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# British Journal of Medical Practitioners

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Cervicogenic headache: It is time to call for more attention

Yili Zhou

Cervicogenic headache (CH) refers to head pain originating from the pathology in the neck. However, the diagnosis of CH is still controversial and it is often misdiagnosed. The author was called to consult a patient in a university hospital not so long ago. The patient was a 28-year-old female with a history of headache for six months. Her headache was described as continuous, dull and achy. It was mainly in the right side occipital and parietal areas. Sometimes she felt a headache behind the eyes. Her headache got worse periodically, several times a month, with nausea, photophobia, and phonophobia. She had no previous history of headache until a whiplash injury six months before. She had been diagnosed as having ‘migraine’ and ‘post-traumatic headache.’ She had used all anti-migraine medications. ‘Nothing was working.’ The patient was admitted into hospital because of ‘intractable headache.’

On the day when the author saw the patient, she was lying on the bed, with the room light turned off and a bed sheet covering her head and eyes. She was given Dilaudid, 2mg/h continuous intravenous (IV) drip, for the headache. The patient had normal results from magnetic resonance imaging (MRI) of the brain and lumbar puncture. According to the patient, no doctors had touched the back of her head and upper neck since admission. The author examined the patient and found a jumping tenderness over the right greater occipital nerve. The patient was given 2ml of 2% lidocaine with 40mg of Kenalog for the right greater occipital nerve (GON) block. Her headache was gone within five minutes and the Dilaudid drip was immediately discontinued. At follow-up four weeks later, the patient was headache-free. This was a typical missed case of CH (occipital neuralgia).

The concept of CH was first introduced by Sjaastad and colleagues in 1983. The International Headache Society published its first diagnostic criteria in 1998 which was revised in 2004. Patients with CH may have histories of head and neck trauma. Pain is often unilateral. Headache is frequently localized in the occipital area. However, pain may also be referred to the frontal, temporal or orbital regions. Headaches may be triggered by neck movement or sustained neck postures. Headache is constant with episodic throbbing attacks, like a migraine. Patients may have other symptoms mimicking a migraine such as nausea, vomiting, photophobia, phonophobia, and blurred vision. Due to the fact that there is a significant overlap of symptoms between CH and migraine without aura, CH is often misdiagnosed as migraine. CH is commonly found in patients after whiplash injuries, especially in the chronic phase.

Anatomical studies have provided a basis for the pathogenesis of CH. The suboccipital nerve (dorsal ramus of C1) innervates the atlanto-occipital (AO) joint and dura matter over the posterior fossa. Therefore, a pathologic condition of AO joint is a potential source for occipital headache. It has been reported that pain from the C2-3 and C3-4 cervical facet joints can radiate to the occipital area, frontotemporal and even periorbital regions. Even pathology in C5 or C6 nerve roots have been reported to cause headache. The trigeminocervical nucleus is a region of the upper cervical spinal cord where sensory nerve fibres in the descending tract of the trigeminal nerve (trigeminal nucleus caudalis) are believed to interact with sensory fibres from the upper cervical roots. This functional convergence of upper cervical and trigeminal sensory pathways allows the bidirectional referral of painful sensations between the neck and trigeminal sensory receptive fields of the face and head.

Clinicians should always put CH in the list of differential diagnoses when they work up a headache patient. A history of head/neck injury, and detailed examination of the occipital and upper cervical area, should be part of the evaluation. Patients with CH may have tenderness over the greater or lesser occipital nerve, cervical facet joints and muscles in the upper or middle cervical region. Diagnostic imaging such as X-ray, computerized tomography (CT) and MRI cannot confirm CH, but can lend support to its diagnosis.

Treatment of CH is empirical. This headache does not respond well to migraine medications. Treatment should be focused on the removal of the pain source from the occipital-cervical junction. Initial therapy should be directed to non-steroidal anti-inflammatory drugs (NSAIDs) and physical therapy modalities. GON block is easy and safe to perform in office. It is effective for the treatment for occipital neuralgia and CH. The author followed a group of patients after GON block. The pain relief effects of GON block lasted an average of 31 days (unpublished data). If patients do not respond to GON block, diagnostic medial branch block and radiofrequency (RF) denervation of the upper cervical facet joints can be considered.
Early studies have reported positive results. A subsequent randomized study found no benefit of RF. However, there were only six cases in each group, which significantly limited the power and validity of the conclusion from that study. Surgical treatment of cervical degenerative disc disease may offer effective pain relief for CH. Jansen reported 60 cases of CH patients treated mainly with C4/5, C5/6 and C6/7 nerve root decompression. More than 63% patients reported long lasting pain freedom or improvement (> 50%).

CH is common, with a prevalence of 0.4% and 2.5% in the general population. However, compared with other common pain conditions, CH is less studied. A Medline search found 6818 abstracts for migraine in 2009, whereas only 86 abstracts on CH were found. CH has not been well studied and it is often misdiagnosed. It is time to call for more attention.

Competing Interests
None Declared

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REFERENCES
Effects of Lornoxicam on the Haemodynamic and Catecholamine Response to Laryngoscopy and Tracheal Intubation

M. Daabiss, M. Hashish, R. AlOtaibi and R. AlDafterdar

Abstract

Background and objectives: Laryngoscopy and tracheal intubation are associated with haemodynamic responses which might increase morbidity and mortality in some patients. Lornoxicam is a non-steroidal anti-inflammatory drug, which when added to fentanyl successfully attenuated the pressor response of intubation. The aim of this study was to evaluate the effect of lornoxicam individually on the haemodynamic response and serum catecholamine levels following laryngoscopy and tracheal intubation.

Methods: Fifty adult patients scheduled for general anaesthesia with endotracheal intubation were enrolled in this randomised, double-blind placebo-controlled study. They were divided into two equal groups to receive intravenously either lornoxicam 16 mg or placebo, half an hour before surgery. Systolic, Diastolic and mean arterial pressure and heart rate were recorded before and after the induction of anaesthesia, and every minute after intubation for 10 minutes. Serum catecholamine levels were measured before induction and 1 minute after intubation.

Results: After induction, there was a significant decrease in blood pressure in both groups. In the control group, a significant increase in serum catecholamine levels 1 minute after intubation as well as a significant increase in the haemodynamic parameters was observed in the first 3 minutes after tracheal intubation (P < 0.05).

Conclusion: Lornoxicam 16 mg attenuates the pressor response to laryngoscopy and intubation of the trachea.

KEYWORDS Tracheal intubation, cardiovascular responses, Laryngoscopy, Lornoxicam, anaesthesia.

Introduction

In 1940, Reid and Brace first described the haemodynamic response to laryngoscopy and intubation due to noxious stimuli of the upper airway. Evidence from laboratory data demonstrates that epipharyngeal and laryngopharyngeal stimulation augments cervical sympathetic activity in the efferent fibres to the heart. This explains the increase in plasma levels of norepinephrine and, to a lesser extent, epinephrine, which occur during airway instrumentation. The rise in the pulse rate and blood pressure is usually transient occurring 30 seconds after intubation and lasting for less than 10 minutes. Usually these changes are well tolerated by healthy individuals. However, these changes may be fatal in patients with hypertension, coronary artery disease or intracranial hypertension. Numerous agents have therefore been utilised to blunt these stimulatory effects on the cardiovascular system induced by laryngoscopy and endotracheal intubation such as deepening of anaesthesia, pretreatment with vasodilators such as nitroglycerin, beta-blockers, and opioids etc.

Lornoxicam is a nonsteroidal anti-inflammatory drug (NSAID) that belongs chemically to the oxicams and has been successfully used as a perioperative analgesic agent with a better safety profile regarding renal and hepatic function tests, in addition to better gastrointestinal tract tolerability compared to selective COX-inhibitors. Riad and Moussa reported that lornoxicam added to fentanyl attenuates the haemodynamic response to laryngoscopy and tracheal intubation in the elderly. Other than this, few data are available regarding the efficacy of lornoxicam in controlling the haemodynamic variations during the peri-intubation period. Therefore the present study was designed as a double-blind randomised placebo-controlled trial to investigate the effect of lornoxicam individually on the haemodynamic response and serum catecholamine levels following laryngoscopy and tracheal intubation.

Methods:

After obtaining the approval of the Hospital Research & Ethical Committee and patients informed consent, fifty ASA I patients, aged 18-40 years, scheduled for elective surgical procedures under general anaesthesia requiring endotracheal intubation, were enrolled in this randomised, double-blinded placebo-controlled study. Those who had taken drugs that could influence haemodynamic and autonomic function, were excluded from the study. Further exclusion criteria consisted of patients with risk of pulmonary aspiration, predictably difficult airways or obesity (body mass index (BMI) > 30%) and patients with a known allergy to NSAIDs.

In a double-blind fashion and using a sealed envelope technique, patients were randomly allocated to one of two groups to receive intravenous injection (i.v.) of either
Lornoxicam 16 mg diluted in 4 ml (Group L, n = 25) or placebo received saline 4 ml (Group S, n = 25) half an hour before induction of anaesthesia as the time taken by lornoxicam to reach peak plasma concentration (Tmax) was determined to be 0.5 h $^{-1}$. Since lornoxicam is yellow while placebo is a clear fluid, syringes containing both solutions were prepared covered in a double blind fashion, by a collaborator not involved in data recording. The same collaborator administered drugs while a blind observer collected data.

Patients were not premedicated. In the holding area, an i.v. cannula was inserted and an i.v. infusion of Lactated Ringer’s 10 ml Kg$^{-1}$ was started half an hour before induction of anaesthesia. Additionally, a 16-gauge i.v. catheter, attached to a stopcock and flushing device, was inserted into an antecubital vein of the contralateral arm to collect blood samples. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and arterial oxygen saturation (SpO$_2$) were recorded before induction (baseline value).

After 3 min of pre-oxygenation, anaesthesia was induced with propofol 2.5mg Kg$^{-1}$ and cisatracurium 0.15 mg kg$^{-1}$ to facilitate tracheal intubation which was performed using direct laryngoscopy when neuromuscular block was achieved by train of four-Guard monitor. SBP, DBP, MAP and HR were recorded before and after administration of the i.v. anaesthetic, immediately after intubation and cuff inflation, and every minute (min) for 10 mins. after intubation. All intubations were performed by a single anaesthetist, the duration of laryngoscopy and intubation were limited to the minimum possible time and were recorded. Data from patients in whom intubation required longer than 20 seconds (sec) were excluded.

Blood samples were drawn before (baseline) and 1 min. after intubation and cuff inflation for measurement of serum catecholamine concentrations. The samples were collected into pre-chilled tubes containing EDTA/Na and immediately centrifuged. Plasma concentrations of epinephrine and norepinephrine were measured in duplicate by using high-pressure liquid chromatography $^{10}$. After tracheal intubation, patients were ventilated to normocapnia with sevoflurane (2-3% end tidal) in 50% oxygen in air. Two mins. after intubation (after collecting the blood sample), all patients received fentanyl i.v. 1.5 µg kg$^{-1}$ and were monitored with ECG, SBP, DBP, MAP, SpO$_2$ and end tidal carbon dioxide (EtCO$_2$). All measurements were completed before skin incision. At the end of surgery, muscle relaxation was reversed and patients were extubated.

Statistical analysis was performed using SPSS version 17. Numerical data are presented as mean ± SD. Statistical comparisons among the groups were performed using unpaired t-test. Haemodynamic responses to induction and intubation in a given group were analysed using a paired t-test. The number of subjects enrolled was based on a power calculation of finding a 20% difference between the two groups in MAP and HR from the baseline values at alpha error of 0.05 and beta of 0.2. Categorical data were expressed as numbers and were analysed by using the $^2$ test where appropriate. A P value <0.05 was considered statistically significant.

**Results:**

The two groups were comparable in demographic profile, duration of laryngoscopy and intubation as well as baseline haemodynamic parameters (table 1).

**Table 1: Demographic, baseline haemodynamic characteristics and duration of laryngoscopy**

<table>
<thead>
<tr>
<th>Group (S (Saline)</th>
<th>Group L (Lornoxicam)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>25</td>
</tr>
<tr>
<td>Sex (female/male)</td>
<td>10/15</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>31.5 ± 5.6</td>
</tr>
<tr>
<td>ASA (I/II)</td>
<td>19/6</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>69.7 ± 4.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167.9 ± 8.6</td>
</tr>
<tr>
<td>Duration of laryngoscopy and intubation (sec)</td>
<td>14.9 (1.7)</td>
</tr>
<tr>
<td>HR/ minute</td>
<td>80.13±8.69</td>
</tr>
<tr>
<td>MAP mmHg</td>
<td>89.97±10.1</td>
</tr>
<tr>
<td>Systolic BP mmHg</td>
<td>120.2±11.2</td>
</tr>
<tr>
<td>Diastolic BP mmHg</td>
<td>78.7±9.91</td>
</tr>
</tbody>
</table>

**Table 2: Changes in Heart rate/minute**

<table>
<thead>
<tr>
<th>Group (S (Saline)</th>
<th>Group L (Lornoxicam)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>After induction</td>
<td>85.15±10.76</td>
<td>.626</td>
</tr>
<tr>
<td>0 minute after intubation</td>
<td>106±14.3</td>
<td>.000*</td>
</tr>
<tr>
<td>1 minute</td>
<td>101.71±11.15</td>
<td>.000*</td>
</tr>
<tr>
<td>2 minute</td>
<td>97.39±12.07</td>
<td>.019*</td>
</tr>
<tr>
<td>3 minute</td>
<td>95.48±12.95</td>
<td>.036*</td>
</tr>
</tbody>
</table>

**Table 3: Changes in mean arterial pressure mmHg**

<table>
<thead>
<tr>
<th>Group (S (Saline)</th>
<th>Group L (Lornoxicam)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>After induction</td>
<td>84.65±8.3</td>
<td>.055</td>
</tr>
<tr>
<td>0 minute after intubation</td>
<td>129±16.54</td>
<td>.000*</td>
</tr>
<tr>
<td>1 minute</td>
<td>119.95±18.2</td>
<td>.000*</td>
</tr>
<tr>
<td>2 minute</td>
<td>105.33±13.15</td>
<td>.008*</td>
</tr>
<tr>
<td>3 minute</td>
<td>96.1±10.11</td>
<td>.024*</td>
</tr>
</tbody>
</table>

(mean ± SD). *P ≤ 0.05 is statistically significant change.
All tracheal intubations were performed successfully by the same anaesthetist at the first attempt. Following the induction of anaesthesia; SBP, DBP and MAP decreased in both groups (fig. 1 and 2).

After intubation the attenuation of the increase in SAP, DBP, MAP and HR in group L was statistically significant compared to group S, and then remained significant until 3 mins. after intubation. Haemodynamic variables are summarised in tables 2,3,4,5. The maximum rise in MAP and HR in group S at intubation was 30.5% and 42% respectively. While in group L the maximum rise in MAP and HR was 7.1% and 6.2% respectively over the entire observation period. After that, SBP, DBP, MAP and HR decreased gradually in both groups to values similar to those noted before induction. Furthermore, blood samples collected one minute following intubation showed a significant increase in serum epinephrine and norepinephrine concentrations in group S compared to group L in the same observation period (fig. 3) (table 6).
Table 6: Changes in serum catecholamine level nmol/L

<table>
<thead>
<tr>
<th></th>
<th>Group S (Saline)</th>
<th>Group L (Lornoxicam)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>Pre intubation</td>
<td>1.95±.119</td>
<td>1.79±.104</td>
</tr>
<tr>
<td></td>
<td>1 min postintubation</td>
<td>2.06±.112</td>
<td>1.81±.087</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>Pre intubation</td>
<td>1.11±.635</td>
<td>1.09±.51</td>
</tr>
<tr>
<td></td>
<td>1 min postintubation</td>
<td>1.49±.903</td>
<td>1.10±.524</td>
</tr>
</tbody>
</table>

(mean ± SD). *P ≤ 0.05 is statistically significant change

Discussion:

Lornoxicam has been successfully used in prevention and treatment of postoperative pain [15]. It was reported that i.v. 8 mg of lornoxicam was equianalgesic with 20 mg of morphine [15], 50 mg of pethidine [15], while 16 mg of lornoxicam had a superior analgesic effect compared with 100 mg of tramadol [14] and was comparable to 100 µg of fentanyl as intraoperative analgesia in mild to moderate day case ENT surgical procedures [15].

Our results showed a significant fall in SBP, DBP and MAP in both groups after induction. This might be due to the vasodilatation associated with the administration of propofol. Patients in both groups exhibited an increase in heart rate since no medicine other than Lornoxicam was added to propofol to decrease pain on injection. Propofol can cause significant tachycardia from pain in addition to reflex tachycardia due to a decrease in SVR. As the SBP, DBP and MAP rose significantly for the first 3 minutes after intubation in the control group, a further reduction in SVR due to the vasodilator effect of sevoflurane is the probable reason for the return of the MAP to nearly baseline values over the entire observation period. The fall in HR over the same period might be partly due to the bradycardia associated with fentanyl administered 2 minutes after intubation in both groups.

In our study, lornoxicam attenuated the pressor response to laryngoscopy and tracheal intubation; SBP, DBP, MAP and HR were significantly lower in L group compared to S group in the first 3 min after intubation. This may be attributable to the analgesic action of lornoxicam mediated through the antiprostaglandin effect of COX inhibition, the release of endogenous dynorphin and β-endorphin [15], a decrease in peripheral and central prostaglandin production, as well as it exerting some of its analgesic activity via the central nervous system [17].

In agreement with our results, Bruder and colleagues [15] reported that laryngoscopy and intubation violate the patient’s protective airway reflexes with marked reflex changes in the cardiovascular system and lead to an average increase in blood pressure by 40-50% and a 20% increase in heart rate. Kihara and colleagues [15], when comparing the haemodynamic response to direct laryngoscopy with the intubating laryngeal mask and the Trachlight device, reported that the HR increased compared with preoperative baseline values in all groups. Moreover, both systolic and diastolic pressure increased after tracheal intubation for 2 mins. with the highest values in the hypertensive group receiving direct laryngoscopy.

In a previous study done by Riad and Moussa [7], i.v. administration of 8 mg lornoxicam half an hour before surgery added to fentanyl 1 µg Kg⁻¹ during induction of anaesthesia was found to attenuate the haemodynamic response to laryngoscopy and tracheal intubation in the elderly. However, it was unclear whether this was attributed to the drug’s narcotic effect. Therefore, our study was designed to evaluate the use of lornoxicam individually, in a single i.v. administration of 16 mg lornoxicam half an hour before surgery. Lornoxicam 8 mg was not used as it was proven to have an inadequate analgesic effect [15].

There have been a few studies which have measured catecholamine levels after intubation. Our results are consistent with those of Russell et al [2] and Shrihman et al [20] who reported significant elevations in serum levels of norepinephrine and epinephrine following laryngoscopy and tracheal intubation. Hassan and colleagues [24] concluded that during laryngoscopy and endotracheal intubation, placing the tube through the cords and inflating the cuff in the infraglottic region contributes significantly to sympathoadrenal response caused by supraglottic stimulation.

When assessing techniques to ameliorate the cardiovascular responses to intubation; the drugs used to induce anaesthesia may influence the results. We induced anaesthesia with propofol which produces hypotension. This may compensate in part for the cardiovascular changes attributable to laryngoscopy and tracheal intubation. This could be considered a limitation of the present study. The omission of opioids during the induction of anaesthesia in healthy young patients should not be a concern.

In conclusion, pretreatment with lornoxicam in the doses given in this study, attenuates the pressor response to laryngoscopy and the intubation of the trachea.

Competing Interests
None declared
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Seroprevalence of Co-infection of Hepatitis B and Hepatitis C Genotypes among Adult Female Population of Karachi, Pakistan

Shazia Tabassum Hakim, Samina Noorali, Meaghan Ashby, Anisah Bagasra, Shahana U. Kazmi and Omar Bagasra

ABSTRACT

Background: Both Hepatitis B virus (HBV) and Hepatitis C virus (HCV) are aetiological agents of acute and chronic liver disease existing throughout the world. The high genetic variability of HBV and HCV genome is reflected by eight genotypes (A to H) and six genotypes (1 to 6), respectively. Each genotype has a characteristic geographical distribution, which is important epidemiologically. Previous studies from the province of Sindh, Pakistan have reported that genotypes D and A as well as D and B are prevalent HBV genotypes, and for HCV genotypes 3a and 3b to be dominant. The aim of this study was to investigate the prevalence of co-infection of both HBV and HCV genotypes in physically healthy females at two universities in Karachi, Sindh, Pakistan and HBV diagnosed patients.

Methodology: Blood was collected from a total of 4000 healthy female volunteer students and 28 HBV diagnosed patients. Serum samples obtained were screened for Hepatitis B surface antigen (HBsAg), anti-HBs antibodies and anti-HCV antibodies by immunochromatography and ELISA. Genotyping was carried out for 6 HBV genotypes (A through F) and 6 HCV genotypes (1 through 6). Genotyping data of HBV and HCV positive individuals are described.

Results: Out of 4028 volunteers, 172 (4.3%) tested positive for HBsAg. All 172 serum samples were genotyped by PCR for both HBV and HCV. Out of 172 HBsAg positive samples, 89 (51.7%) showed a single HBV genotype D infection, followed by genotypes A (6.4%), F (4.6%), B (3.5%), E (1.7%), and C (1.7%). Out of 43 positive for HCV by PCR from the two universities and Anklesaria Hospital, 65.1% showed infection with 3a, followed by genotypes 5a (11.6%), 6a (11.6%), 3b (9.3%) and 2a (2.3%). Hence, the co-infection rate of both these viruses is 25% (43/172) among HBsAg positive individuals.

Conclusion: Genotype D for HBV and genotype 3a for HCV appears to be the dominant genotype prevalent in Karachi’s population and co-infection of both these viruses does exist in HBsAg positive individuals.

KEYWORDS
Hepatitis B virus, Hepatitis C virus, type-specific primer-based genotyping

Introduction

Both Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) are diseases characterized by a high global prevalence, complex clinical course, and limited effectiveness of currently available antiviral therapy. Approximately 2 billion people worldwide have been infected with the HBV and about 350 million live with chronic infection. An estimated 600,000 persons die each year due to the acute or chronic consequences of HBV. WHO also estimates that about 200 million people, or 3% of the world’s population, are infected with HCV and 3 to 4 million persons are newly infected each year. This results in 170 million chronic carriers globally at risk of developing liver cirrhosis and/or liver cancer. Hence, HBV and HCV infections account for a substantial proportion of liver diseases worldwide.

These viruses have some differences, like HBV belongs to the Hepadnaviridae family and HCV belongs to the Flaviviridae family. HBV has a circular, partially double-stranded DNA genome of approximately 3.2 kb, whereas HCV has a single RNA strand genome of approximately 9.6 kb. HBV and HCV show some common biological features. Both HBV and HCV show a large heterogeneity of their viral genomes producing various genotypes. Based on genomic nucleotide sequence divergence of greater than 8%, HBV has been classified into eight genotypes labeled A through H. Different isolates of HCV show substantial nucleotide sequence variation distributed throughout the genome. Regions encoding the envelope proteins are the most variable, whereas the 5’ non-coding region (NCR) is the most conserved. Because it is the most conserved with minor heterogeneity, several researchers have considered the 5’ NCR the region of choice for virus detection by reverse transcription (RT)-PCR. Sequence analysis performed on isolates from different geographical areas around the world has revealed the presence of different genotypes, genotypes 1 to 6. A typing scheme using restriction fragment length polymorphism analysis of the 5’ NCR was able to differentiate the six major genotypes. Hence both HBV and HCV genotypes display significant differences in their global distribution and prevalence, making genotyping a useful method for determining the source of HBV and HCV transmission in an infected localized population.

Many studies have been conducted to study the prevalence of HBV and HCV co-infection among HIV-infected individuals and intravenous drug users globally. There are only a few studies relevant to the epidemiology of these types of infection.
in the normal healthy population. The objective in this study was to determine the seroprevalence of HBV and HCV, co-infection of both these viruses and their genotypes, among an apparently healthy female population as well as from known HBV patients in Karachi, a major city in the province of Sindh, Pakistan. This study is also aimed at providing the baseline data on HBV/HCV co-infection, in order to gain a better understanding of the public health issues in Pakistan. We evaluated the antigen, antibody and genotypes of both HBV and HCV in 144 otherwise healthy female individuals and 28 diagnosed HBV patients.

Materials and Methods

Study duration: From March 2002 to October 2006 & April 2009

Study participants: Total 4000 blood serum samples were collected from healthy female student volunteers and 28 serum samples (April 2009) from already diagnosed Hepatitis B positive patients, aged 16 to 65 years from two Karachi universities and one Karachi hospital. University samples were obtained through the Department of Microbiology, University of Karachi and the Department of Microbiology, Jinnah University for Women. Hospital samples were obtained through the Pathological Laboratory of Burgor Anklesaria Nursing Home and Hospital.

Ethical Consent: Signed informed consent forms were collected from all volunteers following Institutional Review Board policies of the respective institutes.

Pre study screening: All 4028 volunteers had health checkups by a medical doctor before collection of specimens, they were asked about their history of jaundice, blood transfusion, sexual contacts, and exposure to needles, and if they had undergone any surgical and dental procedures.

Biochemical & Hematological screening: On completion of the medical checkups, volunteers were asked to give 5mL of blood for different haematological [(complete blood picture (CP), haemoglobin percentage (Hb%) and erythrocyte sedimentation rate (ESR)] and 10mL for different biochemical tests [(direct bilirubin, indirect bilirubin, total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP)]. Serological analysis: Samples were also subjected to serological analysis for hepatitis B surface Antigen (HBsAg), HBs antibodies and HCV antibodies using rapid immunochromatography kits (ICT, Australia and Abbott, USA). Confirmatory test for HBsAg was done by using ELISA (IMX, Abbott, USA).

All the above mentioned preliminary tests were conducted at the respective institutes in Karachi. Out of 4000 female volunteers from the two universities, 144 otherwise healthy females tested positive for HBsAg. 2 out of the 144 HBsAg positive females were also found to be positive for anti-HCV antibodies. The other 28 positive HBV patients from Anklesaria Hospital were only tested for HBsAg and all 28 were positive for HBsAg. Hence, a total of 172 HBV positive samples (144 + 28 = 172) including the 39 HCV positive serum samples obtained from Karachi were used for genotypic evaluation at Claflin University, South Carolina, USA. Specific ethnicity was not determined but we assume these study participants represent a collection of different ethnic groups in Pakistan.

DNA/RNA extraction and amplification of 172 HBV positive samples: DNA was extracted for HBV, and RNA was extracted for HCV analysis from 200µL of all 172 positive HBV serum samples using PureLink™ Viral RNA/DNA Mini Kit according to manufacturer’s instructions (Invitrogen, CA). Amplification was carried out using puReTaq Ready –To-Go PCR Beads (Amersham Biosciences, UK).

Determination of HBV and HCV genotypes by nested PCR: The primer sets for first-round PCR and second-round PCR, PCR amplification protocol, and primers for both HBV and HCV genomes and genotyping amplification for all 172 samples followed previously reported methods. First round amplification targeted 1063bp for the HBV genome and 470bp for the HCV genome. These respective PCR products for both HBV and HCV were used as a template for genotyping different HBV genotypes A to F and HCV genotypes from 1 to 6. HBV A through HBV F genotypes and HCV 1 through 6 genotypes for each sample were determined by separating the genotype-specific DNA bands on 2% agarose gels, stained with ethidium bromide. The sizes of PCR products were estimated according to the migration pattern of a 50bp DNA ladder (Promega, WI).

Results

Before screening for HBV status, all 4000 healthy female volunteers from the Department of Microbiology, University of Karachi, and the Department of Microbiology, Jinnah University for Women were subjected to routine physical checkups for exclusion criteria i.e., either they were apparently unhealthy or malnourished (23 volunteers were excluded). All 4000 serum samples were screened by immunochromatography for the presence of HBsAg, anti HBs antibodies and anti-HCV antibodies. Positive results were confirmed by ELISA. Out of 4000 subjects 144 (3.6%) tested positive for HB surface antigen (HBsAg), 2 (0.05%) were positive for anti-HCV antibodies, and 3856 (96.4%) were negative for HBsAg and 3998 (99.95%) were negative for HCV antibodies by both immunochromatography and ELISA. Out of these 144 individuals who tested positive for HBsAg, 20 (13.8%) were positive for anti-HB surface antibodies and 2 (1.4%) tested positive for anti-HCV antibodies. The rest of the 28 serum samples obtained from already diagnosed HBV positive samples from Anklesaria Hospital were only tested for HBsAg and were all positive for HBsAg.
The haematological parameters: WBC count, RBC count, hematocrit and platelet count of the 172 HBsAg positive individuals were within the normal recommended range of values, while mean Hb% was 9.8±1.6 g/dL. Direct bilirubin (0 to 0.3 mg/dL), indirect bilirubin (0.1 - 1.0 mg/dL), total serum bilirubin (0.3 to 1.9 mg/dL), ALT (0 - 36 U/L), AST (0 - 31 U/L) and alkaline phosphatase (20 - 125 U/L) were also within the normal range for 129 HBsAg positive individuals, except for the raised ALT (>36 U/L) and AST (>31 U/L) levels in 38 participants with a previous history of jaundice who were also positive for HBsAg.

All 172 samples that were positive for HBsAg were confirmed for the presence of different HBV genotypes as well as for different HCV genotypes by PCR to see the co-infection of both these viruses. Genotyping was carried out at the South Carolina Center for Biotechnology, Department of Biology, Claflin University, Orangeburg, SC, U.S.A. For HBV: Mix A primers were targeted to amplify genotypes A, B and C, and primers for Mix B were targeted to amplify genotypes D, E and F. For HCV: primers for Mix A were targeted to amplify genotypes 1a, 1b, 1c, 3a, 3c and 4. Primers of Mix B for HCV were targeted to amplify genotypes 2a, 2b, 2c, 3b, 5a, and 6a.

Table 1. Prevalence of both single and co-infection of HBV genotypes among the apparently healthy female student sample and known HBV positive patients from Anklesaria hospital in Karachi.

<table>
<thead>
<tr>
<th>2 Universities</th>
<th>Samples</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total HBV</strong></td>
<td>144</td>
<td></td>
</tr>
<tr>
<td>Genotype D</td>
<td>70</td>
<td>48.6%</td>
</tr>
<tr>
<td>Genotype A</td>
<td>8</td>
<td>5.5%</td>
</tr>
<tr>
<td>Genotype F</td>
<td>7</td>
<td>4.9%</td>
</tr>
<tr>
<td>Genotype B</td>
<td>5</td>
<td>3.5%</td>
</tr>
<tr>
<td>Genotype E</td>
<td>5</td>
<td>2.1%</td>
</tr>
<tr>
<td>Genotype C</td>
<td>2</td>
<td>1.4%</td>
</tr>
<tr>
<td><strong>Co-infections of HBV Genotypes</strong></td>
<td><strong>49/144</strong></td>
<td><strong>34%</strong></td>
</tr>
<tr>
<td>Genotype B/D</td>
<td>50/144</td>
<td>20.8%</td>
</tr>
<tr>
<td>Genotype A/D</td>
<td>11/144</td>
<td>7.6%</td>
</tr>
<tr>
<td>Genotype A/F</td>
<td>4/144</td>
<td>2.8%</td>
</tr>
<tr>
<td>Genotype B/C</td>
<td>4/144</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anklesaria Hospital</th>
<th>Samples</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total HBV</strong></td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Genotype D</td>
<td>19</td>
<td>67.9%</td>
</tr>
<tr>
<td>Genotype A</td>
<td>5</td>
<td>10.7%</td>
</tr>
<tr>
<td>Genotype B</td>
<td>1</td>
<td>3.6%</td>
</tr>
<tr>
<td>Genotype C</td>
<td>1</td>
<td>3.6%</td>
</tr>
<tr>
<td>Genotype F</td>
<td>1</td>
<td>3.6%</td>
</tr>
<tr>
<td><strong>Co-infections of HBV Genotypes</strong></td>
<td><strong>5/28</strong></td>
<td><strong>10.7%</strong></td>
</tr>
<tr>
<td>Genotype B/A</td>
<td>5/28</td>
<td>10.7%</td>
</tr>
</tbody>
</table>

Table 1 illustrates the prevalence of both single and co-infection of HBV genotypes from both the universities in Karachi and Anklesaria hospital. Representative 10 samples in Fig. 1 show single and co-infections for HBV.

Besides looking at the HBV genotypic status of these 172 patients by PCR, we also looked at the HCV genotypic status of the positive HBV patients by PCR so as to see if there was existence of co-infection of the two viruses i.e. HBV and HCV in the same individuals as only 2 samples tested positive for anti-HCV antibodies by rapid immunochromatography. Table 2 shows the prevalence of HCV genotypes among the apparently healthy female student population from the 2 universities in Karachi and known HBV individuals samples obtained from Anklesaria hospital. Fig. 2 shows different HCV genotype infection in the 10 representative samples shown in Fig. 1 showing HBV infection with different genotypes.

To summarize the results it was found that out of 172 HBsAg positive samples from the two universities (144 HBV samples) and Anklesaria Hospital (28 HBV samples), 89 (51.7%) were genotype D, 11 were genotype A (6.4%), 8 were genotype F (4.6%), 6 were genotype B (3.5%), 3 were genotype E (1.7%), and 3 were genotype C (1.7%). Out of 43 positive for HCV by PCR from the two universities (39/144 HBV samples) and Anklesaria Hospital (4/28 HBV samples), 65.1% (28/43) showed infection with 3a, followed by genotypes 5a (5/43 =
11.6%), 6a (5/43 = 11.6%), 3b (4/43 = 9.3%) and 2a (1/43 = 2.3%).

Table 2. Prevalence of HCV genotypes among the apparently healthy female student sample, and known HBV individuals from Anklesaria hospital in Karachi.

<table>
<thead>
<tr>
<th>2 Universities</th>
<th>Samples</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total HCV/Total HBV</td>
<td>59/144</td>
<td>27.1%</td>
</tr>
<tr>
<td>Genotype 3a</td>
<td>26/39</td>
<td>66.6%</td>
</tr>
<tr>
<td>Genotype 6a</td>
<td>5/39</td>
<td>12.8%</td>
</tr>
<tr>
<td>Genotype 3b</td>
<td>4/39</td>
<td>10.3%</td>
</tr>
<tr>
<td>Genotype 5a</td>
<td>4/39</td>
<td>10.3%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anklesaria Hospital</th>
<th>Samples</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total HCV/HBV</td>
<td>4/28</td>
<td>14.3%</td>
</tr>
<tr>
<td>Genotype 3a</td>
<td>2/28</td>
<td>7.14%</td>
</tr>
<tr>
<td>Genotype 2a</td>
<td>1/28</td>
<td>3.6%</td>
</tr>
<tr>
<td>Genotype 5a</td>
<td>1/28</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

Figure 2: The sizes of the genotype-specific bands for HCV amplified by PCR genotyping method are as follows: genotype 2a, 190 bp; genotype 3a, 258 bp; genotype 3b, 232 bp; genotype 5a, 417 bp; and genotype 6a, 300 bp.

Discussion

Viral hepatitis due to HBV and HCV has significant morbidity and mortality worldwide. The global prevalence of HCV is 3% and the carrier rate of HBsAg varies from 0.1% to 0.2% in Britain and the USA, to 3% in Greece and southern Italy and up to 15% in Africa and the Asia. Pakistan is highly endemic with HBV. Studies are too limited to give a clear picture of the prevalence of HBV at the national level, especially among apparently healthy individuals. Most previous studies targeted different small groups of individuals with some clinical indications, so they do not accurately reflect the overall prevalence in Pakistan. Our previous study was conducted on a first group of 4000 healthy female students from the two universities i.e., Department of Microbiology, University of Karachi and Department of Microbiology, Jinnah University for Women for the prevalence of HBV. We have reported earlier that genotype D appears to be the dominant genotype prevalent in Karachi, Pakistan’s apparently healthy female population, and genotype B appears to be the next most prevalent genotype. In this study we checked the prevalence of both HBV and HCV in a second group of 4000 healthy female students from the same two universities in Karachi mentioned above, as well as the already 28 diagnosed HBV patients from Anklesaria Hospital in Karachi, Pakistan.

Both HBV and HCV are present in the Pakistani population and there are varying reports of disease prevalence. HCV is one of the silent killer infections spreading undetected in Pakistan because there are often no clinical symptoms and, when HCV is diagnosed, considerable damage has already been done to the patient. In Pakistan alone, the prevalence of HBsAg has been reported to be from 0.99% to 10% in different groups of individuals and 2.2% to 14% for HCV antibodies. A recent study conducted in Pakistan showed that out of 5707 young men tested, 95 (1.70%) were positive for anti-HCV and 167 (2.93%) for HBsAg. Our previous study showed the prevalence of HBsAg among young otherwise healthy women to be 4.5%. A present study shows that the prevalence of HBsAg in otherwise young healthy women to be 3.6%, with 0.98% testing positive for anti-HCV antibodies. On the basis of other studies conducted in different provinces of Pakistan, we can say that there is a variation in the prevalence of HBsAg and HCV antibodies in the Pakistani population as the population sample selected is limited to a particular area or segment of the provinces.

HBV and HCV genotyping is important to track the route and pathogenesis of the virus. In particular, the variants may differ in their patterns of serologic reactivity, pathogenicity, virulence, and response to therapy. Both HBV and HCV has genetic variations which correspond to the geographic distribution and has been classified into 8 genotypes (A to H) on the basis of whole genome sequence diversity of greater than 8% and 6 genotypes (1 to 6) using restriction fragment length polymorphism analysis of the 5’ non-coding region (NCR), respectively.

In this study genotyping was carried out for 6 HBV genotypes (A through F) and 6 HCV genotypes (1 through 6). This study suggests that the HBV D genotype is the most prevalent (114/144 = 79.2%) among otherwise healthy females alone or in co-infection with other HBV genotypes in Karachi, Sindh, Pakistan. In our previous study HBV D genotype was found to be ubiquitous (100%) among otherwise healthy females alone.
or in co-infection with other HBV genotypes in Karachi followed by genotype B. The earlier two studies conducted for prevalence of HBV genotypes in known hepatitis B positive patients in Pakistan report the prevalence of genotypes HBV A (68%) and HBV D (100%) in the province of Sindh. Interestingly, in this study we also found the HBV D genotype to be the prevalent genotype but it was followed by genotypes HBV A (5.5%) and HBV F (4.9%). The prevalence of genotype HBV B in this study was found to be 3.5% as our earlier study has shown the prevalence of genotype B in otherwise healthy females to be 16.1%.

Among the 28 diagnosed HBV patients from Anklesaria Hospital, 67.9% showed HBV genotype D infection followed by genotype A infection (10.7%). In this group of 28 HBV positive patients we also saw infections with genotypes B and D, A and D, C and D as well as B and C (20.8%, 7.6%, 2.8% and 2.8%) among these otherwise healthy females.

As far as the HCV status of these 144 otherwise healthy females who were HBV positive is concerned only 2 (1.4%) tested positive for HCV antibodies by rapid immunochromatography. But the PCR results showed 39 (27.1%) of these 144 otherwise healthy females that were HBV positive for different genotypes were also positive for HCV including the 2 otherwise healthy females that were HBV positive for different genotypes. Of the 39 HCV positive otherwise healthy females, we found the predominant HCV genotype to be 3a (66.6%) followed by genotypes 6a (12.8%), 3b (10.3%), and 5a (10.3%) infections. The earlier study conducted with samples from women at the two universities in Pakistan had shown that among the HCV positive apparently healthy females 51.44% were genotype 3a, 24.03% exhibited a mix of genotype 3a and 3b, 15.86% were genotype 3b, and 4.80% were genotype 1b. Interestingly, among the group of 28 diagnosed HBV patients, the prevalence of HCV 3a genotype infection was dominant but was 7.1% much lower than that found in the otherwise healthy females, followed by infections with genotypes 2a (3.6%) and 5a (3.6%). Hence we see there is 25% co-infection of both these viruses i.e., HBV and HCV among the HBsAg positive individuals. The sample of 28 HBV positive patients was from a hospital located in the center of the metropolis that represents an area of Karachi where sanitation, malnourishment, illiteracy, and lack of awareness is very common. Prostitution can also be considered as one factor in some of the localities of Karachi in the spread of both HBV and HCV.

**Conclusion**

In conclusion, genotype D appears to be the dominant HBV genotype and genotype 3a for HCV appears to be prevalent in Sindh, Pakistan’s otherwise healthy young female population as well as in HBV diagnosed individuals. Co-infection of both the viruses i.e., HBV and HCV exists among HBsAg positive individuals. The young female participants were advised to seek appropriate medical care for both their own benefit and public health benefit.

**Acknowledgements**

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**Competing Interests**

None declared

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Email: Shaz971@yahoo.com

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Psychological Distress in Carers of People with Mental Disorders

Aadil Jan Shah, Ovais Wadoo and Javed Latoo

Abstract

The recent literature on carers' burden in mental disorders is reviewed. Families bear the major responsibility for such care. Carers face mental ill health as a direct consequence of their caring role and experience higher rates of mental ill health than the general population. The production of burden in carers is a complex process and is related to gender, age, health status, ethnic and cultural affiliation, lack of social support, coping style, in addition to the stressors of the disorder itself. Carers appear to suffer from at least moderate levels of psychological symptomatology. The behavioural problems associated with mental disorders further increase the stress levels of carers. The findings from the review afford a comprehensive understanding of the care-giving situation with its outcomes, and its practical application in devising effective support strategies for family carers.

Keywords: Carers, caregivers, care recipients, psychological distress, burden, stress, mental disorders.

Introduction

Carers play a vital role in supporting family members who are sick, infirm or disabled.¹ There is no doubt that the families of those with mental disorders are affected by the condition of their near ones. Families not only provide practical help and personal care but also give emotional support to their relative with a mental disorder. Therefore the affected person is dependent on the carer, and their well-being is directly related to the nature and quality of the care provided by the carer. These demands can bring significant levels of stress for the carer and can affect their overall quality of life including work, socializing and relationships. Research into the impact of caregiving shows that one-third to one-half of carers suffer significant psychological distress and experience higher rates of mental ill health than the general population. Being a carer can raise difficult personal issues about duty, responsibility, adequacy and guilt.² Caring for a relative with a mental health problem is not a static process since the needs of the care recipient alter as their condition changes. The role of the carer can be more demanding and difficult if the care recipient’s mental disorder is associated with behavioural problems or physical disability. Over the past few decades, research into the impact of caregiving has led to an improved understanding of this subject including the interventions that help. It has now been realized that developing constructive working relationships with carers, and considering their needs, is an essential part of service provision for people with mental disorders who require and receive care from their relatives.

The aim of this review was to examine the relationship between caring, psychological distress, and the factors that help caregivers successfully manage their role.

‘Family burden’ - The role of families as carers

Caring for someone with a mental disorder can affect the dynamics of a family. It takes up most of the carers’ time and energy. The family’s responsibility in providing care for people with mental disorders has increased in the past three decades. This has been mainly due to a trend towards community care and the de-institutionalization of psychiatric patients.³ This shift has resulted in the transferral of the day-to-day care of people with mental disorders to family members. Up to 90% of people with mental disorders live with relatives who provide them with long-term practical and emotional support.⁴, ⁵ Carer burden increases with more patient contact and when patients live with their families.⁶ Strong associations have been noted between burden (especially isolation, disappointment and emotional involvement), caregivers’ perceived health and sense of coherence, adjusted for age and relationship.⁷

‘Family burden’ has been adopted to identify the objective and subjective difficulties experienced by relatives of people with long-term mental disorders.⁸ Objective burden relates to the practical problems experienced by relatives such as the disruption of family relationships, constraints in social, leisure and work activities, financial difficulties, and negative impact on their own physical health. Subjective burden describes the psychological reactions which relatives experience, e.g. a feeling of loss, sadness, anxiety and embarrassment in social situations, the stress of coping with disturbing behaviours, and the frustration caused by changing relationships.⁹ Grief may also be involved. This may be grief for the loss of the person’s former personality, achievements and contributions, as well as the loss of family lifestyle.¹⁰ This grief can lead to unconscious hostility and anger.¹¹
The impact of caring on carers' mental health

The vehicles of psychological stress have been conceptualized as adjustment to change,\textsuperscript{11} daily hassles,\textsuperscript{12} and role strains.\textsuperscript{13} Lazarus and Folkman (1984)\textsuperscript{14} define stress as 'a particular relationship between the person and the environment that is appraised by the person as taxing or exceeding his or her resources and endangering his or her well being.' The association between feelings of burden and the overall caregiver role is well documented.\textsuperscript{15} Caregivers provide assistance with activities of daily living, emotional support to the patient, and dealing with incontinence, feeding, and mobility. Due to high burden and responsibilities, caregivers experience poorer self-reported health, engage in fewer health promotion actions than non-caregivers, and report lower life satisfaction.\textsuperscript{16, 17}

The overarching theme from the findings is that carers and care recipients do not believe that care recipients' basic needs are being met, which causes them a great deal of distress and anger towards services and increases carer burden. Carers assert that the needs of care recipients and carers are interconnected and should not be seen as separate.\textsuperscript{18} The stress in carers is best understood by Pearlin’s stress-process model as shown in Figure 1.

Figure 1: Pearlin’s stress–process model of stress in carers (adapted from Pearlin et al, 1990)

The burden and depressive symptoms sustained by carers have been the two most widely studied care-giving outcomes. Reports indicate that depressive symptoms are twice as common among caregivers than non-caregivers.\textsuperscript{19} Family caregivers who have significantly depressed mood may be adversely affected in their ability to perform desirable health-maintenance or self-care behaviours in response to symptoms.\textsuperscript{20} Family caregivers experience more physical and mental distress than non-caregivers in the same age group.\textsuperscript{16} Several studies suggest that many caregivers are at risk of experiencing clinical depression.\textsuperscript{21} Nearly half of the caregivers in some studies were reported to meet the diagnostic criteria for depression whilst in the care-giving role, although they had never been diagnosed with depression prior to their assumption of this role. It has been proven that if the problem behaviours and the functional impairment in the care recipients is worse, the strain score is higher and the carer is more likely to be depressed.\textsuperscript{24} The societal implications of this are underscored by reports indicating that the stressed caregiver is more likely to institutionalize the care recipient.\textsuperscript{25, 26}

The impact of caring for different mental disorders

The impact of caring for different mental disorders, and associated risk factors, is shown in table 1. Although only limited data is available on the psychological distress experienced by the carers of people with other mental disorders, it seems that these disorders have a significant impact on families. Obsessive-compulsive disorder has a considerable impact on families and can lead to a reduction in social activities, causing isolation over time.\textsuperscript{38} People with obsessive-compulsive symptoms frequently involve their relatives in rituals.\textsuperscript{38} This can lead to an increase in anger and criticism towards them which has a negative impact on treatment outcomes.\textsuperscript{38} Caring for patients with eating disorders can be overwhelming for the carer. Available data suggest that the impact on carers of persons with anorexia nervosa may be even higher than for psychoses.\textsuperscript{39} Studies on bulimia nervosa indicate that carers have significant emotional and practical needs.\textsuperscript{40}
### Table 1: The impact of caring for different mental disorders and associated risk factors

<table>
<thead>
<tr>
<th>Mental Disorder</th>
<th>Risk factors</th>
<th>Impact on the carer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>High disability, very severe symptoms, poor support from professionals, poor support from social networks, less practical social support, violence.</td>
<td>Guilt, loss, helplessness, fear, vulnerability, cumulative feelings of defeat, anxiety, resentment, and anger are commonly reported by caregivers.</td>
</tr>
<tr>
<td>Dementia</td>
<td>Decline in cognitive and functional status, behavioural disturbances, dependency on assistance</td>
<td>Anger, grief, loneliness and resentment.</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>Symptoms, changes in family roles, cyclic nature of bipolar disorder, moderate or severe distress.</td>
<td>Significant distress, marked difficulties in maintaining social and leisure activities, decrease in total family income, considerable strains in marital relationships. Psychological consequences during critical periods also persisting in the intervals between episodes in bipolar disorder, poorer physical health, limited activity, and greater health service utilization than non-caregivers.</td>
</tr>
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</table>

### Table 2: Risk factors for carer psychological distress

<table>
<thead>
<tr>
<th>Caregiver factors</th>
<th>Research findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
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</table>
| • Women have higher rates of depression than men in the care-giving role.  
| • 39% of female caregivers, compared to 16% of male caregivers, qualified as being at-risk for clinical depression on The Center for Epidemiologic Studies-Depression Scale (CES-D).  
| • A randomized controlled trial found that women were more likely than men to comply with a home environmental modification intervention, implement recommended strategies, and derive greater benefits.  
| • Male carers tend to have more of a ‘managerial’ style that allows them to distance themselves from the stressful situation to some degree by delegating tasks.  |
| Age               |  
| • Age-associated impairments in physical competence make the provision of care more difficult for older caregivers.  
| • There is a positive association of age and caregiver burden in Whites, but a negative association for African-Americans suggesting that older African-Americans are less likely to experience care-giving as physically burdensome.  |
| Caregiver health  |  
| • Caregiver health has also been identified as a significant predictor of caregiver depression.  
| • Poorer physical health among caregivers than age-matched peers. Such health problems are linked to an increased risk of depression.  
| • Longitudinal studies demonstrated that caregivers are at a greater risk, than non-care-giving age-matched controls, for developing mild hypertension and have an increased tendency to develop a serious illness as well as increased risk for all-cause mortality.  |
| Ethnicity         |  
| • Ethnicity has substantial impact on the care-giving experience.  
| • Comprehensive reviews of the literature have identified differences in the stress process, psychological outcomes, and service utilization among caregivers of different racial and ethnic backgrounds.  
| • Studies consistently show important differences in perceived burden and depression among African-American, White, and Hispanic family caregivers.  
| • Caucasian caregivers tend to report greater depression and appraise care-giving as more stressful than African-American caregivers.  
| • Hispanic caregivers report greater depression and behavioural burden than Caucasians and African-Americans.  |
| Social support    |  
| • Social support has profound effects on caregiver outcomes.  
| • More social support corresponds to less depressive symptomatology and lower perceived burden.  
| • Care-giving is associated with a decline in social support, and increased isolation and withdrawal.  
| • Social support and caregiver burden have been found to mediate depression in caregivers.  
| • Social support has other important functions in that carers may find out about services from people who have used them before and form a network with others in similar situations.  |
Factors associated with psychological distress of the carer

Risks for carer psychological distress or depression are related to gender, age, health status, ethnic and cultural affiliation, lack of social support, as well as certain other characteristics related to the caregiver (table 2).  

Some of the patient factors related to psychological distress in carers are: behavioural disturbances, functional impairments, physical impairments, cognitive impairments, and fear that their relative may attempt suicide.

The frequency with which behavioural disturbances are manifested by the patient has been identified as the strongest predictor of caregiver distress and plays a significant role in the caregivers decision to institutionalize the patient. The literature consistently demonstrates that the frequency of behavioural problems is a more reliable predictor of caregiver burden and depression than are the functional and cognitive impairments of the individual. Carers face unfamiliar and unpredictable situations which increases stress and anxiety. Anxiety may be increased by behavioural problems of patients who cannot be successfully managed on a consistent basis. Anxiety is associated with depression, stress, and physical ill health.

Findings regarding the relationship of functional impairment and negative caregiver outcomes have been inconclusive. Some studies document a weak association of objective measures of patient functional status and caregiver burden/depression, whereas others report a stronger relationship. Carers have reported great anxiety due to fear that their relative may attempt suicide. Carers of people with both physical and cognitive impairments have higher scores for objective burden of caring than those caring for people with either type of impairment alone. In contrast, scores for limitations on their own lives were higher among women caring for people with cognitive impairments (with or without physical impairments).

Coping styles and interventions to reduce psychological distress in carers

There is increasing interest in examining the factors that help caregivers successfully manage their role, while minimizing the effect on their mood and general well-being. Much of this research has been done within the general framework of stress and coping theory, examining coping styles of caregivers and the relationship between types of coping styles and reported symptoms of depression. A variety of interventions have been developed which support caregivers (table 3). Interventions include: training and education programs, information-technology based support, and formal approaches to planning care which take into account the specific needs of carers, sometimes using specially designated nurses or other members of the health care team.

Ballard et al (1995) demonstrates that a higher level of carer education regarding dementia increases carers’ feelings of competency. This is more likely to reduce their expectations of their dependents’ abilities. Previous studies which have looked at these coping strategies and feelings of competence have shown that unrealistic expectations of a dependant increases carers’ risk of depression, and conversely a reduction of carers’ expectations is associated with lower rates of depression. Caregivers who maintain positive feelings towards their relative have a greater level of commitment to caring and a lower level of perceived strain. Furthermore, carers who experience feelings of powerlessness, lack of control, and unpreparedness have higher levels of depression. The most effective treatments in depression of carers appear to be a combination of education and emotional support.

Spiritual support can also be considered a coping resource and has been studied in older African-Americans and older Mexican-Americans. Previous work examining the role of spiritual support observed that African-American caregivers report higher spiritual rewards for caregiving, and reliance on prayer and church support.

Religious coping plays a paramount role, and it is often present at higher levels for African-Americans and Hispanics. For REACH caregivers, Coon et al (2004) found that religious coping is greater for Hispanic and African-American than for White caregivers. Religious involvement is frequently associated with more access to social support as well.

Anecdotal literature suggests that caregivers who use more active coping strategies, such as problem solving, experience fewer symptoms of depression than those who rely on more passive methods. Significant associations have been reported between positive strategies for managing disturbed behaviour, active strategies for managing the meaning of the illness, and reduced levels of caregiver depression. An important role for health-care professionals is in helping caregivers enhance their coping skills, supporting existing skills, and facilitating the development of new ones.
Care-giving has some positive associations for caregivers, including pride in fulfilling spousal responsibilities, enhanced closeness with a care receiver, and satisfaction with one’s competence. These perceived uplifts of care-giving are associated with lower levels of caregiver burden and depression. However perceived uplifts are more common among caregivers of colour than among Whites.

High quality of informal relationships, and the presence of informal support, is related to lower caregiver depression and less deterioration in the emotional health for African-American caregivers, but not for Whites. Support of caregivers by others help to alleviate stress if the supporter is understanding and empathic. In one study, caring for a family member was not perceived to be a burden, and caregivers reported notable limitations on their social networks and social activities. They reported higher levels of unemployment than would be expected for the general population and were over-represented in lower income groups. Family carers are at high risk of social and economic disadvantage and at high risk of mental health challenges. Highly stressed persons may not be able to benefit from attempted social support of others as much as moderately stressed persons.

Caregivers need to have the opportunity to learn more effective ways of coping with stress. If they can learn new ways to cope, they can reduce their anxiety and reliance on treatments. Bourgeois et al (1997) report that caregiver’s behavioural skills and effective self-management training programmes result in a lower frequency of patient behavioural problems and helps to improve the caregiver’s mood. Stevens and Burgio (2000) designed a caregiver intervention that teaches caregivers behavioural management skills to address problem behaviours exhibited by individuals with dementia, as well as problem-solving strategies to increase pleasant activities for the caregiver. Passive coping styles have been associated with greater burden. Persons who use an escape-avoidance type of coping are known to have more depression and interpersonal conflicts.

Psychotherapy may be of some benefit in patients with early dementia but, due to cognitive loss, some adaptation of the technique is required and the involvement of carers is often necessary. Cognitive-behavioural family intervention can have significant benefits in carers of patients with dementia and has a positive impact on patient behaviour. From a cognitive perspective, care-giving plays an important invisible part, which consists of interpreting the care receiver’s behaviour, reflecting on the best way to adjust to it, and defining care objectives. The interventions requiring active participation by the caregivers and those based on cognitive behavioural therapy can produce significant reductions in burden, anxiety and depression than those focused on knowledge acquisition.

Among caregivers with depressive symptoms, 19% used antidepressants, 23% antianxiety drugs, and 2% sedative hypnotics. African-American caregivers were less likely than Whites to be taking antidepressants. In their study, Kales et al (2004) reported use of herbal products in 18% of elderly subjects with depression and/or dementia and in 16% of their caregivers.

In the Burdz et al (1988) study, respite care proved to have a positive effect on the burden experienced by the caregivers, and it also had a positive effect, against all expectations, on the cognitive and physical functioning of the persons with dementia.

There are more than twenty instruments that could be used as outcome measures with mental health carers and have good psychometric properties. They can measure (i) carers’ well-being, (ii) the experience of care-giving and (iii) carers’ needs for professional support. The caregiver burden scale and the sense of coherence scale seem to be highly useful for identifying carers at risk of stress, the pattern of burden, and coping strategies. Nurses can help family caregivers to identify their negative experiences about care-giving and can help them reflect upon their coping strategies to find balance in their situation. Risk groups of caregivers may be identified, especially those with a low perceived health and sense of coherence, for early interventions to reduce burden.

Conclusion

The impact of caring for someone with mental illness brings the risks of mental ill health to the carer in the form of emotional stress, depressive symptoms, or clinical depression. Most individuals with mental disorders live in their own homes and are cared for by a family member. The caring process can be very taxing and exhausting, especially if the care recipient has a severe mental disorder. Providing such long-term care can be a source of significant stress. The behavioural problems associated with mental disorders further increase the stress levels of the carer and therefore impacts significantly on their mental health.

Carers face mental ill health as a direct consequence of their caring role and experience higher rates of mental ill health than the general population. This leads to negative effects on the quality of life of the carer and the standard of care delivered. Efforts to identify and treat caregiver psychological distress will need to be multidisciplinary, require consideration of the cultural context of the patient and caregiver, and focus on multiple risk factors simultaneously. The findings of the review underline the importance for early identification of carers, effective carer support, health promotion, monitoring high-risk groups, and timing appropriate interventions.

Competing Interests
None Declared
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Vitiligo Management: An Update

Imran Majid

Abstract

Vitiligo is one of the commonest skin disorders with a presumed autoimmune aetiology. The management options for this disease have undergone a sea of change over the last two or three decades and we are now in a much better position to treat this disease than in the past. Treatment options such as Narrowband Ultraviolet B (NB-UVB), Targeted Phototherapy, and Excimer laser on the medical front, in addition to epidermal cell transplantation and melanocyte culture transplants on the surgical front, have all revolutionized the management of this psychologically devastating disease.

Introduction

Vitiligo is one of the oldest and commonest skin disorders affecting approximately 1-2% of the human population. The disease shows no regard to the ethnic, racial or socioeconomic background of the affected sufferers. The cosmetic impact of this disease is tremendous and its psychological impact devastating particularly in coloured races. The aetiopathogenesis of this disease is now much better understood compared with a decade earlier but much remains unknown. In parallel with these developments on the aetiological front, a lot of new advances have been made on the therapeutic front as well. With these new therapeutic options, we are currently in a much better position to treat this disease than we were a decade or two earlier. So, how far and how satisfactorily are we able to treat this disorder now? What are the new treatment options available for this disorder and how far have they helped a dermatologist to claim a cure for this disorder? These are some of the questions that will be addressed in this paper.

New advances in management

Medical therapies

The most recent advances on the medical front have been Narrowband Ultraviolet B (NB-UVB) therapy, Targeted Ultraviolet B (UVB), Excimer laser therapies, topical immunomodulator treatment in the form of topical calcineurin inhibitors, topical pseudocatalase, and topical Vitamin D analogues in combination with Ultraviolet (UV) light.

NB-UVB

NB-UVB, using UV-lamps with a peak emission of around 311nm has now emerged as the treatment of first choice in generalized vitiligo as well as vitiligo vulgaris (patchy vitiligo). The efficacy of NB-UVB in vitiligo was first demonstrated by Westerhof and Nieuwboer-Krobotova in 1997. Since then there have been a large number of clinical studies that have demonstrated the therapeutic benefit of NB-UVB in vitiligo patients. The mechanism of action of NB-UVB in vitiligo is through induction of local immunosuppression and stimulation of the proliferation of melanocytes in the skin and the outer root sheath of hair follicles. There is a stimulatory effect on melanogenesis and on the production of Melanocyte Stimulating Hormone (MSH). Comparison studies have shown a significantly enhanced rate of repigmentation with NB-UVB compared with topical Psoralen and Ultraviolet A (PUVA) therapy. Furthermore, the incidence of adverse effects seen commonly with topical PUVA, such as phototoxicity, is significantly reduced with the use of NB-UVB. NB-UVB has shown a number of advantages over PUVA in vitiligo patients in addition to its excellent efficacy. These advantages include its extremely low side-effect profile particularly on the systemic front, its established safety in children, and safety in pregnant females. NB-UVB also has considerably better patient compliance as there is no need to time the exposure with any drug intake or any need for eye protection beyond treatment exposure time. A recent double-blind randomized study comparing NB-UVB with PUVA demonstrated a much better efficacy with NB-UVB. The study found that repigmentation achieved with NB-UVB was much better with respect to colour matching with uninvolved skin, and this was also more persistent than that achieved with PUVA.

In addition NB-UVB has been used in childhood vitiligo with excellent results. No additional adverse effects were seen in children with NB-UVB as compared with those in adults. Furthermore, given the long-term safety profile of NB-UVB in comparison with PUVA as far as skin malignancies are
NB-UVB is now preferred over all other treatment options in the management of generalized vitiligo in both adults and children.

**Table 1: Aetiological hypothesis of vitiligo**

<table>
<thead>
<tr>
<th>Aetiological hypothesis</th>
<th>Brief explanation</th>
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<tbody>
<tr>
<td><strong>Autoimmune hypothesis</strong></td>
<td>Believes that vitiligo occurs because of destruction of melanocytes by an immune mechanism. Most favoured theory at present, supported by many recent in-vitro studies.</td>
</tr>
<tr>
<td><strong>Auto-cytotoxic hypothesis</strong></td>
<td>Believes that vitiligo occurs because of accumulation of toxic metabolites in the melanocytes secondary to a defect in their metabolic clearance of the toxins.</td>
</tr>
<tr>
<td><strong>Neurogenic hypothesis</strong></td>
<td>Believes that vitiligo is because of an altered reaction to neuropeptides, catecholamines and their metabolites by epidermal melanocytes.</td>
</tr>
<tr>
<td><strong>Biochemical hypothesis</strong></td>
<td>Believes that over-secretion of hydrobiopterin, a cofactor of tyrosine hydroxylase results in accumulation of catecholamines that in turn results in formation of reactive oxygen species in the melanocytes. These reactive oxygen species are thought to cause destruction of affected melanocytes in vitiligo patients.</td>
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</table>

NB-UVB has been used in combination with different topical agents to increase its efficacy and thus shorten the total duration of treatment. Treatment options that have been used with NB-UVB in vitiligo till date include topical tacrolimus, pimecrolimus, vitamin D analogues and even topical psoralen. While some studies have shown a synergistic effect with these combinations, others have found the efficacy of the combinations to be similar to NB-UVB alone. In one half-body comparison study, topical placental extract was used in combination with NB-UVB but the combination was shown to offer no added benefit than NB-UVB alone. Therefore, the ideal topical agent to be combined with NB-UVB remains unknown.

**Laser Therapy**

Excimer laser, which uses Xenon-Chlorine (Xe-Cl) gas and produces a monochromatic laser light of 308nm wavelength, is another innovative treatment option for vitiligo. The laser system has been used with increasing frequency over the last few years for targeted treatment of individual vitiligo lesions. The laser is used either alone or in combination with topical immunomodulator or PUVA-sol therapy. Treatment with this laser is claimed to give extremely good and early results in both localized and segmental vitiligo. In a pilot study on 18 patients with 29 affected areas 57% of lesions showed varying degrees of repigmentation after just six exposures over two weeks. The figure was increased to 87% after 12 treatments over four weeks. Another recent study has reported a repigmentation of >75% in 61% of lesions after 30 treatments with Excimer laser. Repigmentation was found to be better on the face and trunk than on the extremities.

Topical therapies, particularly topical tacrolimus, have been used in combination with Excimer laser. This combination has been claimed to be more effective than Excimer laser alone. In a randomized right-left comparison study with 14 patients, Excimer light monotherapy was compared with a combination of Excimer laser with topical tacrolimus. While 20% of lesions treated with Excimer laser alone achieved >75% repigmentation, the same degree of repigmentation was obtained in 70% lesions with the combination treatment. Topical methoxsalen has also been used in combination with Excimer laser phototherapy and this has been claimed to have worked better than laser therapy alone.

The advantage of Excimer laser therapy over conventional UVB therapy is the targeted mode of treatment with no exposure of the uninvolved skin. Moreover, the onset of repigmentation is earlier with Excimer laser therapy than with UVB therapy.

**Targeted UVB therapy**

This is another recent innovation in vitiligo management that has arrived over the last few years. The beauty with this therapy is that it delivers high intensity UVB light only to the affected vitiliginous areas, avoiding any exposure to the uninvolved skin. This not only decreases the cumulative UVB dose received by an individual patient, but is also claimed to improve the efficacy of treatment quite significantly.

Targeted UVB therapy, as expected, finds its use more in the treatment of focal and segmental types of vitiligo. In fact, the first study with targeted UVB therapy was done on eight patients with segmental vitiligo. Five of these patients achieved >75% repigmentation of their lesions with this therapy.

Targeted UVB therapy offers certain advantages over Excimer laser phototherapy. The treatment is safer and more efficacious compared with conventional UVB therapy, and almost as efficacious but much less costly than Excimer laser therapy.

**Systemic immunomodulator therapy**

Vitiligo is thought to be an immune-mediated disease and thus immune-suppressive and immunomodulator agents have been used on a regular basis in this disease. Among the immunosuppressants, systemic steroids have been the most commonly used. However, systemic steroid therapy has always been associated with a high incidence of adverse effects especially in children which is the age-group most commonly affected. To overcome this limitation, steroids have been given in pulse or even in mini-pulse form. A prospective study involving 14 patients with progressive or static vitiligo showed cessation of disease activity and a repigmentation rate of 10-
60% after high-dose methylprednisolone pulse therapy administered on three consecutive days.27 Systemic steroids have also been administered in a mini-pulse form on two consecutive days every week, known as Oral Minipulse (OMP) therapy. The first study demonstrating the efficacy of OMP with oral betamethasone (0.1mg/kg with a maximum of 5mg) was described in 1991.28 In a later study29 on childhood vitiligo, betamethasone was replaced by oral methylprednisolone and combined with topical fluticasone ointment on the vitiligo lesions. The disease was arrested in >90% of patients, and >65% of children achieved good to excellent (>50%) repigmentation of their vitiligo lesions.29

Topical Vitamin D analogues

Vitamin D analogues, particularly Calcipotriol, have been used topically either alone or in combination with topical steroids in the management of vitiligo. The basis for the use of these agents is that Vitamin D3 affects the growth and differentiation of both melanocytes and keratinocytes. This has been further proved by the demonstration of receptors for 1 alpha-dihydroxyvitamin D3 on the melanocytes. These receptors are believed to have a role in stimulating melanogenesis.29 Vitamin D analogues have given variable results in the treatment of vitiligo in different studies. These agents have also been used in combination with UV-light (including NB-UVB) and topical steroids with variable results.30,31,32

Topical immunomodulators

Topical immunomodulators, such as tacrolimus and pimecrolimus, have been the most promising recent additions to topical vitiligo therapy. In fact because of their efficacy and a remarkable safety profile the use of these agents in vitiligo has shown a consistently increasing trend over the last few years. These agents can be safely administered in young children, as they don’t cause any atrophy or telangiectasia of the skin even after prolonged use. There is also no risk of hypothalamic-pituitary-adrenal (HPA) axis suppression as seen with the widespread use of potent topical steroids.30 The first study that demonstrated the efficacy of tacrolimus in vitiligo was published in 2002.34 In this study tacrolimus was used in six patients with generalized vitiligo and five of them achieved >50% repigmentation of their lesions by the end of study period.34 Since then many additional studies have been published on this subject and have clearly demonstrated the role of topical tacrolimus in vitiligo. The best results with topical immunomodulator therapy have been seen on exposed parts of the body such as the face and neck and, as with any other therapy, the acral parts of the body respond the least.34,35 Similar results were obtained with the use of topical pimecrolimus in vitiligo patients.36

Pseudocatalase

Pseudocatalase has been used in combination with Dead Sea climatotherapy or UVB exposure for the treatment of vitiligo. The basis for the use of this agent in vitiligo is the evidence of oxidative stress and high H2O2 levels in the lesional skin.37 While some earlier studies38 demonstrated excellent results with this agent in inducing repigmentation in vitiligo, later studies have cast doubts on its efficacy.39 Pseudocatalase is used topically on the lesional skin, and this is followed by UVB exposure to the whole body or to the lesional skin. The combination is claimed to correct the oxidative stress on melanocytes in vitiligo patients and thus lead to correction of the depigmentation.

Topical 5-Fluorouracil

Topical 5-fluorouracil is supposed to induce repigmentation of vitiligo lesions by overstimulation of follicular melanocytes which migrate to the epidermis during epithelialization.39 This form of topical therapy can be combined with spot dermabrasion of the vitiligo lesions to improve the repigmentation response. In a study by Sethi et al,40 a response rate of 73.3% was observed with a combination of spot dermabrasion and topical 5-fluorouracil after a treatment period of six months.40

Surgical therapies

Surgical therapies for vitiligo have further increased the percentage cure of the disease by an appreciable degree, with the consequent increase of their use in the management of unresponsive vitiligo both in India and abroad. These surgical therapies, as a rule, are indicated in those patients who have a stable (non-progressive) disease of at least one year and not responding to medical treatment. In general the most important advantage with these procedures is that the chances of repigmentation of lesions are in the range of 90-100%. Moreover, these interventions are becoming better and easier to perform with every passing day.

Different surgical therapies that have been attempted in the management of vitiligo include autologous suction blister grafting, split-thickness grafting, punch grafting, smash grafting, single follicular unit grafting, cultured epidermal suspensions and autologous melanocyte culture grafting. All these grafting procedures, except the melanocyte culture grafting, are easy to perform and do not require any sophisticated instruments. These grafting techniques have now been divided into two types, tissue grafts and cellular grafts, depending on whether whole epidermal/dermal tissue is transplanted or the individual cellular compartment.
Tissue grafting technique

Suction blister grafting

Here, thin epidermal grafts are taken from suction blisters on the donor site, usually on the buttocks or thighs. These suction blisters are produced by applying sufficient negative pressure on the skin at the donor site by using a suction apparatus or syringes with three-way cannulae. The epidermal grafts are then transplanted on to dermabraded vitiligo lesions. This leads to repigmentation of the recipient areas with an excellent cosmetic matching. The ease of the procedure, the high success rate and the excellent cosmetic results have all made suction blister grafting the procedure of choice in vitiligo grafting.41

Split thickness grafting

In this grafting technique a thin split thickness graft is taken from a donor site with the help of a dermatome, Humby’s knife, Silver’s knife or a simple shaving blade. This graft is then transplanted on to dermabraded recipient areas. This technique also gives excellent cosmetic matching after repigmentation and the incidence of repigmentation in this technique is also quite high. In fact, most comparison studies on grafting techniques in vitiligo have shown that maximum repigmentation is achieved with either suction blister grafting or split thickness grafting.41

The advantage of partial thickness grafting over the suction blister method is that a relatively larger area of vitiligo can be tackled in a single sitting. Both partial thickness skin grafting as well as suction blister grafting can be followed up by NB-UVB to achieve faster and better results.

Miniature punch grafting

Here full-thickness punch grafts of 1.0 to 2.0 mm diameter are taken from a suitable donor site and then transplanted on to similar punch shaped beds on the recipient vitiligo lesions. The recipient area is then treated with either PUVA/PUVA-sol or topical steroids leading to spread of pigment from the transplanted punches to the surrounding skin. With time the whole of the recipient area gets repigmented. The advantages of this procedure are that it is easy to perform and can take care of a relatively larger vitiligo area compared with the above two procedures. Also vitiligo lesions with irregular or geographical shapes can be treated with this procedure. However there are certain limitations. There is the risk of ‘cobblestone appearance’, ‘polka-dot appearance’, and hypertrophic changes at the recipient site.41 All these side effects can be minimized by proper patient selection and by use of smaller sized punches of 1.0 to 1.5 mm diameter. Miniature punch grafting is presently the commonest surgical procedure performed in India on vitiligo patients.

Follicular unit grafting

In this technique, single-hair follicular units are harvested/prepared from a suitable donor area as in the case of hair transplantation. These follicular units are then cut above the level of the follicular bulb and then transplanted into vitiligo lesions. The idea behind this technique is that the melanocytes in the follicular unit are ‘donated’ to the vitiliginous skin and serve as a source of pigment at the recipient site. The repigmentation process here simulates the normal process of repigmentation of vitiliginous skin quite closely and thus gives an excellent cosmetic result. This procedure combines the advantages of punch grafting with the excellent cosmetic results of split thickness or blister grafting techniques.42 The procedure is however tedious and needs good expertise on the part of the cosmetic surgeon.

Smash grafting

In this technique, a partial thickness graft is taken and is ‘smashed’, or cut into very small pieces, by means of a surgical blade on a suitable surface such as a glass slide. This ‘smashed’ tissue is then transplanted on to the dermabraded recipient skin and covered with a special powder or corrugated tube dressing so as to keep the smash-graft undisturbed on the recipient area. The advantage of this technique, over a simple partial thickness grafting, is that thicker grafts can be used with a good cosmetic result. The procedure has been indicated for those who are relatively inexperienced and cannot take an ideal, thin and transparent partial thickness graft from the donor area.44

Cellular grafting techniques

Non-cultured epidermal suspensions

Here a split-thickness graft is taken from a donor area and then incubated overnight. On the next day the cells are mechanically separated using trypsin-EDTA solution and then centrifuged to prepare a suspension. This cell suspension is then applied to the dermabraded vitiligo lesions, and a collagen dressing is applied to keep it in place. A relatively large area of vitiligo, about ten times the size of the donor graft can be taken care of with this procedure.45 The recipient area however has to be treated with either NB-UVB or PUVA for two to three months to achieve the desired pigmentation.

Melanocyte culture transplantation

This is a relatively more advanced grafting procedure where, once again, a split-thickness graft is taken from a donor area and incubated in an appropriate culture medium to grow the melanocytes or the keratinocytes-melanocyte combination in vitro. The cultured cells are then applied onto laser dermabraded, or even mechanically abraded, lesional skin.46,47 The procedure is obviously more difficult to perform, as it needs the advanced laboratory facilities for melanocyte culture. However the results with this procedure are excellent and a relatively large area of involved skin can be tackled by a single donor graft.
Narrowband UVB therapy either alone or in combination with immunomodulators, Vitamin D analogues etc.

Excimer laser therapy

Targeted UVB phototherapy

Topical immunomodulators

Topical Vitamin D analogues

Topical pseudocatalase with UVB

Oral minipulse steroid therapy

Suction blister skin grafting

Partial thickness skin grafting

Miniature punch grafting

Follicular skin grafting

Smash grafting

Non-cultured epidermal cell transplant

Melanocyte culture transplant

Table 2: New treatment options in vitiligo

<table>
<thead>
<tr>
<th>Medical therapies and phototherapy</th>
<th>Surgical therapies</th>
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<tbody>
<tr>
<td>Narrowband UVB therapy either alone or in combination with immunomodulators, Vitamin D analogues etc.</td>
<td>Suction blister skin grafting</td>
</tr>
<tr>
<td>Excimer laser therapy</td>
<td>Partial thickness skin grafting</td>
</tr>
<tr>
<td>Targeted UVB phototherapy</td>
<td>Miniature punch grafting</td>
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<tr>
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<td>Topical pseudocatalase with UVB</td>
<td>Non-cultured epidermal cell transplant</td>
</tr>
<tr>
<td>Oral minipulse steroid therapy</td>
<td>Melanocyte culture transplant</td>
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Psychological aspects of infertility

Prasanta Kumar Deka, Swarnali Sarma

ABSTRACT
Infertility is the inability to naturally conceive, carry or deliver a healthy child. The World Health Organization definition based on 24 months of trying to get pregnant is recommended as the definition that is useful in clinical practice and research among different disciplines. All over the World it affects an estimated 10%-15% of couples of reproductive age. In recent years, the number of couples seeking treatment for infertility has dramatically increased. There is less information about effective psychiatric treatments for this population; however, there is some data to support the use of psychotherapeutic interventions. The stress of the non-fulfilment of a wish for a child has been associated with emotional squeal such as anger, depression, anxiety, marital problems and feelings of worthlessness among the parents. In general, among infertile couples, women show higher levels of distress than their male partners. Various research studies support the theory that distress is associated with lower pregnancy rates among women pursuing infertility treatment. Since psychological factors play an important role in the pathogenesis of infertility, exploration of this is also an important task to manage this devastating problem, which has cultural and social impact.

KEYWORDS
Infertility, Psychology, Depression

Introduction

Most experts define infertility as not being able to get pregnant after at least one year of trying. Women who are able to get pregnant but then have recurrent miscarriages are also said to be infertile. The infertility definition made a difference. The World Health Organization definition based on 24 months of trying to get pregnant is recommended as the definition that is useful in clinical practice and research among different disciplines.¹

Magnitude of the Problem

It is a growing problem and across virtually all cultures and societies almost all over the World and affects an estimated 10%-15% of couples of reproductive age. In recent years, the number of couples seeking treatment for infertility has dramatically increased due to factors such as postponement of childbearing in women, development of newer and more successful techniques for infertility treatment, and increasing awareness of available services. This increasing participation in fertility treatment has raised awareness and inspired investigation into the psychological ramifications of infertility. Consideration has been given to the association between psychiatric illness and infertility. Researchers have also looked into the psychological impact of infertility per se and of the prolonged exposure to intrusive infertility treatments on mood and well-being. There is less information about effective psychiatric treatments for this population; however, there is some data to support the use of psychotherapeutic interventions².

Why infertility has a psychological effect on the couple?

Parenthood is one of the major transitions in adult life for both men and women. The stress of the non-fulfilment of a wish for a child has been associated with emotional squeal such as anger, depression, anxiety, marital problems and feelings of worthlessness. Partners may become more anxious to conceive, ironically increasing sexual dysfunction and social isolation. Marital discord often develops in infertile couples, especially when they are under pressure to make medical decisions. Couples experience stigma, sense of loss, and diminished self-esteem in the setting of their infertility³.

Male and female partner respond differently

In general, in infertile couples women show higher levels of distress than their male partners⁴; however, men’s responses to infertility closely approximate the intensity of women’s responses when infertility is attributed to a male factor⁵. Both men and women experience a sense of loss of identity and have pronounced feelings of defectiveness and incompetence. Women trying to conceive often have clinical depression rates similar to women who have heart disease or cancer. Even couples undertaking IVF face considerable stress. Emotional stress and marital difficulties are greater in couples where the infertility lies with the man. Therefore the psychological impact of infertility can be devastating to the infertile person and to their partner.
Factors influencing psychological stress

According to one study done in Sweden, three separate factors seem to contribute to the psychological stress men and women experience as a result of their infertility. The three factors, in order of importance for the women were,
1. "Having Children is a Major Focus of Life"
2. "The Female Role and Social Pressure"
3. "Effect on Sexual Life"

The men in the study reversed the order of importance of factors 1 and 2. The third factor was equally significant to both the men and women. It was also shown that women experienced their infertility more strongly than the men. Women also showed a more intense desire to have a baby than men.5

Behaviour of the couple as a result of infertility

Stress, depression and anxiety are described as common consequences of infertility. A number of studies have found that the incidence of depression in infertile couples presenting for infertility treatment is significantly higher than in fertile controls, with prevalence estimates of major depression in the range of 15%-54%.6,7,8,9. Anxiety has also been shown to be significantly higher in infertile couples when compared to the general population, with 8%-28% of infertile couples reporting clinically significant anxiety10. The causal role of psychological disturbances in the development of infertility is still a matter of debate. A study of 58 women from Lapane and colleagues reported a 2-fold increase in risk of infertility among women with a history of depressive symptoms; however, they were unable to control for other factors that may also influence fertility, including cigarette smoking, alcohol use, decreased libido and body mass index11.

Psychological factors may also affect the reproductive capacity

Although infertility has an effect on a couple’s mental health, different psychological factors have been shown to affect the reproductive ability of both partners. Proposed mechanisms through which depression could directly affect infertility involve the physiology of the depressed state such as elevated prolactin levels, disruption of the hypothalamic-pituitary-adrenal axis, and thyroid dysfunction. One study of 10 depressed and 13 normal women suggests that depression is associated with abnormal regulation of luteinizing hormone, a hormone that regulates ovulation12. Changes in immune function associated with stress and depression may also adversely affect reproductive function13. Further studies are needed to distinguish the direct effects of depression or anxiety from associated behaviours (e.g., low libido, smoking, alcohol use) that may interfere with reproductive success. Since stress is also associated with similar physiological changes, this raises the possibility that a history of high levels of cumulative stress associated with recurrent depression or anxiety may also be a causative factor.

Result of treatment

While many couples presenting for infertility treatment have high levels of psychological distress associated with infertility, the process of assisted reproduction itself is also associated with increased levels of anxiety, depression and stress14. A growing number of research studies have examined the impact of infertility treatment at different stages, with most focusing on the impact of failed IVF trials15. Comparisons between women undergoing repeated IVF cycles and first-time participants have also suggested that ongoing treatment may lead to an increase in depressive symptoms16. The data, however, is still controversial since other studies have found minimal psychological disturbance induced by the infertility treatment process or IVF failure17,18. In light of the discrepancy in results, there has been increasing interest in the factors that contribute to drop out from infertility treatment since this population is often not included or decline to participate in studies. Whereas cost or refusal of physicians to continue treatment have been cited as reasons for discontinuing treatment, recent research suggests that a significant number of drop outs are due to psychological factors19,20,21. The outcome of infertility treatment may also be influenced by psychological factors. A number of studies have examined stress and mood state as predictors of pregnancy rates among women pursuing infertility treatment2,16,22,23,24,25.

Conclusion

In light of all the data suggesting that psychological symptoms may interfere with fertility, success of infertility treatment and the ability to tolerate ongoing treatment; interest in addressing these issues during infertility treatment has grown. Since psychological factors play an important role in the pathogenesis of infertility, exploration of this is also an important task to manage this devastating problem, which has cultural and social impact.

Competing Interests
None Declared

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Infertility, Assisted Reproduction and Mental Health.


Coronary vasospasm in a patient with respiratory failure: A case report and a brief review

Mujeeb Sheikh, Satjit Adlakha, Steven Bruhl and Shaffi Kanjwal

ABSTRACT
Coronary vasospasm is an episodic, augmented, contractile response of coronary smooth muscles to variety of stimuli in the setting of established endothelial dysfunction. Various physiological including cold, stress and pathological factors like smoking, and ethanol have been well known to precipitate vasospasm. Despite these omnipresent factors, coronary vasospasm has become infrequent, in particular due to judicious use of medication including calcium channel blockers, statins and aspirin. We present a case of severe coronary vasospasm resulting in haemodynamic instability, in a patient with hypoxic respiratory failure. Recurrent symptomatic episodes required coronary angiography for the diagnosis and patient was successfully treated with calcium channel blockers.

KEYWORDS
Myocardial infarction; respiratory failure; coronary vasospasm; Diltiazem

Introduction
Myocardial ischemia from coronary artery vasospasm can lead to variety of presentation including stable angina, unstable angina, myocardial infarction and sudden death. Although, pathognomonic clinical scenario includes symptom of chest pain, transient ST-segment elevation on the electrocardiogram (ECG), and vasospasm on a coronary angiography, atypical presentations have also been reported. Various known physiological factors including stress, cold, hyperventilation and pharmacological agents including cocaine, ethanol, 5-Fluouracil, and triptans can precipitate a vasospastic attack. We report a case of ST-segment elevation due to right coronary artery vasospasm, in patient with hypoxic respiratory failure, and successful treatment with calcium channel blockers.

Case description
A 56 year old man was admitted for the repair of a large ventral incisional hernia. The patient had a prior history of morbid obesity, chronic obstructive pulmonary disease (COPD), hypertension and cigarette smoking. The postoperative course was complicated by bilateral pneumonia leading to respiratory failure requiring mechanical ventilation. An electrocardiogram at the time of intubation was essentially normal. Aside from bilateral rhonchi and crackles on lung auscultation, the rest of the physical examination findings were unremarkable. Arterial blood gases at the time of intubation demonstrated PH 7.33, PO2 58 mmHg, PCO2 65 mmHg, HCO3- 20 mmol/L, suggestive of hypoxia and concomitant respiratory acidosis. Baseline laboratory studies including cardiac enzymes were within normal limits. The patient was treated with intravenous vancomycin for methicillin-resistant staphylococcus pneumonia. On postoperative day 4, the patient had recurrent episodes of transient ST-elevation on a bedside monitor (Fig.1).

Figure 1

These episodes lasted for 3-5 minutes and were associated with significant bradycardia and hypotension. In view of recurrent episodes, haemodynamic instability, and underlying risk factors of coronary artery disease, cardiac catheterization was performed. Coronary angiography revealed a 90% stenosis with haziness of the mid-right coronary artery without any other significant epicardial disease. An intravascular ultrasound (IVUS) was performed and was followed by administration of 100 mcg of intracoronary nitroglycerin; the lesion was reduced to almost 20%. (Fig.2). The diagnosis of prinzmetal’s angina was made, based on clinical course and angiographic results and prompt therapy with diltiazem (120 mg per day) was initiated.
The patient had no further recurrences of similar episodes during the hospitalization and on follow up at 3 months.

![Figure 2](image)

The diagnosis of prinzmetals angina was made, based on clinical course and angiographic results and prompt therapy with diltiazem (120 mg per day) was initiated. The patient had no further recurrences of similar episodes during the hospitalization and on follow up at 3 months.

**Discussion**

The prevalence of vasospasm has been reported to be higher in Japanese and Korean population as compared to the western population. A recent multi-institute survey in Japan documented spasm in 921 (40.9%) of the 2251 consecutive patients who underwent angiography for angina pectoris. In contrast to the traditional risk factors for atherosclerotic coronary artery disease, the incidence of smoking, age and dyslipidaemia has been reported higher in patients with coronary vasospasm.

Endothelial dysfunction is now considered to be the major inciting factor in the pathogenesis of the vasospasm. Vasospastic angina (VA) with normal coronary arteries on the angiography, impaired endothelial-dependent and endothelial-independent vasodilatation has been frequently observed in these patients. Vascular tone is normally regulated by production of vasodilator factors like nitrous oxide (NO), prostacyclin and vasoconstricting agents like endothelin-1. In the presence of dysfunctional endothelium the agents that normally cause vasodilatation lead to paradoxical vasoconstriction, due to direct muscle stimulation, like acetylcholine.

Stress, whether physical or mental stress has been shown to induce coronary vasospasm and myocardial ischemia. In a study by Kim et al, coronary spastic angina was diagnosed in 292 patients out of 672 coronary spasm provocation tests. Among 292 patients, 21 (7.2%) had myocardial infarction and 14 out of these 21 had experienced severe emotional stress before the event. Recently, animal studies have also shown that high circulatory level of stress hormones (cortisol) exaggerate coronary vasoconstriction through Rho-Kinase activation. Hypoxia has been seen in animal models to predispose to vasospasm through superoxide formation, which leads to loss of vasodilator function of NO.

The ECG changes that occur during attack include ST-segment elevation, and or peaking of T wave from total or subtotal coronary occlusion. In some cases spasm can involve more than one artery leading to ST-segment elevation in multiple leads, which may predispose to ventricular tachycardia or fibrillation. Coronary spasm is diagnosed by angiography, and spasm can occur at the site of atherosclerotic plaque or in normal segment of the coronary artery. In patients with unequivocal diagnosis, provocative tests including administration of acetylcholine, hyperventilation to induce spasm may be required for the diagnosis.

Current first line therapy involves use of calcium channel blockers (CCB) alone or in combination with long acting nitrates. In a study comparing the effect of long acting nitrates (Isosorbide dinitrate 40mg/day) versus calcium channel blockers (amlodipine 5mg/day or long acting nifedipine 20mg/day) on coronary endothelium and vasoconstriction between patients with normal or minimally diseased coronary artery, treatment with long acting nitrates was associated with less favourable effects on coronary endothelial functions. Sudden withdrawal of CCB in patients with known vasospasm can lead to rebound of symptoms and may prove dangerous. In patients with refractory symptoms alpha-blockers, nicorandil have been used. Although beta blockers are believed to enhance vasospasm, Betaxalol, a selective beta-1 blocker, has been found to be effective in the treatment of variant angina due to its vasorelaxing effects.

In addition, elimination of or control of all other risk factors or precipitants is very important for successful treatment. In drug refractory cases the percutaneous coronary intervention or coronary artery bypass graft has been performed for the ischemia relief.

Our patient had multiple precipitating factors for vasospasm. Endothelial dysfunction from severe physical illness and sepsis could have precipitated the VA. Furthermore, hypoxia from respiratory failure could have also been an inciting agent and cannot be ruled out. It is worth mentioning that intensive care unit patients frequently have coexistence of both the underlying risk factors and the precipitating factors for vasospasm, yet VA as a clinical syndrome is uncommonly seen or reported.

**Conclusion:**

The clinician needs to be aware of coronary artery vasospasm as it can pose a serious medical threat. Early diagnosis and treatment may result in improved outcomes from vasospastic angina.
Competing Interests
None Declared

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REFERENCES

Elevated pancreatic enzymes within the content of liver abscess in a patient with a history of chronic pancreatitis

Muhammad Z Bawany and Thomas Sodeman

Introduction

Liver abscess accounts for 48% of visceral abscesses and presents with significant morbidity and mortality. The overall incidence of pyogenic liver abscess is 3.6 per 100,000 populations, however; elevated pancreatic enzymes within the content of a liver abscess have never been reported in the literature.

Case report

A 36-year-old African American male with a history of chronic pancreatitis presented to the emergency department for abdominal pain in the epigastric area along with nausea, vomiting, diarrhoea, fever. His symptoms began 3-4 days before presentation. The abdominal pain was dull in nature and 6/10 in intensity, non-radiating. His past medical history was significant for HTN, diabetes mellitus and chronic diarrhoea secondary to chronic pancreatitis.

On admission the patient was alert and oriented, blood pressure was 97/44 mm Hg, heart rate 16 beats per minute, respiration 16 per minute, oxygen saturation 94% on room air and temperature 102°F. Abdominal examination revealed hyperactive bowel sounds and tenderness in the epigastrium & RUQ. Liver span was 14 cm. The rest of the examination was unremarkable.

Laboratory work revealed: Haemoglobin 9.8 g/dl, WBC 22.1 Thou/mm3 with segmented neutrophils of 81% and 9% bands, BUN 54 mg/dl, Cr 4.7 mg/dl, total protein 10.4 g/dl, albumin 1.8 g/dl, total bilirubin 1.1 mg/dl, direct bilirubin 0.3 mg/dl, AST 98 IU/L, ALT 38 IU/L, alkaline phosphatase 250 IU/L, amylase 81 units/L, lipase 10 units/L, lactate 2.3 mmol/L and INR 1.39.

The patient was started on fluids and meropenem for broad spectrum coverage. However his condition worsened and he developed acute respiratory distress syndrome secondary to sepsis necessitating intubation. Due to his abdominal pain he underwent a computer tomography (CT) scan of the abdomen, which revealed pancreatic calcifications and multiple liver abscesses; the largest measuring 7.5cm in the right lobe of the liver (Figure 1).

As the patient’s condition did not improve, he underwent liver abscess drainage. Fluid analysis showed ph 4.0, LDH 39 units/L, glucose 81 mg/dl, protein 1.6 g/dl, lipase of 16 units/L and amylase 68 units/L. The presence of amylase and lipase in the liver abscess without any evidence of a fistula between liver and pancreas on CT scan was unexpected, therefore it was decided to leave the catheter in situ for continuous drainage. 3 Even though his blood and fluid cultures remained negative during the hospital stay he was continued on antibiotics, which may have meant that the initial antibiotic therapy rendered the blood cultures negative. The success of management was assessed with a hepatic CT 10 days post drainage and was demonstrated by the observation of improvement in the patient’s general condition, as indicated by normal temperature, decreased draining catheter output and the resolution of deranged laboratory values. The catheter was then removed and the patient was discharged.
Discussion

Liver abscesses develop via seeding through portal circulation, directly via spread from biliary infections or from surgical or penetrating wounds and also from systemic organs via haematogenous spread. In our case the most reasonable explanation was through the involvement of portal circulation due to recurrent pancreatitis.

The morbidity and mortality rate for liver abscesses ranges from 2 – 12 % depending on the severity of underlying co-morbidities. 2 The clinical manifestations, as in our case, are characterized by abdominal pain (50-75%), fever (90%), nausea and vomiting. Other symptoms may include weight loss, malaise and diarrhoea. On physical exam RUQ tenderness, guarding, rebound tenderness, hepatomegaly and occasional jaundice can be appreciated. The diagnosis of a liver abscess can be made by radiographic imaging followed by aspiration and culture of the abscess material. Liver abscesses can be either polymicrobial or monomicrobial, unlike in the case with our patient, whose abscess was sterile. Depending on the microbial results additional sources of infection should be evaluated. Drainage of abscesses can be percutaneous or open surgical. Percutaneous drainage with coverage of antibiotics was successful in our patient.

Conclusion

In summary, we present a case of pancreato-liver abscess in a patient with a history of chronic calcified pancreatitis. It was treated with antibiotics and percutaneous drainage, with satisfactory resolution. To our knowledge this has never been reported in the literature and more work needs to be done to understand the pathophysiology of elevated pancreatic enzymes in the context of a liver abscess in a patient with a history of chronic pancreatitis.

Competing Interests
None declared

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Giant Cerebral Hydatid Cyst in a Child- A Case Report and Review of Literature

Ali Nemati, Ahmad Kamgarpour, Murtaza Rashid and Sahar Sohrabi Nazari

ABSTRACT
Cystic hydatidosis is a rare disease which mainly involves the liver and lungs, and rarely the brain. Cysts may be single or multiple. A 6-year-old boy presented with the chief complaint of ataxia. Brain imaging revealed a huge cystic structure involving the right side of the brain. A diagnosis of brain hydatid cyst was made and the patient was operated on. A large cyst was successfully delivered without rupture. Anthelmintic medication was started and the patient was discharged with full recovery of neurological function. Hydatid cysts must be considered as a differential diagnosis in patients with cystic lesions of the brain, especially in children. Surgery remains the standard method of treatment, and care must be taken in order to recover the cyst without rupture to avoid severe complications and recurrence.

KEYWORDS
Hydatid cyst; Brain; Imaging; Surgery

Introduction
A hydatid cyst is the larval stage of a small tapeworm, Echinococcus granulosus. This is an emerging zoonotic parasitic disease throughout the world, thought to cause an annual loss of US $193,529,740.1 Hydatid cysts are more prevalent in Australia, New Zealand, South America, Russia, France, China, India, the Middle East and Mediterranean countries.2,3,4 They are most commonly (about 50-75%) seen in children and young adults.4,5,6 The liver is the most common organ involved (77%), followed by the lungs (43%).7,8,9,10 However, some researchers report that the lung is the most common organ involved in children, possibly due to bypass of the liver by lymphatics, and higher incidental findings in the lungs when children are assessed for other respiratory infections.8,11,12,13 Hydatid cysts have been reported in the brain (2%),3,5,6,7,8,14,15 heart (2%),8,10,13,16 kidneys (2%),9,10,11 orbit (1%),17,18 spinal cord (1%),5,19 spleen,5,18 spermatic cord20 and soft tissues.9 However, in the Mediterranean region, the incidence of brain hydatid cysts have been reported higher (7.4-8.8%).21 Surgery remains the treatment of choice, although recently some new modalities have been described.5,8,22 Careful removal of the lesion is of considerable importance, otherwise fatal complications are inevitable.23,24,25 We describe the case of a 6 year old boy who came to our department with various neurological manifestations. The main purpose of this study is to demonstrate the unusual symptoms of the patient and the enormity of the operated cyst, which was fully resected without rupture.

Case Report
A 6-year-old boy was referred to our Neurosurgery Department with a four week history of ataxia and left sided weakness. His vital signs were normal and his Glasgow Coma Scale (GCS) was 15. The symptoms had started about six months ago with numbness and paraesthesia of the toes. Subsequently he developed intermittent nausea and vomiting. He then started to develop left sided weakness and finally ataxia. He also had a few focal convulsions but did not complain of headache. Fundoscopy revealed bilateral frank papilloedema. On examination, the patient had nystagmus and a positive Romberg’s test. Laboratory data showed mild leucocytosis without any significant rise in eosinophils, and liver enzymes were normal. The enzyme-linked immunosorbent assay (ELISA) for hydatid cysts was negative. Plain chest X-ray and ultrasound scan of the abdomen and pelvis were also normal. Brain computed tomography (CT scan) of the frontal and parietal lobes demonstrated a single large, spherical, well-defined, thin-walled homogenous cyst, with an inner density similar to that of cerebrospinal fluid (CSF), and a wall which did not show enhancement [fig 1(a)].

This cystic structure caused a mass effect and a midline shift towards the left, as well as hydrocephalus, possibly due to obstruction. Magnetic resonance imaging (MRI) of the brain showed cystic signal intensity similar to that of CSF, without ring enhancement or oedema [fig 2].
Fig 1 (a): Pre-operative unenhanced CT scan which shows a large CSF density cystic lesion on the right side causing mass effect and midline shift to the left. There is no peri-lesional oedema. Fig 1 (b): Post-operative CT scan of the lesion shows a large void which can lead to dangerous collapse. Mild haematoma is also seen.

Fig 2 (a): T1-weighted axial MRI of the brain demonstrates a cyst density similar to CSF. Fig 2 (b): T2-weighted MRI shows no ring enhancement or oedema. The periventricular hyperintensity of the left side is probably due to obstructive hydrocephalus.

Fig 3: This shows the cyst removed in toto after operation. The cyst appears creamy and smooth.

After summation of all the above data, the diagnosis of a hydatid cyst was made and a right frontotemporoparietal craniotomy was performed. A large cystic structure (14×14×12 cm) was delivered with utmost care to avoid rupture and spillage [fig 3]. A hydatid cyst was confirmed by pathology reports. A post-operative CT scan showed a large space without any residual matter [fig 1(b)]. Post-operatively, albendazole 15 mg/kg was started and continued for four weeks. The patient showed marked improvement in his neurological deficit and was discharged after one week with close follow-up.

Discussion/Review Of Literature

Life Cycle

Hydatidosis is caused by Echinococcus granulosus, which occurs mainly in dogs. Humans who act as intermediate hosts get infected incidentally by ingesting eggs from the faeces of the infected animal. The eggs hatch inside the intestines and penetrate the walls, entering blood vessels and eventually reach the liver where they may form cysts or move on towards the lungs. Even after pulmonary filter, a few still make it to the systemic circulation and can lodge in almost any part of the body, including the brain, heart and bones. Brain hydatid cysts are relatively rare and only account for up to 2% of total cases. The actual percentage may be higher than what we have in literature, due to under-reporting. Brain hydatid cysts can be primary (single) or secondary (multiple). The latter are thought to arise from the multiple scolices released from the left side of the heart following cyst rupture in the heart or due to spontaneous, traumatic or surgical rupture of a solitary cranial cyst. Cysts mostly involve the territory of the middle cerebral artery but other regions like intraventricular, posterior fossa and the orbit have also been reported. The wall of the cyst consists of an inner endocyst (germinal layer) and outer ectocyst (laminated layer). The host reacts to the cyst forming a pericyst (fibrous capsule), which provides nutrients to the parasite. In the brain, due to minimal reaction, the pericyst is very thin. The endocyst produce scolices which bud into the cyst cavity and may sediment within the hydatid cavity, commonly known as hydatid sand.

Presentation and Diagnosis

Most hydatid cysts are acquired in childhood and are manifested during early adulthood. Cysts develop insidiously, usually being asymptomatic initially, and present with protean clinical and imaging features. In previous studies the most common presenting symptoms were headache and vomiting. In the literature, patients reported ataxia, diplopia, hemiparesis, abducens nerve palsy and even coma. Surprisingly, in the present study the patient did not have a headache and presented with parasithea and numbness of the toes. Later he developed left sided weakness, convulsions and finally ataxia, which correlate with previous studies. Diagnosis of a hydatid cyst can sometimes be confused with other space occupying lesions of the brain, especially abscesses, neoplasms and arachnoid cysts. In this study the patient had bilateral frank papilloedema which is also mentioned in earlier reports. The Casoni and Weinberg tests, indirect haemagglutination, eosinophilia and ELISA are used in diagnosing hydatid cysts, but as brain tissue evokes minimal response many results tend to be false negatives. In our case also, serology for hydatid cyst was
negative. CT scan and MRI are used frequently in diagnosing the cystic lesions.5,8,14,23,32,33 However, MRI is considered superior in demonstrating the cyst rim.5,8,11,21,23,32,34 On CT scan, a solitary cyst appears as well-defined, spherical, smooth, thin-walled and homogeneous, with an inner density similar to CSF, and non-enhancing walls.11,29,32 There may appear iso-dense to hyper-dense on CT scan5,8, and rarely, may become calcified.11,29,32 There is usually no surrounding brain parenchymal oedema, which if exists along with ring enhancement, indicates inflammation and infection.7,11,32,33,34 Ring enhancement and peri-lesional oedema differentiates brain abscesses and cystic neoplasms from uncomplicated hydatid cysts.5,8 These findings can in fact sometimes cause dilemma and misdiagnosis and lead to catastrophic events.14 The cyst shows low signal intensity on T1-weighted, and high signal intensity on T2-weighted MRI.5 MRI may also show peri-lesional oedema not seen on regular CT scan imaging.5 MRI may prove superior in determining exact cyst location, presence of super-added infections and cystic contents, and also in surgical planning and ruling out other diagnostic possibilities.14,35 We strongly recommend MRI for better evaluation of cystic brain lesions. Spontaneous cystic rupture can lead to different appearances depending on which layers have been obliterated, and produce some specific signs.5 When only the endocyst ruptures, cyst contents are held by the outer pericyst giving a peculiar water lily sign, which is pathognomic.5,8

Treatment

Though still in infancy, medical therapy for small or inoperable brain hydatid cysts has been promising. Albendazole alone or in combination with other compounds, such as praziquantel, has been reported with favourable results as an adjunct and, in certain circumstances, as the primary mode of treatment.2,5,35-37 It is reported that albendazole results in the disappearance of up to 48% of cysts and a substantial reduction in size of the cysts in another 28%.7 The duration of the treatment is four weeks or more, and recently many authors have favoured a prolonged therapy. The change in levels of cyst markers such as alanine, succinate, acetate and lactate, measured before and during treatment on Proton Magnetic Resonance Spectroscopy (MRS), correlate well with shrinkage and resolution of cyst findings on conventional MRI and help in evaluating the efficacy of chemotherapy.35 Cysts may drain into ventricles or rupture completely, causing spillage of contents into the subarachnoid space, leading to fatal anaphylactic shock, meningoitis or local recurrence.5,5,22,27 Surgery is the mainstay for treating intracranial hydatid cysts and the aim is to excise the cysts entirely without rupture, which can otherwise lead to catastrophic events as described earlier.2,3,14,25. The Dowling-Orlando technique remains the preferred method, in which the cyst can be delivered by lowering the head of the operating table and instilling warm saline between the cyst and the surrounding brain.40 Even minimal spillage can cause deleterious effects (1 ml of hydatid sand contains 400,000 scolices).14 The thin cyst wall, periventricular location and micro-adhesions to the parenchyma are the main problems encountered during the surgical procedure.1,22 The large cavity remaining after the cystic removal can lead to many serious complications, such as cortical collapse, hyperpyrexia, brain oedema and cardio-respiratory failure.5 Recurrence remains a major concern, which is managed by both antihelminthic chemotherapy and surgery. In a study conducted by Ciurea et al, 25% of the patients had recurrence, which highlights the need for long term follow up.23 In the present study, due to the huge size of the cyst and progressive neurological deficit, it was not wise to completely rely on medical therapy. Surgery was performed and post-operatively albenzazole was started as an adjunct. We recommend that for treating brain hydatid cyst, the size of the cyst, multiplicity, location and neurological deficit must all be taken into consideration.

Competing Interests
None Declared

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Post MTAS: A Survey of the first MMC Surgical Trainees in the Oxford Deanery

Khurram K Khan, Karen A Eley, Bettina Lieske, and Mr Bob Soin

Abstract

Introduction: The nationwide implementation of ‘run-through’ training in 2007, based upon the new system of postgraduate medical training known as Modernising Medical Careers (MMC), was the subject of much debate as to the suitability of the selection process, and the feasibility of the new system itself. One year after the start of the new Specialty Training (ST) grade this study obtains the views of core surgical trainees in the Oxford Deanery.

Methods: Forty-six trainees in ST1, ST2, Fixed Term Specialty Training Appointment (FTSTA) 1 and FTSTA2 posts completed questionnaires at three and nine months from appointments in August 2007.

Results: Fifty two percent (n=24) of respondents were appointed to their training posts from Round 1a, with 67% (n=16) to ST1 or ST2 level. Despite 61% (n=28) having initially selected Oxford as their first choice deanery, 93% (n=43) now wished to remain in the region for further training, with 57% (n=27) of all trainees satisfied with their current position. At three months, only 9% (n=4) felt well informed regarding their surgical training, and 28% (n=13) well supported by their seniors; however, six months later these figures had risen to 64% (n=29) and 60% (n=24) respectively. Nearly half (43%, n=20) of surgical trainees had looked into moving abroad to train, and two thirds had considered leaving surgery all together. From August 2008, 70% (n=9) of ST2 trainees and 57% (n=4) of FTSTA2 trainees had obtained ST3 positions, with all but one in their desired surgical specialty.

Conclusion: Despite MMC’s difficult introduction into higher specialist training, the majority of trainees surveyed expressed encouraging levels of job satisfaction, felt increasingly well informed and well supported, and had successfully negotiated the initial stages of the ‘run-through’ track. With continuing debate surrounding how MMC-based surgical training will work within the confines of National Health Service (NHS) provision and the European Working Time Directive, we present the opinions and outcomes of the first cohort of ‘run-through’ surgical trainees.

Keywords

Surgical training, MMC, ST trainee, FTSTA trainee

Introduction

The Department of Health’s Modernising Medical Careers (MMC) has been uniformly implemented into specialty training across the United Kingdom (UK). This began with the controversial and subsequently redundant Medical Training Application System (MTAS) selection process in Spring 2007, and ended with the first MMC specialty training posts commencing in August 2007. During the application process itself one preliminary study reported that 85% of candidates demonstrated decreased levels of enjoyment in their work, and 43% caring less about patient care.¹ The emergency introduction of the ‘golden ticket’ Round 1b guaranteed interview - though arguably justified in the face of a flawed application system - was a cause of further discontent and division amongst junior trainees and the consultants responsible for appointing them.

For surgical training in particular, the advent of the MMC initiative combined with the European Working Time Directive (EWTD) represents an estimated 50% reduction in the amount of specialist training hours when compared to the previous system.² This has raised concerns not only from current consultants, but also from the already increased number of surgical trainees having to share the same caseload. A previous survey of Ear, Nose, and Throat senior house officers reported 71% were willing to opt out of the EWTD to safeguard their training and patient care.³

In the Oxford Deanery the selection process of shortlisted surgical trainees in Rounds 1a and 1b consisted of six stations assessing curriculum vitae, portfolio, clinical examination, data interpretation, and pre- and post-operative management (totalling one hour). Candidates were offered generic or specialty themed Core Training (CT) posts at Specialty Training (ST) 1 or 2, or Fixed Term Speciality Training Appointments (FTSTA) 1 or 2, depending upon the candidate's ranking at interview (plus application form for Round 1a) irrespective of specialty preference. Following acceptance, individual appointments were made based on candidates ranking job preferences. Round 2 appointments were made at a local level via traditional selection methods. The most recent information from the deanery states that those trainees who received an offer of run-through training in the region will be guaranteed an interview for an ST3 post in surgery, however individual specialty preference and job allocation will be determined by re-ranking based on continuous appraisal during the core surgical training years, further Higher Specialist Training interviews, and training numbers available.
The media coverage that surrounded MTAS clearly highlighted the dissatisfaction amongst trainees and consultants leading up to and during the application process, but no study has yet assessed the views of surgical trainees following the start of their new MMC-based training posts. This survey aimed to obtain the views and outcomes of core surgical trainees in the Oxford Deanery.

Methods

At three and nine months following the commencement of speciality training posts, questionnaires were distributed to junior surgeons (CT 1-2) in the Oxford Deanery School of Surgery. Questions were structured to obtain information about level of experience and qualification(s), current and desired surgical speciality, job satisfaction, attitudes towards ‘run-through’ training and levels of support. In the Oxford Deanery there were 40 appointments at CT1 (18 ST1 and 22 FTSTA), and 29 at CT2 (17 ST2 and 12 FTSTA) in August 2007. Data were expressed as the mean ± standard deviation (SD). Statistical comparison was performed using Mann-Whitney’s U test, with the significance level at p<0.05.

Results

The questionnaire was completed by a total of 46 and 45 surgical trainees at three and nine months respectively. At the three-month time point this represented 67% of all trainees in the Oxford Deanery School of Surgery (male: female, 33:13) and included 11 at ST1, 16 at ST2, 11 at FTSTA1, and 8 at FTSTA2. Of these 52% (n=24) had obtained their post via Round 1a, 41% (n=19) via Round 1b, and 7% (n=3) via Round 2. At both CT1 (ST1 & FTSTA1) and CT2 (ST2 & FTSTA2), trainees were on average 3.7 ± 1.9 years post graduation (from time surveyed; CT1 range 1-11 years, CT2 range 3-8 years); 16% (n=7) of all trainees had previously studied Medicine at Oxford University, and 93% had studied medicine in the UK. (Figures 1a, 1b). Most popular desired specialities at three and nine months are displayed in figure 2. Of the 46 respondents, all had worked in the speciality of their career choice during the course of the year.

At time of appointment, 52% of trainees had completed the Membership to the Royal College of Surgeons (MRCS) exams, and 35% (n=16) of all trainees had completed a higher degree. (Figure 3). Furthermore, 22% (n=10) felt that there should be a further exam in addition to the MRCS to rank candidates for appointment to higher specialist training (ST3 onwards), with half of this number having already obtained their MRCS.

Those who had been allocated to ‘run-through’ ST posts were more satisfied with the concept of run-through training than those in FTSTA posts (where scores were assigned on a scale from 1 - very unsatisfied, to 5 - very satisfied), with the mean score at three months for ST trainees 4.1 ± 1.4, and FTSTA trainees 2.0 ± 1.4 (p<0.01), and at nine months 3.7 ± 1.1 for ST trainees versus 2.1 ± 1.1 for FTSTA trainees (p<0.01). Job satisfaction levels between these two groups of trainees were similar: at three months, mean score 3.5 ± 1.3 in ST posts versus 4.1 ± 0.8 in FTSTA posts (p>0.05), and at nine months,
mean score 3.5 ± 1.0 in ST posts versus 3.2 ± 1.3 in FTSTA posts (p>0.05). In addition, a similar comparison between ST and FTSTA trainees was found when determining if trainees had thought about leaving surgery. On a scale where a score of 1 – never thought of leaving surgery to 5 – very frequently thought of leaving surgery, the mean score at three months was 2.3 ± 1.4 for ST trainees versus 3.0 ± 1.6 for FTSTA trainees (p>0.05), and at nine months 2.2 ± 1.4 for ST trainees versus 2.9 ± 1.5 for FTSTA trainees (p>0.05). (Figures 4a, 4b).

In fact, 43% (n=20) of all trainees surveyed reported having enquired about surgical training in another country, with 4% (n=2, both UK Medical School graduates) stating that if unsuccessful in securing a training post in their desired specialty for August 2008, they would move abroad to train.

At three months, 9% (n=4) of all trainees felt well-informed about what will happen in the future regarding their training, with 20% (n=9, ST to FTSTA ratio 2:7) responding that had they been better informed prior to August 2007, then they would not have accepted their current post, and 28% (n=13) felt well-supported by their senior colleagues with regard to their future training. However at nine months from appointment, 69% (n=29) of all trainees felt well informed, and nearly two thirds well supported by their seniors (n=27). (Figure 5). Ninety three percent (n=43) of applicants wished to remain in the region for their future training, with 61% (n=28) having initially selected Oxford as their first choice deanery.

The majority of both ST2 (85%, n=11) and FTSTA2 (71%, n=5) trainees secured ST3 posts from August 2008, mainly within the Oxford Deanery, and all within their desired surgical specialty. All ST1 (n=16) trainees successfully moved into ST2 posts, and the majority of FTSTA1 (78%, n=7) trainees secured CT positions. (Table 1).

<table>
<thead>
<tr>
<th>Grade (n)</th>
<th>August 2008 Post (n)</th>
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<tbody>
<tr>
<td>ST1 (16)</td>
<td>ST2 (16)</td>
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<tr>
<td>FTSTA1 (9)</td>
<td>CT1 (3)</td>
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<td></td>
<td>FTSTA (2)</td>
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<td>GP Trainee (1)</td>
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<td>FTSTA2 (7)</td>
<td>ST3 (5)</td>
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<td></td>
<td>ST1 Radiology (1)</td>
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<td></td>
<td>CT2 (1)</td>
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Table 1. ST2 and FTSTA2 trainee outcomes from August 2008

Discussion

MMC has and will have profound implications on the way junior doctors will henceforth be trained in the National Health Service (NHS). Last year’s difficult introduction into specialist training, has for obvious reasons, directly affected the perceptions of trainees having to negotiate their careers through the ‘transition’ period.1, 6 This survey provides an interesting insight into the demographics, current viewpoints, and outcomes of the first cohort of MMC surgical trainees in the Oxford Deanery.

Just over half of all trainees in the survey were appointed after Round 1a (52%, n=24) of which two thirds (n=16) were to ST posts; a further 41% (n=19) were appointed after Round 1b, of which roughly half (n=9) were to ST posts. This highlights the large number of very good surgical trainees that may have been left unemployed had MTAS interim measures not been introduced to permit all candidates the opportunity of at least one interview, and that in the Oxford Deanery at least, candidates were given an equal chance of obtaining a ‘run-through’ post between the two rounds. Despite MMC person specifications at the time of application stating that MRCS was
not an absolute requirement for entry at ST1-2, 52% (n=24) had completed their MRCS, with a further 20% (n=9) having completed at least Part I or more.

Overall job satisfaction levels were good amongst all trainees (mean score 3.7 ± 1.1), with 57% (n=26) still agreeing with the concept of 'run-through' training, and hence MMC. This view is maintained despite the problems associated with last years application process, and in the face of an uncertain future. However, nearly half (43%, n=20) of trainees had enquired about training abroad, with several committed to leaving the UK next year if unable to obtain their desired surgical specialty. With the average cost to train a UK medical graduate being at least £150,000,7 and the amount of dedication and effort needed to embark on a surgical career thereafter, care must be taken to improve morale amongst junior surgeons, and to provide adequate and timely information. Encouragingly, between the two time points surveyed, levels of senior support and how well informed surgical trainees felt with regards to their training, increased from 28% to 60% and from 9% to 69% respectively; this may be secondary to a combination of extensive effort from the Deanery and the Royal College of Surgery to address trainee concerns.

The realistic future of those in FTSTA posts is cause for concern. This is highlighted in the recently released Tooke Report, in which it is stated they are “in danger of becoming the next ‘lost tribe’, the very category of doctor MMC sought to avoid”, but at the same time that “core [training] should not repeat the errors of previous SHO arrangements and must be time limited”.6 Those in FTSTA posts face higher levels of future uncertainty than their ST colleagues, and this was reflected in reporting a higher likelihood of consideration of alternative careers outside of surgery. However, both groups of trainees demonstrated statistically similar scores when questioned about how frequently they had thought of leaving surgery (2.3 ± 1.4 for ST trainees versus 3.0 ± 1.6 for FTSTA trainees, p<0.05), and 71% of FTSTA2 trainees surveyed within the Oxford Deanery went on to secure ST3 level posts in their desired specialty.

The authors note the limitations inherent to surveys in general namely the validity and reliability of responses obtained to questions asked due to the self-report method of data collection, the questionnaire entirely constructing the information obtained, and that the data does not capture the decision process that produced the observed outcomes and is therefore descriptive rather than explanatory. More specifically, the authors note that candidates who were successful in obtaining an ST3 post may have been more likely to complete the questionnaire, leading to further potential bias.

**Conclusion**

MMC has crossed the threshold into higher specialist training, and the first cohorts of MMC surgeons are being trained. The majority of trainees we surveyed expressed good levels of job satisfaction, had successfully negotiated their first year of the new system, and encouragingly felt better informed and supported over the course of their first year. However, this study encompassed a proportion of surgical trainees in one Deanery in the UK, and further study on a larger scale at regular time intervals is certainly warranted. Consequent to the problems of MMC’s difficult introduction, positive steps included travelling tours by the Royal College of Surgeons (England), and in the Oxford Deanery at least, regional meetings to address concerns and expectations, and outline the realistic future for surgical trainees. Perhaps a key determinant of sustainability for MMC in surgery in 2008 and beyond will be the relative success of the Intercollegiate Surgical Curriculum Programme (ISCP), and this represents a significant area for further study.

**COMPETING INTERESTS**

None declared

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**REFERENCES**


Female urinary incontinence - primary care management

Anita Sharma

Urinary incontinence is a common and distressing condition. It is an underreported problem because of the stigma associated with the condition and many patients simply suffer in silence.

Definition
Urinary incontinence is defined as involuntary leakage of urine.

Prevalence
It has been estimated that in the United Kingdom (UK) 9.6 million women are affected by bladder problems. An overactive bladder itself affects five million adults, nearly 1 in 5 of the over-40 population. Prevalence is estimated to be 15% among healthy older adults and 65% of old frail adults. It is twice as common in women than men. It can affect women of all ages including after childbirth. In a cross-sectional survey of adult females attending a primary care practice in the UK, nearly half had urinary incontinence but only a small minority sought help. Forty-two per cent of women affected wait up to 15 years before seeking treatment.

Types
1. Stress incontinence: This is involuntary urine leakage on exertion such as coughing/laughing/sneezing or exercise. Stress incontinence is due to an incompetent urethral sphincter. It is largely caused by childbirth thus young women can develop this problem. Other causes include pelvic surgery or hysterectomy.

2. Urge incontinence: This is involuntary urinary leakage associated with urgency (a compelling desire to urinate that is difficult to defer) and is due to detrusor overactivity leading to detrusor contraction. Urge incontinence often appears later in life. Frequency or nocturia, with low volume of urine voided, are signs of an overactive bladder that can occur with or without urge incontinence. An overactive bladder affects both genders and its prevalence rises with age, affecting 16.7% of those aged 40 in North America and Europe. An overactive bladder should be managed in the same manner as urge incontinence.

3. Overflow incontinence

4. Mixed incontinence: This is both stress and urge incontinence.

Risk factors
The most important risk factor is being female. Others are:

- Obesity
- Pregnancy and childbirth
- Obstruction - tumours in the pelvis or impacted stool
- Hysterectomy
- Neurological disease
- Cognitive impairment

Burden
In 2001 the annual estimated cost of dealing with bladder problems was £353.6 million. This included expenditure on pads. It is expected to be much higher now. Only a small proportion of the above amount was spent on drugs, the remainder being spent on secondary care and surgical treatment.

Bearing this in mind, it makes sense that the general practitioner (GP) is ideally placed to screen and manage these patients in primary care. It is not necessary to refer all patients to secondary care. With the ever-increasing pressure on GPs to reduce unnecessary referrals, there is now a scope for commissioning this service. However, management of an overactive bladder is not part of the Quality and Outcome Framework - could be one reason why GPs are not keen or enthusiastic.

Primary care management
History
A good history makes the initial diagnosis. Ask the woman whether she leaks on coughing, sneezing or exertion (stress) or whether she has an urgent need to pass urine before the leakage (urge). If she gives a history of both, she probably has mixed incontinence.

A history of nocturia or frequency with low urinary volume means an overactive bladder. This should be managed in the same way as urge incontinence. Previous surgery, or an obstetric and gynaecology history, may give further clues as to the type of incontinence.
Examination

- Abdominal examination - any palpable mass. This may be a palpable bladder, an ovarian cyst, or a large fibroid.
- Pelvic examination - Prolapse, enlarged uterus due to fibroid. Inspection of the pelvic floor may show visible stress incontinence on straining or coughing.
- Per-rectal (PR) examination if suspicion of constipation or faecal incontinence.

Investigations

- Routine urine check for sugar and protein.
- Mid-stream urine (MSU) to exclude urinary infection.
- Bladder diary for three days. Ask the woman to complete a diary of time and fluid volume - intake and output with episodes of urinary leakage and her activity at that time. The charts are available from pharmaceutical companies (keep the booklets in your examination room).
- National Institute for Health and Clinical Excellence (NICE) states that the use of cystometry, ambulatory urodynamics or video-urodynamics is not recommended before commencing non-surgical treatment.11

Treatment

Treatment depends on the type of incontinence. Pregnancy and childbirth are known risk factors and there is evidence that pelvic floor exercises during pregnancy reduce the risk. The exercises should be taught by the midwife during antenatal classes.

- For stress incontinence, the first line therapy is three months of pelvic floor exercises. These should be taught by the practice nurse. An instruction leaflet on its own is not enough. There is good evidence that advising about pelvic floor exercises is an appropriate treatment for women with persistent postpartum urinary incontinence.12
- For urge incontinence, bladder training is the first step. The patient should be taught to gradually increase the time between voids.
- Lifestyle advice in all with a body mass index (BMI) over 30kg/m².11
- Household modifications, mobility aids, downstairs toilets can help an elderly patient struggling to reach the toilet in time.
- Regular prompting of patients, by residential or nursing home staff, to visit the toilet can make a considerable difference rather than putting a pad on.
- Patients with an overactive bladder should be advised to reduce their caffeine and alcohol intake.
- Encourage the patient to drink two litres of fluid a day. Many women reduce their fluid intake hoping that this would help the symptom control, but less fluid intake can lead to concentrated urine which can result in bladder irritation.

- Antimuscarinic drugs such as oxybutynin can be used if bladder training is not successful. NICE recommends that immediate-release oxybutynin should be given as a first line.11 Transdermal oxybutynin can be given if oral oxybutynin is not tolerated. Compliance is often a problem because of side effects e.g. dry mouth, constipation, dry eyes, blurred vision, dizziness and cognitive impairment. Contraindications are acute angle glaucoma, myasthenia gravis, severe ulcerative colitis and gastrointestinal obstruction.
- NICE does not recommend duloxetine as a first or second line treatment for stress incontinence. It can be considered if there are persisting side effects with oxybutynin.
- Desmopressin or tricyclic antidepressants can be used in women with nocturia.
- The role of hormone replacement therapy (HRT) is debatable. Although oestrogens may improve atrophic vaginitis, there is no evidence that oestrogens by themselves are beneficial in incontinence.13
- Pads and catheters should only be issued on prescription if all treatment options have failed and the patient is waiting to see a specialist. These are coping aids.

Referral to secondary care

GPs should refer patients to a urogynaecologist or a surgeon who has experience in this field. Extra-contractual referrals are not favoured by Primary Care Trusts (PCTs) - try convincing your PCT!

Refer if there is:

- Pelvic mass
- Frank haematuria
- Symptomatic prolapse
- Suspected neurological disease
- Urogenital fistula
- Previous pelvic surgery
- Failure of conservative measures and anticholinergic drugs.

Useful patient information

www.continence-foundation.org.uk

Competing Interests
None declared

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REFERENCES

Online Interview with Dr David Fearnley

Dr David Fearnley, aged 41, is a Consultant Forensic Psychiatrist at Ashworth Hospital, a high secure psychiatric hospital in Merseyside, UK. He is also the Medical Director of Mersey Care NHS Trust, which is a large mental health and learning disability trust and one of three in England that have a high secure service. As Medical Director he is responsible for the performance of over 175 doctors, 50 pharmacists and has the lead responsibility for R&D and information governance. He is the College Special Advisor on Appraisal at the Royal College of Psychiatrists and has an interest in the development of management and leadership skills in doctors.

How long have you been working in your specialty?

Which aspect of your work do you find most satisfying?
I have always found clinical work satisfying, and particularly when it becomes linked to wider service changes. I think this is why I decided to take on management responsibilities in addition to my clinical work so that I could continue to work at this interface.

What achievements are you most proud of in your medical career?
I have been particularly pleased whenever I have passed my exams and I have been able to make progress in my career. Also, in 2009 I won the inaugural Royal College of Psychiatrists Psychiatrist of the Year award, largely because of my innovative approach to involving service users and carers in their treatment.

Which part of your job do you enjoy the least?
I find that I dislike having to read poorly written reports because of the limited time available to do other things!

What are your views about the current status of medical training in your country and what do you think needs to change?
In my view, medical training in England is of an exceptionally high standard although more emphasis will need to be brought into training around management and leadership.

How would you encourage more medical students into entering your specialty?
I think medical students should be exposed to mental health services as soon as possible, to see not only the clinical aspects but appreciate the organisational structures.

What qualities do you think a good trainee should possess?
I think trainees should develop a sense of respect for everybody they work with including the service users and carers, particularly when they feel under pressure. This is, in my opinion, the hallmark of somebody who will make a great clinician.

What is the most important advice you could offer to a new trainee?
I think new trainees should create habits in terms of acquiring new knowledge (particularly evidence based knowledge) so that they build up a sense of lifelong learning that extends beyond clinical examinations.
What qualities do you think a good trainer should possess?
A good trainer should be approachable and accessible, with a willingness to challenge the status quo but also show interest in the life of the trainee.

Do you think doctors are over-regulated compared with other professions?
The medical profession is entering the phase of increased regulation through revalidation. I think this is an acceptable position in view of the enormous privilege that practicing medicine offers and the need to assure the public that doctors are fit to practise.

Is there any aspect of current health policies in your country that are de-professionalising doctors? If yes what should be done to counter this trend?
I think doctors are becoming better at identifying certain tasks that others are equally capable of undertaking. I think doctors should be continually seeking out areas of healthcare that they alone have the skills, knowledge and attitude to be responsible for.

Which scientific paper/publication has influenced you the most?
I have found the work of the Cochrane Collaboration (rather than a single publication) to influence me considerably because it made me aware, through the work of the Archie Cochrane, the importance of standing back and comparing more than one study whenever possible.

What single area of medical research in your speciality should be given priority?
I think the overlap between mental illness and personality disorder is not understood well enough and yet is a major reason for patients remaining in secure care longer than perhaps they might need to in the future.

What is the most challenging area in your speciality that needs further development?
As a medical manager, I think that more needs to be done to encourage doctors to see management and leadership as part of their role as a professional and to gain competencies and confidence in these areas during their undergraduate and postgraduate training.

Which changes would substantially improve the quality of healthcare in your country?
Healthcare delivery in the UK is undergoing change following the publication of the coalition government’s White Paper in health, and it is encouraging clinicians, particularly GPs, to take part in commissioning. I think this, alongside a focus on better outcome measures is likely to improve the quality of healthcare.

Do you think doctors can make a valuable contribution to healthcare management? If so how?
I think doctors are in a unique position following years of clinical training to make decisions in terms of management and leadership. They should be able to transfer their ability to manage particular cases over time to managing projects and resources both in operational and strategic terms.

How has the political environment affected your work?
The NHS has an element of political oversight that does influence the work, particularly in the high secure service where public protection is a key factor.

What are your interests outside of work?
My time outside work is spent almost exclusively with my family.

If you were not a doctor, what would you do?
I would like to be a writer (although I doubt I have the skills to do so successfully!)