J Obstet Gynecol India Vol. 55, No. 5 : September/October 2005 Pg 410-414

REVIEW ARTICLE

The Journal of Obstetrics and Gynecology of India

Embolisation in fibroids

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Uterine artery embolization (UAE) is one of the multiple modalities in the armamentarium available for the management of uterine fibroids. It was first described in English literature by Ravina and colleagues in 1995 [1]. They used the procedure in 16 patients. In the beginning they offered embolization as palliative management in women who presented with high operative risks i.e. thromboembolic accidents, severe obesity, diabetes, and AIDS. Subsequently, it was offered as an alternative to surgery in women who did not want to become pregnant and in whom a major surgical procedure of myomectomy or hysterectomy was indicated. With a mean follow-up of 20 months (range 11-48), symptoms resolved in 11 patients while three patients improved partially.Two failures required surgery. The main consequence was pelvic pain which was seen in 14 of 16 patients.

Today, UAE is offered for fibroids either as an alternative to surgery or as a pre-operative measure when the surgeon anticipates a difficult myomectomy or hysterectomy. It can be especially useful in women who are at high risk for surgery. Since May 2001, at the King Edward Memorial Hospital, Mumbai, 48 patients have undergone UAE for fibroids, either as a definitive procedure (34 patients) or as a pre-operative measure (14 patients).

Patients who desire to conserve their uteri have the option of medical management by GnRH analogues, myomectomy or embolization. GnRH analogues are useful in reducing the size and vascularity of the uterus in a patient who is to undergo surgery. Myomectomy carries the risk of recurrence. In a series of 622 patients who underwent myomectomy between 1970 and 1984, the cumulative 10 year recurrence rate was 27% [2]. Women who gave birth to a child had a 10 year recurrence rate of 16% as compared to 28% in those who did not. The risk of recurrence was 1.2 in those with two or three myomas removed and 2.1 in those with four myomas removed as compared to that in those from whom a single fibroid was removed.

Paper received on 10/06/2005 ; accepted on 04/07/2005

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Procedure

The procedure is generally done under sedation and local anesthesia, though epidural analgesia may also be utilized. Peri-procedure prophylactic antibiotics are given. The femoral arterial approach is utilised to perform a digital subtraction arteriography of the pelvis by using a 5-French catheter placed above the aortic bifurcation. Contralateral internal iliac arteriography and selective arteriography of the anterior division of the internal iliac artery is performed so as to analyze the uterine artery with a 5-F cobra shaped catheter and with a hydrophilic polymer coated 0.032 inch guide wire. The vessel is embolized with polyvinyl alcohol particles, gel foam or steel coils. The embolizing agent is mixed with saline and contrast medium, and is introduced under fluoroscopic control. Embolizing particles are injected in free-flow till the vessel is completely occluded. This is indicated by complete cessation of forward flow or reflux of contrast material. Selective catheterisation of the feeder vessels is done with the help of microcatheters. The ipsilateral internal iliac artery is then cannulated and the artery embolized in a similar fashion. Occasionally, bilateral femoral punctures are required because the anatomy precludes ipsilateral uterine artery cannulation.

Embolising agents

Polyvinyl alcohol is a semi-permanent occlusive agent with a limited potential for recanalization.The smaller the particle size, the more complete the occlusion of vessels but this is also associated with a higher incidence of post-

procedure side effects. Gelatin sponge has the advantage of being cheap, safe and easily available. It can get completely absorbed by the body within approximately 1 month. Thus menstruation and fertility can be preserved, though the fibroid undergoes infarction. Steel coils induce intra-vascular thrombosis and cause permanent vascular occlusion. They have thrombogenic material such as wool or dacron attached to them. The coils are manipulated into position by the interventional radiologist. Coils are also made from materials other than steel, such as platinum or tungsten.

Mechanism of action

The women are followed up pre- and post-procedure both clinically and by using imaging technics. Sonography, computerized tomography (CT) and magnetic resonance imaging (MRI) have all been utilized. de Souza and Williams [3] did MRI imaging of 11 patients with 45 leiomyomas before and within 30 minutes of the completion of embolization and 1 and 4 months after the procedure. Leiomyomas were generally hyperintense on T2 weighted image, compared with myometrium, although 11 were isointense or hyperintense. After bilateral embolization the myometrium and leiomyoma demonstrated differential perfusion responses. Immediately following the procedure, there was a dramatic reduction in the overall uterine perfusion. However, while perfusion of the myometrium reduced considerably, it was still retained to some extent. Perfusion of the leiomyoma however, virtually stopped. After 1 and 4 months, perfusion of the myometrium recovered to normal levels while leiomyoma perfusion remained poor.

Outcomes

Generally, bilateral embolization is successful in 95 -98 % of women [4,5] and is shown to have 88-90% success rates in treating fibroid related symptoms [4-6]. At KEM Hospital, two patients required a second session to ensure a successful procedure. In Pelage et al's [4] study of 80 women who underwent super selective embolization with polyvinyl alcohol particles, menorrhagia disappeared in 72 patients. Katsumori et al [7] utilized gelatin sponge particles alone to achieve marked or moderate improvement in menorrhagia in 41 of 42 patients (98%) at 4 months and in 20 of 20 (100%) patients 1 year after embolization.

In Vashisht et al's [8] series of 21 patients, the fibroid volume reduced from 310 mL (range 140-457) to 209 mL (range 57-288) after 2 months and 77 mL (range 41-164) after 6 months. Worthington-Kirsch et al [5] reported a mean reduction of 46% in uterine volume over 3 months and Katsumori et al [7] reported a similar reduction (mean reduction of 40% at 4 months and 56% at 1 year) utilizing gelatin sponge. The dominant fibroid's volume showed a mean reduction of 55% (range 22-100%) at 4 months and 70% (range 27-100%) at one year.

Similarly, Huang et al [9] demonstrated satisfactory short-term outcomes, with significant improvement in hematocrit, over 8.1 months (range 6-12) in 40 premenopuasal women with myomas undergoing UAE with gelatin sponge particles and lipiodol. Menstrual flow improved in 29 of 35 patients (83%) and significantly decreased by 78.4%. Menstrual pain improved in 27 of 35 patients (77%) and significantly decreased by 70%. The mean percentage reductions of uterine and myomal volumes were 40.2% and 54.9%, respectively. The major complication rate was 2.56%. There was no correlation between tumor volume reduction and clinical outcome.

Walker and Pelage [10] have reported 400 consecutive UAE for symptomatic fibroids with a mean follow-up of 18.7 months. Menstrual bleeding and pain improved in 84% and 79% respectively. Ninety-seven percent were pleased with the outcome. Three (1%) infective complications required emergency hysterectomy. Twenty-three (6%) patients had clinical failure or recurrence. Twenty-six (7%) had persistent amenorrhoea of which four were under the age of 45. Thirteen (4%) had chronic vaginal discharge which was considered a major irritant. Thirteen pregnancies occurred.

Watson and Walker [11] have reported 114 women who underwent UAE with a median reduction of 58%, in fibroid volume Ninety-one percent of the 114 women had their symptoms resolved or improved following embolization. It is not clear whether these 114 women are a subset of the paper quoted in the earlier paragraph since one of the hospitals is common to both papers.

Ravina et al [12] have recently reported their results of UAE done for fibroids in 454 patients (age range 21-68 years) with menorrhagia or bulk-related symptoms or both, of whom 433 were evaluated. There were 42 failures (9.6%). Six months after the procedure, 391 patients were symptom-free. Follow-up ultrasonic examination showed an average reduction of 55% in dominant myoma's volume at 6 months, and 70% at 1 year. Twenty-seven women became pregnant (30 pregnancies). Complications related to the procedure and requiring surgery, occurred in three cases. Principal complications are amenorrhea and fibroid sloughs. Severe complications are rarely found.

Prollius et al [13] compared 12 women with uteri $\geq 780\ cm^3$ i.e, uterine size larger than 24 weeks gestation, with a

control group of 49 women with uteri < 780 cm^3 at 12 months after embolization. Reduction in dysmenorrhea, menorrhagia and pressure effects, and the rate of complications were similar in both the groups. Only 66% of the study group had a reduction in volume to < 780 cm^3 but satisfaction was similar between the two groups. Women may thus be left with a large uterine volume but without symptoms and must be counseled about the same.

Broder et al [14] compared long term outcomes of 51 uterine artery embolization patients with 30 myomectomy patients, 3 or more years after their procedures. Patients who had undergone an embolization were older (44 vs 38 years; $P < 0.001$) and more likely to have had previous surgeries i.e. myoma biopsies and/or myomectomies (78% vs 3%; $P < 0.001$). The exact number of previous myomectomies is not specified in the article.The embolization patients were more likely to have had a further invasive treatment for myomas (29% vs 3%). Amongst those not needing further management, symptoms improved to an equal extent in both the groups; 92% in the embolization group and 90% in the myomectomy group.

Sometimes, multiple procedures are necessary. An unmarried lady with a past history of myomectomy underwent an embolization for a 32 week size fibroid uterus at KEM Hospital. Though the size regressed partially, menorrhagia persisted and she underwent a second difficult myomectomy for multiple fibroids. Unfortunately, 4 years later, symptomatic fibroids recurred and she opted for a second embolization which has relieved her symptoms with only partial regression of uterine size.

Pregnancy after UAE

An analysis of the 50 published cases [15] of pregnancy after UAE done for various reasons revealed the following complications – spontaneous abortion (22%), malpresentation (17%), small for gestational age babies (7%), premature delivery (28%), cesarean delivery (58%) and postpartum hemorrhage (13%). The reasons for embolization included leiomyomas, uterine arterio-venous malformations, gestational trophoblastic disease, cervical pregnancy, placenta previa, placenta accreta, and abruptio placenta. When considering only those pregnancies following embolizations done for fibroids, the various rates were as follows – spontaneous abortion (32%), malpresentation (22%), small for gestational age babies (9%), premature delivery (22%), cesarean delivery (65%) and postpartum hemorrhage (9%). The authors state that in interpreting these rates, the fact that the caesarean section rate was affected by elective cesarean sections and that two patients's prior myomectomies necessitated operative deliveries should be taken into consideration. The malpresentation rate could also be possibly influenced by residual fibroids.

Complications

The procedure is not free from complications. In 400 consecutive patients undergoing UAE for leiomyomas reported by Spies et al [16] with a minimum of a 3 months followup, there were no deaths. One patient required a hysterectomy and one had an undiagnosed leiomyosarcoma. Periprocedural complication rate was 8.5%. Using ACOG definitions for peri-operative complications the overall morbidity was 5%. The complications, included febrile morbidity in eight patients (2%), hemorrhage in three (0.75%), unintended procedure which included unplanned injury or return to operating room for surgery during the same admission in 10 (2.5%), life-threatening events in two (0.5%) and readmission in 14 (3.5%).

Fatal septicemia has also been reported [17] in a lady who underwent embolization for a 20 week size uterus due to two submucous fibroids not suitable for resection. Seven vials of polyvinyl alcohol particles (335-500 μm diameter) had been used. On day 3 post-procedure she developed a urinary tract infection which was treated. She was readmitted with sepsis and disseminated intravascular coagulation, and underwent a hysterectomy for a necrotic, infarcted fibroid. She subsequently died following multiorgan failure. The report does not mention the pre-operative urine report or blood sugar at any time. Pelage et al [4] have also reported one case of acute septic uterine necrosis in a patient with a large submucous fibroid which necessitated a hysterectomy. Submucous fibroids may cause problems due to sloughing and two women in Katsumori et al's [7] series required readmission for the treatment of large sloughing submucous fibroids.

In UAE performed in sheep, small polyvinyl alcohol (PVA) particles had a higher score of uterine necrosis than large particles. PVA particles produced more necrosis than did calibrated micropheres [18]. Thus, use of smaller particles can lead to complications such as uterine necrosis and ovarian ischemia.

Intense post-procedure pelvic pain has been reported in 85% of women [4]. At KEM Hospital, diclofenac suppositories are utilised for peri-procedure pain relief. None of the patients had such severe pain as to warrant epidural analgesia though intramuscular diclofenac was required. In Vashisht et al's [8] series of 21 women who underwent UAE for fibroids, 12 women required patient

controlled analgesia devices. Two women required emergency epidural analgesia following the procedure and two had epidural given electively before the procedure. The mean range of duration of analgesia was 2.5 days. One woman required readmission for pain 6 weeks after the procedure due to fibroid degeneration. Vashisht et al [17] have reported one death and have quoted one more death from Italy due to massive pulmonary embolism 20 hours after the procedure with pelvic vein thrombosis also being identified at autopsy. Occasionally, the postembolization syndrome even warrants a hysterectomy [5].

Pelage et al [4] have reported amenorrhea in 8% of women which reversed in one-third of them. Menopausal symptoms and continued amenorrhea occurred in a 48 year old lady in Katsumori et al's series [7].

Dissection of the uterine artery has also been reported [4,5]. Non-target embolization can lead to a variety of complications ranging from amenorrhea due to ovarian embolization to labial necrosis [19]. Embolic microspheres have even been identified in the ovarian vasculature in a woman who underwent a hysterectomy with bilateral salpingo-oophorectomy for suspected sepsis subsequent to UAE. Histological examination revealed intravascular embolic microspheres (PVA particles) throughout the myometrium as well as in the left ovary [20].

UAE can affect the ovarian reserve. Tulandi et al [21] studied ovarian function in 48 pre-menopausal women with a mean age of 44.1 ± 2.4 years undergoing bilateral UAE for symptomatic fibroids. Baseline serum FSH levels were < 10 mIU/mL in 23 of them. Post-procedure, serum FSH levels gradually increased over a time. A level of >10 mIU/mL was found in seven women 1 month after UAE and in nine women, 3 months after the procedure. However, there was no significant difference in E_2 levels, ovarian volume, number of antral follicles and ovarian stromal blood flow before, 1 month after and 3 months after UAE.

With respect to such data in younger women, in 20 women aged 33-39 years with regular menstrual cycles undergoing UAE for fibroids, Tropeano et al [22] found that there were no significant changes from baseline in the mean day 3 FSH and E_2 levels, ovarian volume measurements, and antral follicle numbers measured at 3, 6 and 12 months after UAE.

Arterial anastomosis between the ovarian artery and the uterine artery is thought to contribute both to failure of embolization and premature menopause. Razavi et al [23] identified three types of anastomoses. In type 1 (21.7%) flow from the ovarian artery to the uterus occured through anastomoses with the main uterine artery. In type II (3.9%) the ovarian artery supplied the fibroid directly while in type III (6.6%), the major blood supply for the ovary was from the uterine artery. After embolization, menopausal signs and symptoms occurred only in those women who were older than 46 years and were seen in 16% (5 of 32) in this age group. Three of the five women had either a type III anastomosis or a type I with bilateral evidence of reflux into the ovarian artery during angiography. Of the six patients in their series with a type II connection, three underwent ovarian artery embolization in addition to uterine artery embolization and two of the remaining three patients reported clinical failure. Razavi et al [23] counsel their patients about the possibility of failure if such an anastomosis exists and perform an ovarian artery embolization at a second sitting if the UAE fails to give symptomatic relief after discussing the risks, benefits and alternatives.

Conclusion

The American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice [24] considers the procedure of UAE for the treatment of symptomatic uterine leiomyomata investigational or relatively contra-indicated in women wishing to retain fertility. Current evidence indicates that, when performed by experienced physicians, the procedure provides good short-term relief of bulk-related symptoms and a reduction in menstrual flow. Complication rates are low, but in rare cases can end in hysterectomy and death. Pregnancy-related outcomes remain understudied. The committee strongly recommends that women who wish to undergo such a procedure should be thoroughly evaluated by an obstetrician-gynecologist so as to facilitate optimal collaboration with interventional radiologists and to ensure the appropriateness of this therapy, taking into account the reproductive wishes of the patient. It recommends that all patients should be adequately informed about potential complications.

Though UAE has a definite role in the management of leiomyomas, published literature is often difficult to analyze and compare in the absence of standard protocols and variations in reporting. The Society for Cardio-vascular and Interventional Radiology has prepared a report which is intended to serve as a guideline for investigators with the goal of improving the validity of conclusions derived from clinical studies of UAE for treatment of leiomyomata [25].

A team approach including both gynecologists and interventional radiologists would be appropriate to manage

women with fibroids. The women need to be informed about the advantages and disadvantages of all the modalities which would be suitable under the circumstances and a joint decision taken as regards the modality to be opted for.

Acknowledgements

I gratefully thank the Department of Radiology of KEM Hospital including Dr Ravi Ramakantan, Dr H Deshmukh, Dr K Rathod and others who are responsible for UAE and Dinesh Rijhwani who helped in the literature search.

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