

Hysterectomy and bilateral oophorectomy for severe premenstrual syndrome

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BACKGROUND: Premenstrual syndrome (PMS) is a chronic, poorly understood psycho-endocrine disorder severely affecting 5% of women. Hormonal therapy which suppresses ovulation is the mainstay of medical treatment, but these interventions are rarely permanent. We evaluated the effectiveness and patient satisfaction with total abdominal hysterectomy/bilateral salpingo-oophorectomy (TAH/BSO) in PMS sufferers, and assessed the post-operative HRT continuation. **METHODS:** All women undergoing TAH/BSO for severe PMS between January 1994 and April 2000 were interviewed and responses recorded by structured questionnaire. **RESULTS:** Forty-seven women were interviewed. Median age was 42 years (interquartile range 39.8–46.6) at the time of surgery. They had suffered with PMS for a mean of 9.68 years (SD 6.8) and received treatment for a mean of 3.57 years (SD 2.0) prior to referral to a gynaecologist. Fifty-two percent were treated with estradiol patches and 48% with estradiol implants prior to TAH/BSO. Ninety-six percent of women were 'satisfied' or 'very satisfied' with TAH/BSO, and 93.6% declared complete resolution of their cyclical symptoms; 93.6% were continuing with HRT usually by implants of estradiol and testosterone for a mean duration of 3.8 years (SD 1.86) post-operatively. **CONCLUSION:** Despite few reports of TAH/BSO as a treatment for severe PMS, we have found surgery, coupled with appropriate HRT, to be an extremely effective and well-accepted permanent cure for PMS.

Key words: HRT/hysterectomy/oophorectomy/premenstrual syndrome

Introduction

Premenstrual syndrome (PMS) is a poorly understood psycho-endocrine condition, which has been reported to affect up to 95% of women (Pennington, 1957). Of these, the majority suffer only mild cyclical symptoms (Slade, 1984), but ~20–40% will suffer a significant impairment of their work, private and social activities (Coppin and Kessel, 1963). These symptoms are severe in 5% of women. It is the latter group who needs definitive treatment. Many display serious behavioural, psychiatric and physical problems during the luteal phase of the cycle leading up to menses.

For such a common condition, we know remarkably little, and to date no biological marker has been identified to aid in the diagnosis. It is related to the ovarian cycle as PMS does not occur prior to puberty, during pregnancy or after the menopause and these are the periods in a woman's life when there is no ovarian cyclicality. This was first recognized in 1979 with the observation that whatever the details of the hormone imbalance, and no doubt they vary from case to case, the ultimate cause of premenstrual tension must be a change in plasma hormone values from the time of ovulation. The symptoms for this common condition can usually be relieved by suppression of ovulation and ablating these cyclical hormone changes, whatever they are, and thus removing the cyclical symptoms of PMS (Studd, 1979). The mainstay

of treatment in our clinics is therefore aimed at the inhibition of the ovarian cycle either by moderately high-dose transdermal estrogens (Magos *et al.*, 1986a; Watson *et al.*, 1989) or by GnRH analogues (Leather *et al.*, 1999). The Mirena intrauterine system (IUS) (Schering Health, West Sussex) may also be used in order to avoid bleeding and the cyclical symptoms of cyclical oral progestogens.

When these medical treatments fail and a patient has completed her family, a hysterectomy may be a suitable course of action. Alternatively, women should be aware that pregnancy will offer a temporary cure. Awaiting the menopause is certainly effective, but may be impractical if it is many years away in young women. There are very few data on hysterectomy and bilateral oophorectomy for severe PMS. We identified two studies evaluating the effectiveness of this procedure. Casson *et al.* (1990) showed it to be effective in 14 patients for physical and psychological symptoms, as well as having a very favourable impact on lifestyle, after first suppressing ovarian steroidogenesis with danazol. Casper and Hearn (1990) also showed a dramatic improvement in mood, general affect, well-being, life satisfaction and overall quality of life in another small study of 14 women.

In this study, we report on the satisfaction rates of a larger cohort of patients who have had bilateral oophorectomy and hysterectomy for PMS in the last 6 years.

Materials and methods

The records of all patients undergoing a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH/BSO) in our units (Chelsea and Westminster and Lister Hospital) over the period between January 1, 1994 and May 31, 2000 were examined. Both NHS and private patients were considered. All patients who had their hysterectomies for the primary indication of PMS were telephoned and questioned according to a structured questionnaire. A total of 53 patients who fitted the criteria were identified; six were untraceable and therefore 47 were included in this study. The women who could not be contacted were sent two letters to their listed address, as well as two letters to their respective primary care physicians. All women who we contacted consented to cooperate with the questionnaire. We recorded patient satisfaction rates, continuation with HRT, problems experienced at surgery and co-existent pathology. All subjects were diagnosed on the basis of having cyclical physical and psychological symptoms associated with PMS. The aim of this particular study was to evaluate how women, with a clinical diagnosis of PMS, rated their health and quality of life following TAH/BSO.

Statistical analysis was performed using SPSS version 9.

Results

A total of 47 women who had a TAH/BSO for severe PMS were identified. A subtotal operation leaving the cervix had been performed at the patient's request in eight patients. The median age of the women was 42 years with an interquartile range (IQR) of between 39.8 and 46.6.

Figure 1 shows a breakdown of their respective ages. Seven women were younger than 40 years and two women were under 30 years of age. They had suffered with severe PMS for a mean of 9.68 years (SD 6.8) prior to referral and had received treatment for a mean of 3.7 years (SD 2.0) before attending our specialist PMS clinic. After referral, they received treatment in our specialist clinics for a further mean of 1.21 years (SD 0.4). This treatment was by transdermal estrogens in the form of estrogen implants (23 out of 47) or patches (24 out of 47) with cyclical progestogens each month for endometrial protection. Fourteen women (31%) had tried both patches and subsequently implants. Table I shows other treatments that were used.

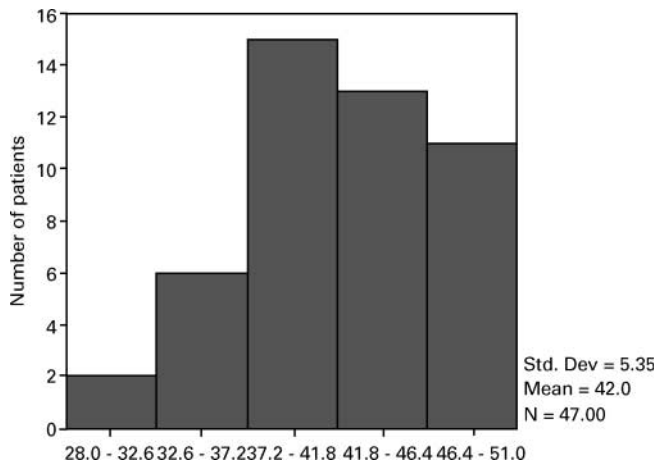


Figure 1. Age at hysterectomy.

Table I. Alternative therapies used

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| Zoladex with add-back therapy (<i>n</i> = 2) |
| Progestasert (<i>n</i> = 1) |
| Fluoxetine (<i>n</i> = 3) |
| Spironolactone (<i>n</i> = 1) |
| Synarel (<i>n</i> = 1) |

Table II. Contributing factors influencing the decision to operate

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| Heavy bleeding (<i>n</i> = 27) |
| Spotting (<i>n</i> = 6) |
| Progestogenic side effects (<i>n</i> = 8) |
| Felt unwell/fed up (<i>n</i> = 21) |
| Desire for TAH/BSO (<i>n</i> = 21) |
| Fibroids (<i>n</i> = 11) |
| Prolapse (<i>n</i> = 1) |
| Other (<i>n</i> = 9) |

A total of 17 women had additional pathology that aided the decision making to proceed to surgery although the principal indication remained PMS. These included fibroids, menorrhagia, endometrial hyperplasia and ovarian cysts (Table II).

Patients suffered from progestogenic side effects in 30% of cases. This led to a change in the type of progestogen, dose of progestogen, duration of usage or, in six cases, the insertion of the Mirena IUS.

Ten patients had no specialist treatment prior to surgery. One of these patients demanded surgery without medical treatment and the other nine women had suffered for a mean of 12.5 years prior to referral in spite of varied medical therapies, and expressed a desire for a surgical menopause plus hormone replacement.

In terms of satisfaction rates following surgery, patients could choose from the categories: 'very satisfied', 'satisfied', 'dissatisfied' and 'very dissatisfied'; 80.9% of women were 'very satisfied' and 14.5% were 'satisfied'. Only two women expressed dissatisfaction, with one woman falling into each category.

As a further yardstick to assess patients' satisfaction, we asked them whether they would recommend surgery to a friend, and 89.4% of our group stated that they would do so.

Six patients reported that they experienced some downside to the surgery. These included bowel problems (patient 'satisfied' but would not recommend surgery to a friend), breathing problems due to sarcoidosis (patient satisfied and would recommend surgery), weight gain (very satisfied and would recommend), pelvic haematoma (very satisfied and would recommend), bleeding problems with longer recovery than expected (very satisfied and would recommend) and urinary retention (very satisfied and would recommend).

Of all women who underwent surgery, 93.6% were still on HRT at the time of the interview: of these, 88.6% received estrogen and testosterone implants, 9.1% were using patches and one case (2.3%) was taking tablets. This implies continuation duration of 3.8 years (SD 1.86) as well as total relief of residual symptoms in 93.6% of these women.

Discussion

Our retrospective study shows that 96% of patients were satisfied with the results of surgery in the form of TAH/BSO for PMS. This demonstrates the effectiveness of TAH/BSO combined with effective hormone replacement for the treatment of severe intractable PMS, and the importance of careful patient selection. These women were attenders of specialist psycho-endocrine clinics, and were clinically evaluated by an expert in the field.

Despite the ever-mounting criticism of surgery, often fuelled in the media, the majority of women included in this study had complete resolution of their symptoms. The women in this study suffered, on average, for nearly 10 years before they were even referred to a specialist clinic and during this period and after referral they had received various unsatisfactory and ineffective treatments for nearly 6 years.

All women involved in our study had completed their families and had no wish to retain their reproductive potential. We would not advise a bilateral salpingo-oophorectomy, with or without hysterectomy, for someone who was contemplating future childbirth. In fact, we would often encourage a woman with PMS who was keen to get pregnant to do so, as, during pregnancy, they often feel extremely well with the associated high endogenous estrogen levels (Vashisht *et al.*, 2003). It is arguable that bilateral oophorectomy would be a simpler surgical method of treating severe PMS, leaving the uterus available if ovum donation is to be considered, but all patients were resolute in their view that they wanted no further pregnancies or periods and the necessary cyclical progestogen for endometrial protection would reproduce many of the cyclical symptoms of PMS.

Whilst we acknowledge that a hysterectomy may not be a necessity for the resolution of PMS symptoms, it facilitates estrogen replacement therapy (ERT) post-operatively. This is particularly important in this group of women as many are progestogen intolerant and, as we are rendering them menopausal at an early age, it is imperative that they are on a well-tolerated and effective form of ERT. Removing the uterus avoids the need for progestogens with their associated adverse effects, and avoids possible bleeding complications. Some have proposed that substances such as natural progesterone may not give rise to some of the adverse effects of synthetic progestogens, but unfortunately natural progesterone has not been shown to be convincingly protective against the effects of oestrogens on the endometrium (Vashisht *et al.*, 2003).

The most common treatments prior to referral included evening primrose oil (EPO), selective serotonin re-uptake inhibitors (SSRIs), calcium and magnesium, and vitamin B6. Many women had also previously tried complementary therapies for symptom relief. Although some positive findings have been reported, a comprehensive review concluded that the evidence is not compelling for any of these therapies (Stevinson and Ernst, 2001).

EPO is believed to work as it contains the polyunsaturated essential fatty acids linoleic and gamma-linolenic acids. These are precursors of prostaglandins PGE₁ and PGE₂.

A meta-analysis by Budeiri *et al.* (1996) did not show significant benefit of EPO in treating PMS. Vitamin B6 is an important cofactor in the synthesis of serotonin and dopamine. These neurotransmitters are also believed by some to be implicated in the pathogenesis of PMS. Wyatt *et al.* (1999) performed a systematic review and found that doses of 100 mg are likely to be of benefit in the treatment of PMS. Some evidence suggests that disturbances in calcium regulation may play a role in the pathogenesis of PMS (Penland and Johnson, 1993). A randomized, double-blind, placebo-controlled multicentre trial (Thys-Jacobs *et al.*, 1998) showed a major benefit in luteal phase symptoms using 1200 mg of calcium carbonate over three menstrual cycles.

It has been shown that women who suffer with PMS have lower levels of serotonin during the luteal phase of the menstrual cycle (Rapkin *et al.*, 1987). This has led to the introduction of SSRIs for sufferers of PMS. Many studies have proved efficacy, and a meta-analysis (Dimmock *et al.*, 2000) identified 29 trials of which 15 were randomized and controlled. Sertraline and fluoxetine were the most commonly used SSRIs, and fluoxetine was found to be the more effective. A recent Cochrane database review (Wyatt *et al.*, 2002) also has very good evidence to support the use of SSRIs in the management of severe PMS.

It is necessary to explore these other modes of treatment. A wide range of different treatment options have been described in the treatment of PMS (Chakmakjian, 1983; O'Brien, 1993), but these were the most commonly used in our cohort of women. By the time of referral, they were already desperate.

After referral, patients were treated with estradiol implants or patches, or GnRH analogues to achieve anovulation. Greenblatt *et al.* (1977) were the first to use estradiol implants in anovulatory doses for the purposes of contraception. Our unit used similar regimens for the specific treatment of severe PMS. In the majority of cases, estrogen treatment will be adequate, and work previously in this unit has shown success rates of 84% with estradiol implants (Magos *et al.*, 1986b) and patches (Watson *et al.*, 1989). This original placebo-controlled patch study used doses of 200 µg twice weekly with crossover after 3 months, but a further study showed 100 mg patches to be equally effective with fewer side effects (Smith *et al.*, 1995). Unfortunately, it is necessary to administer progestogens when using estradiol therapy, in order to protect the endometrium. This can cause severe PMS-like side effects in ~20% of women (Magos *et al.*, 1986b). In addition to progestogen intolerance, women may have other pathology including menorrhagia, fibroids, prolapse or abnormal smears. Even if none of these problems is severe enough to warrant a hysterectomy, it may become a valid option, in the presence of severe PMS. In our study, 17 women had additional pathology, as mentioned above, that aided the decision making to proceed to surgery. They were not, however, primary presenting complaints and were often found to be co-existent pathology at the time of surgery. It is not uncommon to encounter these problems in the general population, and was not the primary indication for surgery.

In the presence of intolerance to progestogens and menorrhagia, the Mirena IUS may be of benefit and possibly prevent some hysterectomies. A recently published study from our unit shows a decrease of up to 50% in the hysterectomy rate since the introduction of the Mirena IUS (Studd *et al.*, 2000) in 1996. Another method of anovulatory treatment would be to use GnRH analogues, using 'add-back' therapy in the form of sequential HRT or tibolone to prevent bone loss. This was shown by Leather *et al.* (1999) to be an effective treatment for severe PMS. For many women who are not receiving treatment by transdermal estrogens, it may be appropriate to use GnRH analogues prior to surgery to confirm an improvement or resolution of symptoms by short-term ovarian suppression.

The majority of women will benefit from one of the above treatment methods and it is in the small group who are refractory to treatment that a TAH/BSO should be offered. It must be remembered that in most cases, these women have been (unsuccessfully) treated for many years previously. There is no benefit if the correct treatment is withheld because of the fear of doing an unfashionable but effective operation. The key is to discuss options with the patient throughout the course of treatment as it is unacceptable for a patient to suffer for years with ineffective treatment only to find out later that she could have been cured by hysterectomy and bilateral oophorectomy. Correct patient selection is of course a necessity, and if there are any suspicions of other possible co-existent diagnoses, for example endogenous depression, then input from other health care professionals such as psychiatrists should be sought.

At a time when the hysterectomy rate is decreasing worldwide, it should be emphasized that surgery is not an easy option for the treatment of PMS but it can be an option in reserve for patients severely incapacitated with symptoms resistant to medical therapy.

It is essential that women continue with HRT following surgery to prevent the long-term effects of estrogen deficiency such as bone loss and urogenital atrophy. Implants of estrogens and testosterone would include replacement of ovarian androgens as well as estrogens. Thus the majority of women in this study received implants as both hormones can be administered simultaneously and implants are still the only licensed method of administering testosterone in the UK. At the time of our study, continuation rates were excellent and other work from our unit has shown continuation rates of 85% at 10 years (Domoney *et al.*, 1999).

Prospective diagnostic criteria were not used in this study. Although such prospective evaluations using Trigg's trend analysis have been used in randomized controlled trials from this unit, in this report the clinical diagnosis was made from the patients' history by an expert in mood and hormonal disorders. For the future, a prospective study looking at changes after surgery in specific symptoms measured by prospective diaries will be performed. We therefore conclude that in a selected group of women, TAH/BSO, coupled with effective HRT, is an extremely effective and well-accepted permanent cure for the symptoms of PMS.

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