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Treating menstrual disorders

Menstrual disorders are commonly seen in general practice. According to an article in the *Medical Journal of Australia*,[1] in the UK each year 1 in 20 women consult their GPs about heavy menstrual bleeding.

Heavy menstrual bleeding is the most common complaint and in most cases has no identifiable pelvic or systemic cause and tends to be called dysfunctional uterine bleeding. Irregular dysfunctional uterine bleeding is generally associated with anovulation. Historically, women experiencing this problem were advised to have a hysterectomy. However, there is a range of new and effective interventions which can be offered for dysfunctional bleeding and other common causes of menstrual disorders such as fibroids and endometriosis.

The authors of this paper present an interesting approach of case studies comparing traditional approaches to common menstrual disorders with more recent developments.

Their first case is that of a 39-year-old overweight woman presenting with regular heavy menstrual bleeding. She had undergone laparoscopic sterilisation. Her uterus was normal, but the endometrium was irregular and thickened. The ovaries were normal. Traditional management might have included a trial of medical therapy, such as luteal-phase progestins. If this failed or was unacceptable, the next step was often an abdominal hysterectomy. Current management would include hysteroscopy or saline infusion sonography to rule out submucous fibroids or large polyps. Subsequent treatment options include insertion of a levonorgestrel-releasing intrauterine system or endometrial ablation. The woman opted for the latter after investigation revealed a normal uterine cavity.

Intrauterine administration of progestins results in higher endometrial concentrations of progestin compared with oral administration, but relatively little systemic absorption. The Mirena system has been shown to produce an 86% reduction in objectively measured menstrual blood loss at 3 months and a 97% reduction at 12 months. The effect continues over a 5-year period. The disadvantage is spotting, particularly during the early months of use.

Endometrial ablation in a minimally invasive therapy that preserves the uterus and is suitable for women who have completed childbearing. New techniques have been introduced recently which can be used in outpatients. Most women are satisfied with the reduction in bleeding, although an estimated 20% require further surgery and 10% eventually undergo hysterectomy. Amenorrhoea cannot be guaranteed and the surgery is not contraceptive. Subsequent pregnancy may be dangerous.

The second case was one of menorrhagia and fibroids in a 45-year-old woman. A trial of an anti-inflammatory drug had failed. Traditional management would probably have included an early resort to major abdominal surgery. A newer approach is clear identification of the position of the fibroids in relation to the endometrial cavity, followed by removal of the submucous fibroids using hysteroscopic techniques with possible endometrial resection.

Microwave endometrial ablation has also been shown to be effective for the management of heavy menstrual bleeding associated with fibroids, as has embolisation of symptomatic uterine fibroids as an alternative to surgical myomectomy.

These newer techniques have the potential to preserve or restore fertility, although this has not yet been fully established in trials.

The third case is of a 26-year-old woman with a history of dysmenorrhoea since menarche and perimenstrual pain on passing bowel motions. She has never been pregnant and, although sexually

active, does not use contraception. She was recently prescribed the oral contraceptive pill with only a small reduction in symptoms.

It should be recognised that these symptoms may be of endometriosis even in a young woman. A new approach would include transvaginal ultrasound examination to rule out ovarian abnormality, followed by laparoscopic surgery or medical therapy, depending on the reason for treatment (pain or infertility) and the severity of the symptoms.

In this case ultrasound revealed bilateral ovarian masses suggestive of endometriomas, which were confirmed on laparoscopy that showed extensive endometriosis. Laparoscopic removal of the endometriomas and excision of the deep endometriosis was performed, leading to a reduction in dysmenorrhoea and bowel symptoms. This was maintained at 6 months, although recurrence is likely.

Traditionally endometriosis has been seen as a condition of later reproductive life. However, it is increasingly acknowledged that endometriosis is also common in younger women.

Possible future developments in the management of menstrual disorders include improved understanding of the mechanisms of menstrual disturbance and the factors that control the establishment and progression of endometriosis. In the latter condition, specific therapies directed at molecular targets regulating the growth of ectopic endometrium are a possibility.

In addition, new roles for established therapies such as the levonorgestrel-releasing intrauterine system are still being explored, including the treatment of symptomatic endometriosis and endometrial hyperplasia.

1. Hickey M, *et al. Med J Aust* 2003; 178: 625 - 628.

HRT: to use or not to use?

Since July 2002, when the findings of the oestrogen plus progestin randomised controlled trial of the Women's Health Initiative (WHI) were released, many women (and their doctors) have been confused about whether or not to use hormone replacement therapy (HRT). A nice article in the *Medical Journal of Australia* attempts to relieve some of this confusion.[1]

As the authors point out, the WHI trial was stopped prematurely because the test statistic for invasive breast cancer exceeded the pre-determined stopping boundary and also because the trial index showed that risks exceeded benefits for users of HRT. Essentially the trial showed that this particular cohort of women using HRT had an increased risk of cardiovascular disease, thromboembolic disease and stroke and a reduced risk of various fractures and colorectal cancer. However, further analysis, taking into account the multiple endpoints required by such a trial, showed that in fact only the changes in the incidence of thromboembolic disease and total and other osteoporotic fracture were significant. The increase in breast cancer risk did not reach statistical significance irrespective of how it was analysed.

The result was that many women stopped HRT prematurely and prescriptions for HRT fell by 50%. Another planned trial looking at issues including quality of life and symptom relief in younger women was cancelled. This leaves many important questions unanswered.

The authors deal separately with issues of symptom relief, cardiovascular disease, cancer, stroke and venous thromboembolism and skeletal effects. About 600 000 Australian women use HRT, three-quarters of whom began HRT to relieve symptoms and improve quality of life. Although these symptoms are not life threatening, they do affect quality of life and HRT remains the most effective proven therapy for relief of those symptoms. Most women stay on HRT for 3 - 5 years and there have been no trials properly evaluating the risk-benefits of long-term use.

Cardiovascular disease is a different matter. Early observational studies suggested that oestrogen replacement therapy (ERT) was associated with a lower incidence of ischaemic heart disease. However, these findings, consistent across a number of observational studies, have not been supported by recent randomised controlled trials of oral continuous combined HRT. The generally accepted reason for the discrepancy is that women in the observational studies were younger, slimmer and included fewer smokers than those in the WHI study. Two secondary prevention trials of HRT and heart disease showed no reduction in heart disease or regression in atherosclerotic plaque in users of HRT or ERT. Currently HRT cannot be advocated for treatment or prevention of coronary artery disease.

The WHI press release highlighted the increased risk of breast cancer. However, the relative risk for invasive breast cancer in the WHI study did not reach statistical significance, although its inclusion in the weighted test statistic was significant for an overall adverse effect of HRT. The absolute increase in risk was 8 cases per 10 000 women per year. There was no difference in total cancer risk as HRT users had a decreased risk of

colorectal cancer. There is no evidence for an increase in breast cancer risk in women under the age of 50 using HRT. Trial findings suggest that long-term HRT leads to a small increase in breast cancer incidence in older women, and reduction in colorectal cancer incidence. However, long-term HRT does not appear to affect mortality.

The relationship between HRT and stroke remains uncertain. However, oral HRT causes a small but significant increase in venous thromboembolism and pulmonary embolism.

The WHI study found a non-significant reduction in hip and vertebral fracture rates and a significant reduction in rates of total fractures and other osteoporotic fractures. HRT still remains the first option for preventing fractures in symptomatic postmenopausal women, and long-term use of HRT to prevent osteoporosis may be appropriate but individual benefits should be weighed against the potential increase in breast cancer with long-term use.

1. Baber RJ, O'Hara JL, Boyle FM. *Med J Aust* 2003; 178: 630-633.

Prescribing habits and visits by drug representatives

A recent article in the *British Medical Journal* is particularly pertinent in the light of the new legislation being tabled in South Africa regarding doctors and drug companies.[1] Similar debates are carrying on in Britain, where drug companies are still allowed to provide all sorts of potential incentives to doctors, which may alter prescribing habits.

In an effort to see exactly what the effect is of frequent visits by drug industry representatives, Chris Watkins and colleagues sent a questionnaire to all general practitioners in 200 English practices selected from the bottom, middle and top fifths of prescribing costs.

They found that GPs who reported weekly contact with drug representatives were more likely to express views that led to unnecessary prescribing than those who reported less frequent contact.

When new drugs became available, GPs who saw drug representatives at least weekly were more likely, as their first course of action, to prescribe the drugs for a few patients and monitor the results. This conflicts with advice given by health commissioners to use published sources of evidence such as the *British National Formulary*.

GPs who see drug representatives most often tend to be those who are isolated from their colleagues and work in deprived areas.

The authors say that this study cannot identify the direction of causality. It may be that the drug representatives actually target GPs who are known to prescribe more. The authors suggest that more research is needed to help primary care trusts in the UK to adopt policies which encourage more cost-effective prescribing.

1. Watkins C, *et al. BMJ* 2003; 326: 1178-1179.

Patterns of functional decline at the end of life

Although there are clinical observations of differences in patterns of functional decline before dying, there is little empirical work to examine such patterns which could have implications for the organisation and delivery of care at the end of life.

This study sets out to determine if functional decline differed among 4 types of illness trajectories — sudden death, cancer death, death from organ failure and frailty. The authors used cohort analysis of data from 4 US regions in the prospective, longitudinal Established Populations for Epidemiological Studies of the Elderly (EPESE) study.

They found that the empirical trajectories of functional decline for the 4 categories differed markedly. Those who died suddenly were highly functional even in the last month before death. Those who died of cancer were highly functional early in their final year, but markedly more disabled 3 months before death. The frail were relatively more disabled in the final year and especially dependent during the last month.

These results are an important first step in getting beyond the 'one-size-fits-all' model for end-of-life care and research. The public image of dying and most scientific evidence for care at the end of life come from studies of those diagnosed with terminal illnesses. But this is not the experience facing most of those in the USA, only 23% of whom die of cancer. Most will die of acute complications of an otherwise chronic condition, usually without a discrete terminal illness.

End-of-life care must also serve those who become increasingly frail even without a life-threatening illness. These frail elderly persons may also die without a clear terminal period. Each group requires a different clinical approach and different types of health service.

Lunney JR, *et al. JAMA* 2003; 289: 2387-2392.