Chronic pelvic pain and menorrhagia: Assessing treatment effectiveness
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Chapter 1

Introduction
Chapter 1

Chronic pelvic pain

Chronic pelvic pain is described in many ways. The most frequently cited definition is cyclical or non-cyclical pain in the lower abdomen or pelvis, of at least six months’ duration, occurring continuously or intermittently, that causes functional disability or limits activities of daily living. Chronic pelvic pain (CPP) has a major impact on health-related quality of life, work attendance and productivity, and health care utilization, accounting for 40% of referrals for diagnostic laparoscopy, and is an important contributor to health care expenditure.

Chronic pelvic pain can be a symptom and also a syndrome in its own right when underlying pathology has been excluded, which may be termed idiopathic CPP. It may encompass dyspareunia, dyschesia, dysuria, or dysmenorrhoea, but it can also be independent of these symptoms. There are several underlying aetiological factors which may overlap, including endometriosis, chronic pelvic inflammatory infection, adhesions, irritable bowel syndrome, interstitial cystitis, and pelvic congestion syndrome.

Analgesics are often the first line of management, and women often try to manage their pain with over the counter painkillers before consulting with their general practitioner. Pharmaceutical approaches considered first include the combined oral contraceptive pill, progestogens or gonadotropin-releasing hormone agonists, yet there are very few randomised data to support their use in idiopathic chronic pelvic pain. Methoxyprogesterone acetate provides more improvement in pain scores than placebo at 3 months (OR: 2.64, 95%CI 1.33 to 5.25; p=0.005, n=146) which is sustained to 6 months whilst on treatment. No improvement in pain scores was seen in a further small trial of the selective serotonin uptake inhibitor sertraline compared to placebo. The combined oral contraceptive pill is frequently prescribed. Only 20-25% of patients respond to conservative treatment. Neuropathic pain treatments are the focus of ongoing investigations following initial promising results, although there is no evidence to suggest CPP is neuropathic in origin.

Given that the symptoms experienced are chronic, varied and non-specific, a differential diagnosis in chronic pelvic pain can be hard to establish and women often present to health care providers repeatedly. This wastes both the patients’ time and NHS resources. The diagnosis of endometriosis may be delayed by over 8 years after first presentation with CPP symptoms, potentially demoralising the patient and missing the opportunity to improve their life quality through early effective treatment, and may provoke women to seek having a hysterectomy with
its inherent risks and consequences. The Royal College of Obstetricians and Gynaecologists guidelines provide a number of suggested initial investigations, including history, microbiological screening and vaginal examination, all with weak evidence for utility.\textsuperscript{12} If no cause of the pain is found, gynaecologist frequently perform a diagnostic laparoscopy.

As diagnoses emerge through careful history and examination and directed investigation, so do treatment strategies. These should be tailored to the needs of individual patients as, whatever the cause, chronic symptoms need long term management. Surgical treatments tend to focus on the organic causes of pelvic pain. Laparoscopic vaporisation or excision of endometriotic lesions is effective in reducing pain.\textsuperscript{11} Division of intraperitoneal adhesions is of unclear benefit.\textsuperscript{7} Interruption of the Lee-Frankenhauser sensory nerve plexuses by laparoscopic uterosacral nerve ablation was thought to alleviate pain, based on mainly observational data.\textsuperscript{14}

A multidisciplinary approach has been advocated\textsuperscript{15} and fits with the biopsychosocial model of pain. Counselling, psychotherapy and attempts to provide reassurance using laparoscopy are employed. Whilst less invasive, psychological approaches are time consuming and may not be acceptable to all women. Trials of cognitive behavioural therapy have been favourable in other chronic pain conditions, but evidence for psychological interventions within chronic pelvic pain is lacking.

**Heavy menstrual bleeding**

Heavy menstrual bleeding is another common problem that can significantly impact on women’s lives, and burden individuals and healthcare systems.\textsuperscript{16} With an annual community prevalence of 25%,\textsuperscript{16} HMB accounts for 20% of gynecologist consultations in the UK,\textsuperscript{18} over 5% of women aged 30-49 consult general practitioners each year in the UK with this problem.\textsuperscript{18} Rates of surgical procedures for HMB are 14.3 per 10,000 in the UK.\textsuperscript{19}

There is discordance between women’s subjective experience of menstruation, actual menstrual blood loss,\textsuperscript{20} and clinicians’ assessment.\textsuperscript{21} Only about half of women presenting to health providers with heavy menstrual bleeding have blood loss greater than the traditional clinical threshold of 80 ml per cycle considered as heavy menstruation.\textsuperscript{20} A shift in emphasis away from menstrual blood loss to a more patient-centered definition, to define heavy menstrual bleeding as that significant as to interfere with women’s physical, emotional and social life, is now advocated, as are the use of patient reported outcomes.\textsuperscript{22}
A range of non-hormonal and hormonal medical treatments are available as first line therapy for women presenting with heavy menstrual bleeding in primary care. For over a decade, the levonorgestrel-releasing intrauterine system (LNG-IUS; [Mirena®]) has been available for heavy menstrual bleeding. Although developed as a contraceptive, it also reduces menstrual blood loss. In 2007, UK guidance introduced the option of LNG-IUS for heavy menstrual bleeding based on limited evidence.

Hysterectomy offers a definitive treatment for heavy menstrual bleeding and guarantees amenorrhea, but it is particularly invasive and carries significant morbidity. It is also expensive – due to the need for general anaesthesia, prolonged hospital stay and delayed recovery.

Endometrial ablative techniques aimed at destruction of the functionally active endometrium, along with some of the underlying myometrium, offer a conservative surgical alternative. The first generation ablative techniques, including endometrial laser ablation, transcervical resection of the endometrium and rollerball endometrial ablation, were all endoscopic procedures. Although they do not guarantee amenorrhea, their effectiveness in comparison with hysterectomy has been demonstrated in a number of randomised controlled trials. However, first generation ablative techniques carry some risks including uterine perforation, cervical laceration, false passage creation, haemorrhage, sepsis and bowel injury.

Second generation ablative techniques represent simpler, quicker and potentially more efficient options of treating heavy menstrual bleeding, which require less skill on the part of the operator. Second generation techniques employ fluid filled thermal balloons, high temperature saline irrigation, 3D bipolar radiofrequency or microwave energy, freezing or photodynamic therapy to cause endometrial destruction. Complications associated with second generation techniques include equipment failure, uterine infection, perforation, visceral burn, bleeding and cyclical pain.

These procedures appear to be as effective as first generation ablative techniques in a limited number of randomised trials and some have the added benefit of being performed under local anaesthetic. However, some women treated by endometrial ablation will eventually require repeat ablation or hysterectomy. A proportion of women will also develop subsequent problems such as post surgical adhesions and pelvic floor dysfunction which may lead to further hospital treatment and surgery.
Aims of the thesis

To provide an overview of the treatments for chronic pelvic pain and of the interventions for heavy menstrual bleeding.

Specific questions:

- What is the effectiveness of LUNA for chronic pelvic pain?
- Are there any subgroups of women who may benefit from LUNA?
- What is the current evidence for psychological treatments for chronic pelvic pain?
- What is the relative effectiveness of hysterectomy, endometrial destruction techniques and the levonorgestrel releasing intra-uterine system for heavy menstrual bleeding?
- What is the relative effectiveness of different second generation endometrial ablation techniques?

Outline of the thesis

Part One: Chronic Pelvic Pain

Chapter 2 reviews the current thinking and evidence base for diagnostic tests and medical, surgical and psychological therapies.

Chapter 3 illustrates the situation regarding use of laparoscopic uterosacral nerve ablation (LUNA) in the UK, presenting the results of a survey of clinicians.

Chapter 4 describes the protocol for the LUNA randomised controlled trial, detailing the outcomes, analytical methods and practicalities of the trial.

Chapter 5 evaluates the clinical effectiveness of LUNA in alleviating chronic pelvic pain in a large randomised controlled trial.

Chapter 6 describes the protocol for an individual patient data meta-analysis of five randomised LUNA trials.

Chapter 7 presents results from the individual patient data meta-analysis, whereupon data from are subject to further subgroup analyses.
Chapter 8 contains a systematic review of the few psychological treatments for chronic pelvic pain.

Part Two: Heavy Menstrual Bleeding

Chapter 9 describes the results of an individual patient data meta-analysis of the clinical effectiveness of hysterectomy, endometrial destruction and the levonorgestrel releasing intra-uterine system.

Chapter 10 extends the previous review to by undertaking an indirect comparison of the relative effectiveness of the different types of second generation endometrial destruction techniques.

Chapter 11 examines the measurement properties of a patient reported questionnaire assessing the impact of heavy menstrual bleeding on women’s lives.

Chapter 12 summarises the previous chapters and describes the results from the studies in this thesis in the context of the current literature. Unanswered questions, implications for clinical practice and directions for future research are discussed and the main conclusions are described.
References


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