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Review

Use of GnRH analogues pre-operatively for hysteroscopic resection of submucous fibroids: a systematic review and meta-analysis

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ABSTRACT

GnRH analogues are commonly used before hysteroscopic myomectomy to make surgery easier and safer, but they are expensive, have potential side effects and lack a robust evidence base to support this practice. We undertook a systematic review of the literature to determine whether, in women with submucous fibroids, pre-operative GnRH analogues were more effective than placebo/no treatment in terms of symptom relief, complications and ease of surgery. The outcomes were patient-reported relief of symptoms, complete resection of the fibroids, operative time and complications. Meta-analysis was performed where appropriate. Two trials including 86 women were identified.

The assessment of symptom relief differed in the two trials: hence it was not possible to combine these data. The relative risk for completion of surgery and mean differences (95% confidence intervals) for operating time and fluid deficit were [0.94 (0.68–1.31); −5.34 min, (−7.55 min to −3.12 min) and −176.2 ml, (−281.05 ml to −71.5 ml)] respectively. Our results suggest that GnRHa may improve some outcomes but there is insufficient evidence to support their routine use prior to hysteroscopic resection of submucous fibroids. More randomised trials are needed to inform definitive conclusions.

Contents

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Introduction

Uterine fibroids are the commonest benign tumours of the female reproductive tract [1]. They are classified according to their anatomic location into subserosal, intramural and submucosal types [2]. Most are asymptomatic and are detected during clinical examination or following ultrasound but occasionally they can present clinically with heavy menstrual bleeding [2,3].

Submucous fibroids distort the endometrial cavity causing heavy and/or irregular bleeding while longer pedunculated submucous fibroids can cause severe dysmenorrhoea [4]. In addition, they have been associated with recurrent miscarriage and infertility [3,5,6].

Hysteroscopic resection of submucous fibroids is an effective therapeutic intervention which, in selected cases, can result in complete symptomatic relief [5,7,8]. Surgery is less technically demanding when fibroids are smaller in size and complete resection of fibroids can be achieved in a single sitting. Resection of larger submucous fibroids is associated with increased blood loss, longer operative time, fluid overload and the need for multiple operations [5,9].

Gonadotropin-releasing hormone (GnRH) analogues are commonly used pre-operatively before myomectomy so as to reduce the size of a fibroid in order to make the surgery easier and safer [6,10,11]. However, GnRH analogues are expensive and have unpleasant side effects, such as menopausal symptoms due to estrogen deprivation [6].

Growth of fibroid tissue is known to be oestrogen-dependent and continuous administration of GnRH analogues can cause temporary suppression of the hypothalamo-pituitary-ovarian axis leading to a hypoestrogenic state [12]. This leads to decreased vascularity, resulting in shrinkage of the fibroid. It is believed that this reduction in size could lead to protrusion of the intramural component of a submucous fibroid, thereby increasing the possibility of complete resection with a corresponding reduction in the chance of recurrence [5,13].

Although GnRH analogues have been used pre-operatively for hysteroscopic resection of fibroids for a long time, robust evidence to support this practice has been weak [14–16]. Observational studies by Perino et al. [14] and Donnez et al. [17] reported that treatment with a GnRH agonist prior to hysteroscopic resection of fibroids was useful, while Campo et al. [18] found that pre-operative administration of GnRH analogues prolonged surgical time. A Cochrane review evaluated the role of pre-operative GnRH analogues prior to myomectomy and hysterectomy [19]. The included trials were mainly focused on the effectiveness of GnRH in providing intra-operative/post-operative benefits at myomectomy and hysterectomy via a laparoscopic versus open approach. This review did not specifically evaluate the role of GnRH prior to hysteroscopic resection of submucous fibroid.

We undertook a systematic review of the literature to determine whether, in women with submucous fibroids, pre-operative GnRH analogues were more effective than placebo/no treatment prior to hysteroscopic resection of these fibroids in terms of symptomatic relief, ability to compete surgery, operating time, complications and technical difficulties.

Materials and methods

Eligibility criteria

We planned to include randomised controlled trials (RCTs) and included women who were undergoing hysteroscopic resection of submucous fibroids. In the treatment arm, women received GnRH analogues within 2 months prior to hysteroscopic resection. For comparison, we examined hysteroscopic resection of such fibroids, without any pre-operative GnRH analogue administration, placebo or any other medical intervention.

Outcome measures

The primary outcome was relief of menstrual symptoms. Secondary outcomes included complete resection of the fibroid, operating time, complications {fluid deficit ($>$1.5 l), excessive intra-operative bleeding, uterine perforation, bowel injury}, recurrence of submucous fibroid, operative difficulty, surgeon's satisfaction, side effects of pre-medication and cost.

Search strategy

We searched all published and unpublished randomised controlled trials (RCTs) of pre-operative GnRH analogues versus no pre-operative GnRH analogues before hysteroscopic resection of fibroids. We restricted our search to papers published in the English language.

We searched the Medline, EMBASE, DARE and CENTRAL data bases (from 1980 to July 2012). In addition, we searched the ongoing clinical trial registries, which included clinical trials.gov (http://www.clinicaltrials.gov/) and the International Clinical Trial Registry Platform. Cross-references identified during the search were also selected if they were not included initially. We used the following terms as either free text terms or MeSH terms and in combination between them: GnRH-a, GnRH, submucous fibroid, fibroid, hysteroscopy, pre-treatment and hysteroscopic resection. In cases where additional information was needed, we contacted the corresponding author of the trial. Relevant studies which fulfilled the inclusion criteria were identified and print-outs of retrieved document were taken.

Data collection and extraction

Assessment of all papers was performed independently and in a standardised manner by two of the authors (MK and TK). Disagreements between these authors were resolved by mutual discussion.