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Advancements In Non-Surgical Management Of Uterine Fibroids: Role Of Gnrh Antagonists And Uterine Artery Embolisation

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ABSTRACT

Uterine fibroids have been treated mainly with resection via hysteroscopy, laparoscopy, or laparotomy, or with hysterectomy. Transcatheter embolisation of the uterine arteries (UAE) has been used to treat obstetric bleeding complications, bleeding from pelvic tumours, and, recently, uterine fibroids. The potential advantages are preservation of the uterus with a minimally invasive technique, avoidance of surgery and surgical complications, and reduced costs. Published reports indicate improvement of bleeding problems in 85-95% of patients within 3-9 months of the procedure and reduction of uterine or fibroid volume by 60-80%. Overall, 60-80% of patients are satisfied with the results of UAE and would recommend the procedure. Many uneventful pregnancies subsequent to UAE have been reported. Diffuse abdominal pain of varying intensity and duration, slight fever, leucocytosis, and signs of peritoneal irritation are common after embolisation. Endometritis, myometrial necrosis (2%), and two deaths (sepsis, pulmonary embolism) have been reported among the 7000 published procedures. The effects of the UAE on ovarian function are unclear. A registration of long-term results, recurrence rates, side effects, and complications would help physicians counsel patients about the role of UAE in the treatment of uterine fibroids.

KEYWORDS: Role of GnRH Antagonists, Uterine Artery Embolism.

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INTRODUCTION

Uterine fibroids constitute the most common benign tumours within the female reproductive system, with an estimated prevalence rate varying between 20% and 77% in premenopausal women. Their aetiology is associated with multiple factors, including genetic predisposition, family history, nulliparity, and obesity, all of which may enhance the probability of fibroid development. The clinical symptoms related to uterine fibroids include menorrhagia (excessive menstrual bleeding), increased urinary frequency, gastrointestinal disturbances, a sensation of pelvic heaviness, and dyspareunia (painful sexual intercourse).There is a significant and growing interest in non-invasive therapeutic approaches for managing symptomatic fibroids, especially among women who aim to preserve their uterine structure. Non-surgical options, including uterine artery embolisation (UAE), offer numerous advantages over traditional surgical procedures such as hysterectomy, which encompass lower complication rates, improved patient satisfaction, and the ability to address individuals with concurrent medical conditions while protecting their reproductive health.(1–3).

OVERVIEW

Uterine fibroids, sometimes called leiomyomas, are common benign tumours in women of reproductive age that often cause excessive menstrual bleeding, pelvic pain, and infertility. In the past, surgical procedures such as myomectomy or hysterectomy were the main options. Recent advances in non-surgical treatment provide effective alternatives that preserve fertility and the uterus. Two gonadotropin-releasing hormone (GnRH) antagonists, elagolix and relugolix, inhibit the synthesis of estrogen, which in turn shrinks the fibroid and eases its symptoms. These oral drugs offer rapid, reversible, and convenient therapy and are often used temporarily or before surgery. Uterine artery embolisation (UAE) is a minimally invasive procedure that shrinks fibroids and reduces their symptoms by stopping blood supply to them. UAE preserves the uterus and offers a faster recovery than surgery. The combination of GnRH and UAE antagonists represents a significant breakthrough in patient-centred fibroid therapy.(4–6).

Role of GnRH Antagonists

GnRH antagonists are a novel therapeutic strategy for the non-surgical management of uterine fibroids. They work by quickly reducing endogenous GnRH, which in turn reduces dose-dependent levels of progesterone and oestradiol. These hormone levels decrease, which reduces the bleeding associated with uterine fibroids. Add-back therapy, which uses hormones like progesterone and estrogen, helps reduce menopausal adverse effects. When used to treat symptomatic fibroids, GnRH antagonists have shown

promising results in clinical trials. (7,8). Caution is advised when introducing new treatment options, with an emphasis on the need for audit and data collection techniques to track adverse effects and evaluate efficacy.

GnRH antagonists are a novel treatment option for premenopausal women with uterine fibroids that does not involve surgery. Their effectiveness in lowering uterine haemorrhage and fibroid volume has been assessed. Eleven randomised clinical studies totalling 4164 participants were included in the meta-analysis, showing that GnRH antagonists produced better outcomes than placebos. A considerable improvement was shown by the relative risk of 5.09 for the control of uterine haemorrhage. Their efficacy in reducing size was demonstrated by the mean difference of -27.36 for the percentage decrease in fibroid volume. In addition, compared to other therapies, GnRH antagonists produced a smaller loss of bone density. In general, GnRH antagonists are thought to be a good non-surgical option for treating uterine fibroids, especially when it comes to symptom management and fibroid size reduction. (8)

The invention offers compositions and techniques for administering a gonadotropin-releasing hormone (GnRH) antagonist to a patient, such as a human patient with uterine fibroids, in order to decrease the volume of menstrual blood loss. Suitable GnRH antagonists that work well with the compositions and techniques outlined here include derivatives of thieno[3,4d]pyrimidines, including3-[2-fluoro-5-(2,3-difluoro-6-methoxybenzyloxy)-4-methoxyphenyI].5,4-dioxo-1,2,3,4-tetrahydrothieno[3,4d]pyrimidine and its choline salt.

The most prevalent type of benign gynecological tumors, uterine leiomyomas, affect 20–40% of women at some point in their lives. These people can be treated with a variety of therapy approaches. In recent years, there has been a significant increase in the use of medicinal treatment for myomas, especially for women who would decline, put off, or are not candidates for surgery. The clinical study of gonadotropin-releasing hormone (GnRH) antagonists, often known as GnRH-ants, has surfaced in recent yearsThis family of medications immediately stops the release of gonadotropins and sex hormones by acting as a pure competitive antagonism on the pituitary gland's GnRH receptor. Relugolix is an oral nonpeptide GnRH-ant that was just granted a marketing authorisation in Japan to treat uterine myoma symptoms. In the United States and Europe, a number of phase III clinical trials are presently being conducted to assess this chemical in this context. (9,10)

UTERINE ARTERY EMBOLISM

Introduction

A minimally invasive procedure called uterine artery embolisation (UAE) is used to treat a number of uterine-related disorders. It is mostly used to treat uterine fibroids, which are tumours that arise from the smooth muscle of the uterus and can cause severe symptoms of bleeding and pressure in women. Resolving arteriovenous malformations with adenomyosis. - Acting as a life-saving surgery for high-risk individuals with placental anomalies or for postpartum hemorrhage. By cutting off the blood flow to the afflicted areas, UAE successfully lessens the symptoms of various illnesses. (11)

Definition of UAE

Uterine artery embolization (UAE) is characterized as a minimally invasive procedural intervention.
This technique is employed in the management of disorders including uterine fibroids, adenomyosis, and arteriovenous malformations.

UAE has the potential to significantly mitigate pressure and hemorrhagic manifestations associated with fibroids.
Furthermore, the procedure is deemed critical for the management of postpartum hemorrhage or for patients at elevated risk due to placental anomalies. (12)

Historical Background and Development of Uterine Artery Embolisation (UAE)

The concept of uterine artery embolisation (UAE) originated from the groundbreaking methodologies in interventional radiology developed to address uterine hemorrhage. During the 1970s, this procedure was initially introduced as a vital intervention for the treatment of acute postpartum hemorrhage, pelvic trauma, and bleeding associated with gynecological malignancies. These innovative interventions demonstrated that the precise occlusion of the uterine arteries could effectively manage hemorrhage while minimizing adverse impacts on the integrity of the uterine structure.

Aiming mainly to reduce intraoperative blood loss, embolization was first used in gynecological surgery in the 1980s as a preparatory procedure before surgical procedures like hysterectomy or myomectomy. Through these incidental uses, researchers discovered that fibroids shrank in size when their vascular supply was cut off, leading them to consider embolization as a possible main treatment option.

The procedure's safety and effectiveness were significantly increased starting in the 2000s by technology advancements, such as improved imaging modalities, advanced catheter systems, and more focused embolic agents. The establishment of detailed post-procedural care standards and standardized patient selection criteria made UAE a reliable and generally accepted therapy option. Nowadays, uterine artery embolization is thought to be a minimally invasive procedure that preserves the uterus while treating symptomatic fibroids and other uterine conditions. Its evolution from a vital life-saving treatment for severe hemorrhage to a common therapeutic approach reflects significant progress in interventional radiology and the treatment of women's reproductive health. (13).

PROCEDURE

Postpartum hemorrhage and uterine fibroids are the main indications for uterine artery embolization (UAE), a minimally invasive technique guided by fluoroscopy and carried out under conscious sedation and local anesthesia. As directed by digital subtraction angiography (DSA) to define anatomy and rule out collateral branches to the bladder, ovaries, or vagina, the procedure starts with vascular access through the femoral artery (or radial artery in some centers) using the Seldinger technique. Next, a selective catheter is advanced into the anterior division of the internal iliac artery, and finally a microcatheter is advanced into the uterine artery.

After achieving super-selective catheterization of fibroid-feeding branches to minimize non-target embolization, embolic agents—such as gel foam, tris-acryl gelatin microspheres, or polyvinyl alcohol particles—are injected gradually under fluoroscopic monitoring to obstruct the uterine blood supply, causing ischemia and fibroid shrinkage. Following embolization, occlusion is confirmed by repeat angiography, and bilateral blockage is ensured by repeating the procedure on the contralateral side. (15)

After the sheath and catheters are removed, a sterile dressing is put on and hemostasis is maintained using closure tools or manual compression. Usually lasting 60 to 90 minutes, the surgery involves ongoing intraoperative monitoring of sedative levels, discomfort, and vital signs. The patient is then monitored for four to six hours as they recuperate in order to evaluate the puncture site and treat any symptoms. UAE is a safe and efficient substitute for surgery in the treatment of uterine fibroids and hemorrhage, with the majority of patients becoming mobile within a few hours and being released within 24 to 72 hours. (16).

CONCLUSION

While preserving the ability to procreate, non-surgical treatment of uterine fibroids offers viable substitutes for surgery. By blocking estrogen and progesterone, GnRH antagonists reduce the growth of fibroids and lessen related symptoms; these effects are safe and reversible. By blocking the arterial supply to fibroids, uterine artery embolization (UAE), a minimally invasive procedure, reduces symptoms and speeds up recovery.

In order to preserve reproductive potential, non-surgical treatment of uterine fibroids offers viable substitutes for surgery. Through the inhibition of estrogen and progesterone, GnRH antagonists reduce the size of fibroids and alleviate related symptoms, with reversible and safe results. A minimally invasive procedure called uterine artery embolization (UAE) blocks the arterial supply to fibroids, reducing discomfort and hastening recovery.

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