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The Effect of Intravenous Tranexamic Acid on Reducing Blood Loss during Myomectomy Operation; Randomized Controlled Study: Review Article

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Abstract
The most frequent benign tumor in females is uterine myoma, which is derived from the myometrium of the uterus. Multiple studies have reported occurrence rates varying between twenty percent and forty percent. The histological diagnosis indicates a significantly higher frequency compared to the clinical diagnosis. Myoma is present in about sixty per cent of females over the age of forty-five. A laparoscopic, abdominal, or robotic myomectomy is an invasive medical operation. The abdominal incision is the most common method for carrying out a myomectomy surgery, as it allows the uterus to be easily closed in layers. The small port hole of laparoscopic myomectomy necessitates the application of supplementary equipment, such as a morcellator. The outcomes of robotic myomectomy have not yet been demonstrated to be greater to those of the laparoscopic technique. Tranexamic acid is one of the agents that is utilized. Tranexamic acid was utilized to decrease the necessity for allogeneic blood transfusions, particularly in cardiac operations, liver transplantation, and certain orthopedic surgical procedures, however, the outcomes were inconsistent. Tranexamic acid (TXA) (Kapron) is a synthetic analog of the amino acid lysine. TXA functions as an antifibrinolytic by reversibly binding to 4 to 5 lysine receptor sites on plasminogen. This prevents fibrin degradation and maintains the matrix structure of fibrin by reducing the conversion of plasminogen to plasmin.
Key words: TXA, uterine myoma, myomectomy

Introduction

The majority of myomas are asymptomatic. The primary determinants of whether a myoma results in complications and symptoms are its location and size. Bloating, abnormal uterine bleeding, painful defecation, abdominal discomfort, infertility, frequent urination or retention, and backache are all significant symptoms. It is correlated to a reduction in the quality of life associated of health. Complications during surgery and after surgery correlated with myomectomy include extra bleeding, , visceral damage, pyrexia, conversion to hysterectomy, thromboembolism, scar dehiscence in future pregnancy, transfusions of blood, and several more. Consequently, it is crucial to ensure that the uterus is properly haemostatic and that the uterus is closed in a layered fashion following a myomectomy to reduce complications (1)**.**

In myomectomy operations, hemorrhage is a significant problem. when dissection is performed through the avascular cleft or is reduced through mechanical or pharmacological techniques, hemorrhage may be controlled. A new Cochrane Library review examined a variety of medications that can be used to minimize the loss of blood during myomectomy (1)**.**

Tranexamic acid shows approximately 8 times the antifibrinolytic activity of an older analogue, ε-aminocaproic acid. Tranexamic acid additionally directly suppresses the activity of plasmin with a weak potency (IC50 = 87 mM). and it has the highest specificity (Ki = 2 mM) between all serine proteases in blocking the active site of urokinase plasminogen activator (uPA) (2)**.**

The effectiveness of tranexamic acid in the treatment of abnormal gynecological hemorrhagic disorders was assessed and studied in numerous randomized clinical investigations. Tranexamic acid's efficacy in managing females with normal reproductive function who have been diagnosed with abnormal bleeding due to uterine fibroids is uncertain (3)**.**

The objective of the current research was to evaluate the effectiveness of placebo and tranexamic acid in reducing the loss of blood during transabdominal myomectomy.

Uterine Fibroids (Leiomyomas)

Leiomyomas are tumors of the smooth muscles of benign origin; women usually suffer from symptoms of uterine fibroids during their child bearing period. The majority of females who have uterine fibroids are asymptomatic; however, they typically experience pressure symptoms, abnormal uterine bleeding, infertility, adverse pregnancy outcomes and pain. Fibroids are the most frequent neoplasm in the female pelvis. Gonadal steroids have influenced the growth and epidemiology of women; however, they aren't necessary contributing to the development of tumors (4)**.**

Blacks races are 2 to 3 times more likely to suffer from leiomyomas compared to white races .

Etiology:

While the exact reasons of myomas are unidentified there were significant advancements in our knowledge of the growth factors, genetic factors, hormonal factors, and molecular biology of these benign tumors. Most myomas are monoclonal, and approximately forty percent of them are chromosomally abnormal. Abnormalities that are frequently observed involve translocations among chromosomes 12 and 14, trisomy of chromosome 12, and deletions of chromosome 7. Chromosomal abnormalities are most commonly to be observed in atypical, large and cellular myomas (5)**.**

Risk factors:

Myomas are a common condition in women, with the majority of females being diagnosed in aged fourteen. Hormonal factors, such as early menarche and family history, can increase or decrease the risk of uterine myomas. Each ten kilogram rise in body weight and body mass index elevates the probability of myomas by twenty-one percent. Obesity results in a rise in biologically available estrogen by increasing the conversion of adrenal androgens to estrone and decreasing sex hormone-binding globulin. Oral contraceptives have no definite relationship with myomas, with some studies finding an elevated probability with oral contraceptives, while others found a decreased risk. The frequency and number of clinically apparent myomas may be reduced by pregnancy, as the postpartum myometrium goes back to its normal blood flow, size of cell and weight. Smoking may reduce the incidence of myomas by reducing androgen conversion to estrone, decreasing bioavailability of estrogen at the target tissue, stimulating higher sex hormone-binding globulin concentrations, increasing or 2-hydroxylation of estradiol. The initiation of myoma formation was supposed to be facilitated by tissue injury, such as cell injury or inflammations caused by environmental agents, hypoxia, or infections. (1)**.**

Classification of myomas:

Primary Classification of leiomyomas is concerned by the presence of myomas by sonograhic examination, it is not concerned by site, size and number of Myomas**).**

Intramural: they may be large enough to distort the uterine cavity or the serosal outline, and they develop in the uterine wall.

Submucosal: it arises from the myometrium just below the endometrial line, they often protrude into the uterine cavity. They are classified into three types: pedunclated fibroids (type 0), fibroids which has less than 50%of its size in the uterine wall (type I) and a third type are fibroids with more than 50% of its size in the uterine wall (type II)**.**

Subserosal: arise from the serosal surface of uterus.

Cervical: arise from the uterine cervix.(6)

Symptoms:

Abnormal uterine bleeding:

It’s the most frequent, excessive menstrual bleeding is the typical pattern with myomas. It cen be responsible for many correlated complications included community problems and decreased activity and work force and anemia. Postmenopausal bleeding and inter-menstrual hemorrhage aren’t common and distinguishing of fibroids and must be well examined to diagnose endometrial disorders and pathology.

Fibroid location is usually the main factor affecting the degree of uterine bleeding: submucosal myoma are frequently associated with menorrhagia, myoma size is of secondary effect on bleeding (7)**.**

Pain and pressure symptoms:

problems associated with bladder emptying, and rarely obstruction, and urinary frequency, are pressure symptoms of fibroids, they are due to irregularity in the shape of the myoma, they may be due to posterior myomas pushing the entire uterus anteriorly, anterior myomas compressing the bladder or rarely ureteric compression lead to silent hydronephrosis.

Fibroid may also place pressure on the rectum causing constipation, they can also lead to back pain, huge myomas may compress the inferior vena cava leading to increased risk of venous thrombosis and embolism (6)**.**

Rapid Myoma Growth:

The presence of uterine sarcoma in premenopausal femaleis frequently indicated by "rapid uterine growth." One sarcoma was identified in an investigation of 371 females (0.26%) who had

surgery on for the rapid growth of suspected myomas. There's no sarcomas have been identified in the 198 females who experienced a 6-week rise in the size of their uterus over a one-year period. The correlation among sarcoma and the rapid development of presumed myomas has yet to be established (8)**.**

Uterine Sarcoma:

Uterine sarcomas are often suspected to be a pelvic malignancy. Nine women aged 64-86 with sarcomas were diagnosed with vaginal bleeding, and abdominal pain, four of whom had gynecologic malignancies, including ovarian cancer, endometrial carcinoma, and presumed uterine sarcoma. A sarcoma was discovered frequently after a females received prolapse operation. Within the SEER database of the United States National Cancer Institute, there were 2098 females diagnosed with sarcomas, with an average age of sixty-three years. Nevertheless, a review revealed that the average age of females that underwent myomectomy was thirty-six years (6)**.**

Diagnosis:

Pelvic Investigation

Typically, a pelvic examination may be used to diagnose clinically significant subserosal and intramural myomas, which are characterized by an irregularly shaped, enlarged, non-tender and firm uterus. The uterine weight and size at pathologic investigation are effectively correlated, particularly in the majority of obese females (body mass index higher than thirty), as determined by bimanual investigation (9)**.**

Imaging

The precise evaluation of the number, position and size, of myomas is essential for the selection of cases for medical treatment, noninvasive processes, or operation. Imaging methods like saline-infusion sonography, sonography, magnetic resonance imaging and hysteroscopy, can confirm myomas diagnosis. Transvaginal sonography is the most accessible and cost-effective method, helping differentiate myomas from additional pelvic disorders. A combination of transabdominal and transvaginal ultrasound is the most effective method for imaging large myomas. Although sonographic appearances may differ, they are typically characterized by symmetrical, clearly established hypoechoic, and heterogeneous masses. Transvaginal ultrasound is dependable for uterus that are less than 375 milliliters in total volume or contain 4 or lesser myomas.

Adenomyosis and myomas can be distinguished using magnetic resonance imaging. Magnetic resonance imaging was more effective than trans-vaginal ultrasound (specificity 79%, sensitivity 59%) in diagnosing adenomyosis in twenty-two females who were scheduled for hysterectomy (specificity 88%, sensitivity 64%). Junctional zone thickness exceeding fifteen millimeters (or twelve millimeters in a nonuniform junctional zone) had been indicative of the presence of adenomyosis. Adenomyosis is also associated with focal, poorly defined areas of either elevated or decreased intensity within the myometrium (6)**.**

Uterine Sarcoma

It can be viable to diagnose leiomyosarcoma prior to surgery. The accuracy of diagnosis was found to be good when initial images are obtained for from forty to sixty sec using total serum lactic acid dehydrogenase (LDH), lactic acid dehydrogenase isoenzyme 3, and gadolinium-simulated magnetic resonance imaging (Gd-DTPA). Within an investigation of eighty-seven females with uterine myomas, ten females with leiomyosarcomas, and 130 females with degenerating myomas, 100% positive predictive value, 100% specificity, 100% diagnostic precision, and 100% negative predictive value have been obtained for leiomyosarcoma (10)**.**

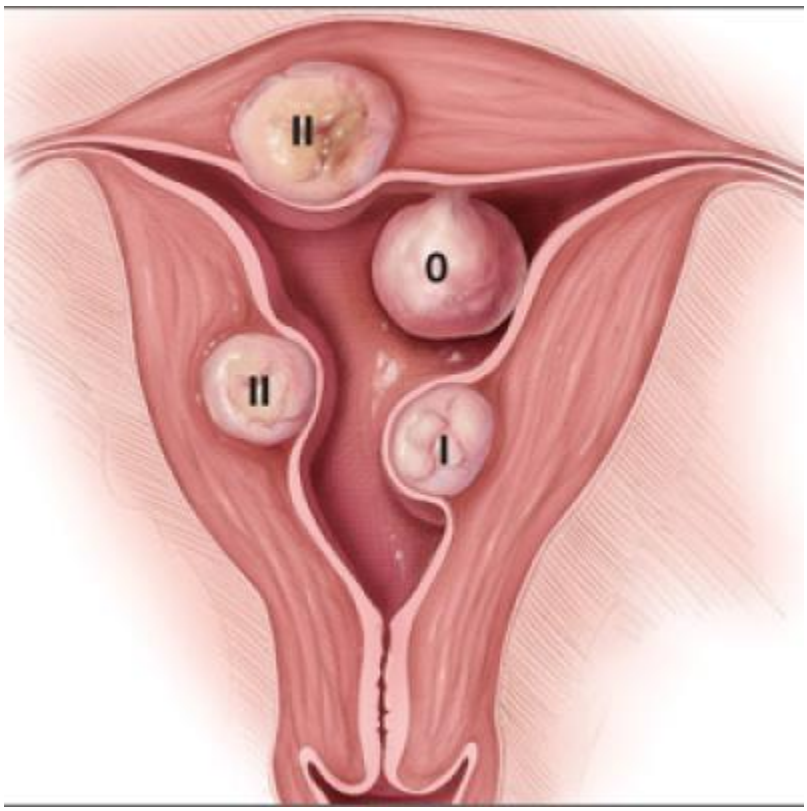

Figure (1): Hysteroscopic classification of submucous fibroids (10)**.**

Management of Uterine fibroids

The main goal of management plan of women with symptomatic fibroids is the symptom relief. Factors affecting the management plan include, symptoms (type and severity), myomas location and size, the patient age and their reproductive and obstetric history (6)**.**

Management options:

Expectant management:

Data regarding asymptomatic fibroids who were expectantly managed are not of high quality, but studies showed that leiomyomas can regress substantially postpartum and that expectant management is a wise option for some cases**.** Annual evaluation is done for follow up of symptoms, fibroid size and patient should be counseled about other management options if the case is progressing (11)**.**

Medical treatment:

Effectiveness of medical management for symptomatic fibroids has not been studied well, through randomized trials "**.**

Hormonal therapy:

Estrogen-progestin contraceptives: it was thought that COC is one of the risk factors for growth of fibroids. Recent studies showed a 17% decrease in the growth risk in current COC users.This data support trial of therapeutic treatment before other invasive options.

Estrogen and progesterone therapy mostly acts through endometrial atrophy (12)

Levonorgestrel intrauterine contraceptive device:

Randomized trials and observational studies suggests the efficacy ofIUD in treatment of mennorhagia and correction of anemia.

The Food and Drug Administration accepted the use of IUDs for managing excessive bleeding during menstruation. It is also used as a contraceptive method for these cases. It is relatively contraindicated in women with intra-cavitary myomas (13)**.**

Progesterone pills, injections and implants:

It may cause growth of myomas but it also help to decrease menstrual bleeding by causing endometrial atrophy (14)**.**

Gonadotropin – releasing hormone agonists:

It acts through increasing the gonadotropin release at first then by down regulation and desensitization creating a clinical state like menopause (hypogonadotrophic hypogonadism). They will cause a reduction of uterine size 35% to 60% within three months, they will also improve anemia (15)**.**

Gonadotropin-releasing hormone antagonists:

They compete with endogenous Gonadotropin releasing hormones for their pituitary receptor (16)**.** They are more used for induction of ovulation so there is no long acting preparation in the market.

Antiprogestins and progesterone receptor modulators (PRMs):

Mifepristone: it can reduce the uterine size up to 74 % which is comparable to that reduction by the use of GnRH agonists. It is approved by the FDA for management of fibroids, however available doses can be used for termination of pregnancy rather than treatment of fibroid.

Ulipristal acetate: it inhibits ovulation with little effect on estradiol. It results in resolution of mennorrhagia in most cases and increased in hemoglobin level (17)**.**

Raloxifene: its role is unclear, clinical trials of raloxifene use in women in child bearing women have not been convincing**.** High doses of Raloxifene may lead to venous thrombosis.

Danazol and gestrinone: they are effective but they are associated with multiple side effects. Danazol inhibits pituitary gonadotrophin release and endometriotic implants, it also inhibits ovarian enzymes that produce estrogen so they cause amenorrhea and inhibit autologous endometrium. It helps to control bleeding but does not reduce the myoma size. Danazol is associated with multiple side effects which are common, they include acne, hirsutism, weight gain, oily skin, depression and mood changes.

Gestrinone can decrease myoma bleeding and volume, it also has the advantage of the carry over effect after its discontinuation (18)**.**

Non-hormonal therapy options include aromatase inhibitors, antifibrinolytic agents, and non-steroidal anti-inflammatory drugs. Aromatase inhibitors can decrease the size and symptoms of leiomyomas, especially during menopause. Antifibrinolytic agents are used for dysfunctional uterine bleeding but not for fibroids. Tranexamic acid is FDA-approved for menorrhagia and women with fibroid-associated excessive bleeding during menstruation. Non-steroidal anti-inflammatory medications are effective in mitigating menstrual pain; however, they have not been approved for the treatment of heavy menstrual bleeding. Interferon therapy has shown to reverse fibroid cell proliferation by inhibiting fibroblastic growth, resulting in a significant shrinkage in myoma size after seven months.

Operating management:

It’s the main line of management for fibroid, hysterectomy is the definite radical procedure, other lines include uterine artery embolization, myomectomy, myolysis, and endometrial ablation magnetic resonance guided focused ultrasound surgery (19)**.**

Hysterectomy:

A hysterectomy is a significant procedure which is suggested for a females when alternative therapies were ineffective.

Myomectomy:

It is preferred for females that haven't full child bearing or that do not want to remove the uterus. It is effective in curing abnormal uterine bleeding and pressure related symptoms but there is a high risk of recurrence from abnormal myocytes who form new clones after myomectomy (20)**.**

Other lines of treatment include:

Endometrial ablation:

For females that have finished childbearing, endometrial ablation is an effective therapy for hemorrhage abnormalities, either in alone or in conjunction with hysteroscopic myomectomy. Pressure symptoms or bulk are uncommon to enhance , because this method doesn't impact subserosal and intramural leiomyomas. An enlarged uterine cavity (uterine length higher than nine centimeters) has been associated with a reduction in the probability of amenorrhea in a newest population-based investigation into endometrial ablation results. However, the presence of either intramural or submucous fibroids failed to contribute to this finding (21)**.**

Myolysis:

The term "myolysis" indicates the cryoablation (cryomyolysis) or laparoscopic thermal coagulation of leiomyoma tissue. Performing this method is simpler than that of myomectomy, that necessitates suturing. Nevertheless, the probability of adhesion formation or rupture during pregnancy can be greater if localized tissue destruction occurs without repair. Nevertheless, a recent device that utilizes radiofrequency ablation is currently being introduced, despite its uncommon utilization in the present day**.**

Uterine artery occlusion:

A potential alternative to UAE is the occlusion of uterine vessels through laparoscopy or a vaginally-placed clamp. However, there is a lack of knowledge in this field (22)**.**

Interventional radiology techniques:

Uterine artery embolization:

Uterine fibroid embolization (UFE) or uterine artery embolization (UAE) is an effective but minimally invasive choice for the treatment of leiomyoma-correlated symptoms. It was stated to have good clinical and technical success. It's a viable alternative for females that aren't interested in optimizing their future fertility and desire to maintain their uterus. Myomas undergo around thirty to forty-six percent shrinkage as a consequence of uterine fibroid embolization.

Magnetic resonance guided focused ultrasound:

A more new therapy choice for uterine leiomyomas in premenopausal females that finished childbearing is magnetic resonance guided focused ultrasound surgery (MRgFUS). This outpatient process involves the combination of numerous waves of ultrasound energy on a small volume of tissue, resulting in its thermal destruction. It is a noninvasive thermo-ablative method (23)**.**

Abdominal Myomectomy:

The uterine leiomyoma is the most common benign tumor in the pelvis of women , and it is most probably responsible for symptoms during the reproductive years. This tumor is well documented since ancient times. The curator of the Egyptology Department at the English Museum in London informed me which the mummies showed calcified pelvic masses which were identified using radiographic methods. These masses are indicative of uterine leiomyoma (24)**.**

Operative technique:

Incision of the uterus: myomas are located at first via palpation of the uterine wall, after that incisions are planned in order not to injure the cornu or uterine vessels if the incision was extended. Classical teaching is to incise the uterus via a vertical incision, for preventing injury of the arcuate uterine arteries which are known to run transversely**.**

Surgeons prefer to plan the uterine incision location from which they can excise most the myomas. They think that using a small number of uterine incisions minimize the adhesions to the serosal wall of the uterus, however there is no data and studies regarding the risk of adhesions and the number of uterine incisions.

Myomectomy: The uterus is deeply incised, extending through the pseudo capsule of the fibroid and the layers of the myometrium. Extending of incision is continued deeply to just below the fibroid capsule which is the least vascular plane where the myoma can be seen initially and was slightly bulge.

The fibroid is covered by a dense vascular layer which supplies a fibroid, while it lacks a vascular pedicle. This was demonstrated through electron microscopy examination of the fibroid (25)**.**

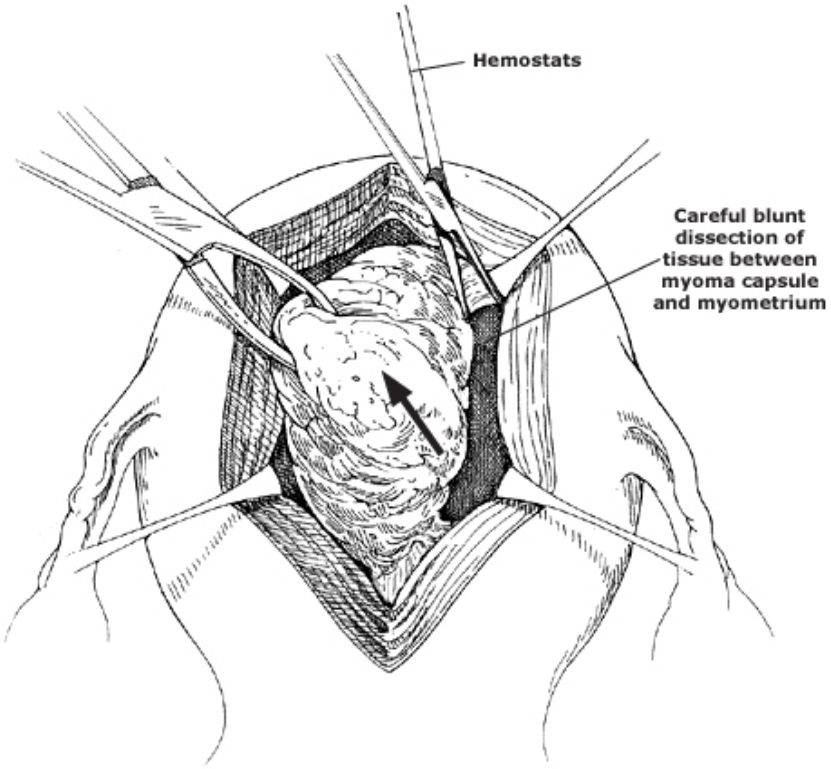

Figure (8): Dissection of myoma during myomectomy

Bonney additionally explained an alternative technique to the posterior myoma, which is referred to as the Bonney hood. This method involves the enucleation of the myoma and a transverse posterior fundal incision. The extra serosa is sutured to the anterior surface of the uterus with fine suture following interrupted sutures in layers are utilized to close the dead space, resulting in a functional anterior incision. This permits a posterior method while simultaneously preventing a posterior deficiency(25)**.**

Complications:

Myomectomy can cause an average blood loss of 200-800 CC, mainly due to an increase in myomas and cavity opening. Transfusions are common, ranging from 2-28% of cases. Hysterectomy can complicate the procedure, causing severe bleeding and uterine artery ligation. Patients may experience fever and infection within 48 hours, with 36-36% experiencing postoperative adhesions. Vascular injuries are uncommon, with only one bladder injury and two intestinal obstructions reported in 97 cases.

Outcome:

Symptom relief: relieve occurs in 80% women undergoing myomectomy. Persistence of myomas: many women will show presence of fibroids in the postoperative follow up but they will not require another treatment because of symptomatic relief that why postoperative imaging is not required unless symptoms persist. presence of myomas after surgery is because they were not removed or they were incompletely removed (26)**.**

Measures to decrease blood loss in myomectomy

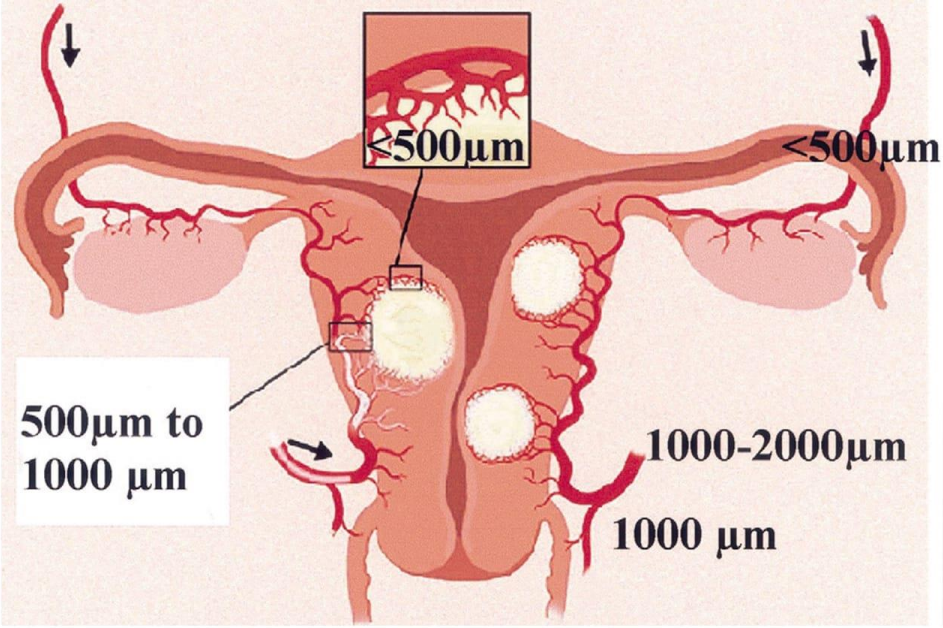

Fig. (13): The arterial blood supply (short arrows) to the uterus and three fibroid tumors are shown in anatomic drawings(F). The perifibroid plexus generally consists of arteries with diameters ranging from 500 to 1000 micrometers within the most patients; the utero-ovarian anastomosis (long arrow) typically has a diameter of fewer than 500 micrometers (26)**.**

Measures to reduction loss of blood in abdominal myomectomy:

Preoperative:

Correction of anemia: Anemia is cause by menorrhagia due to presence of fibroids, anemia prior to surgery rises the probability of transfusion of blood and additionally the mortality and morbidity prior to surgery, iron infusion, blood transfusion, or erythropoiesis stimulating agents are viable options for treating anemia. Administration of gonadotropin releasing hormone agonists before surgery offers certain short-term advantages for females having myomectomy according to reduced loss of blood and decreased uterine size; however, it could complicate the surgical procedure (27)**.**

Intra-operative:

Bleeding can be decreased by: Pharmacological methods, Non-pharmacological methods, and Operative technique

Pharmacological methods:

Vasoconstrictors:

The planned uterine incision site for each fibroid is treated with intra-myometrial vasopressin to minimize the loss of blood. The smooth muscle in the walls of capillaries, small arterioles, and venules is constricted by it through its action. The randomized study outcomes indicate which the blood loss during myomectomy with vasopressin is significantly lower than that with placebo [299 milliliters less] and is either comparable to or lower than the application of a uterine artery tourniquet.

Epinephrine also helps in decreasing loss of blood during abdominal myomectomy. On a randomized investigation, it was observed which intramyometrial injection of bupivacaine with epinephrine decreased blood loss than saline (69 milliliter less) (28)**.**

Uterotonics:

Studies have discovered which blood loss during abdominal myomectomy was significantly decreased by the administration of 400 mcg of vaginal misoprostol one hour prior to operation**.**

The effect of oxytocin in non-pregnant women is inadequately recorded. According to an investigation, the injection of oxytocin during myomectomy didn't decrease blood loss following surgery, as the uterine oxytocin receptor's influence on non-pregnant females is restricted (29)**.**

Tranexamic Acid:

The injection of tranexamic acid intravenously during open myomectomy resulted in a significant decrease in total blood loss, hemoglobin decrease following surgery, period of operation, and transfusion demands**.**

It acts through inhibition of fibrinolysis to control hemorrhahe, it is administered in myomectomy by giving an intravenous bolus of 190 milligram per kilogram with a maximum dosage of 1gram before incising the uterus subsequently, an infusion of one milligram per kilogram dissolved in one litter saline**.** its the Food and Drug Administration accepted for management of uterine bleeding due to fibroids, also helps to control perioperative bleeding in myomectomy (30)**.**

Non-pharmacological methods.

Tourniquets:

The reduction of blood loss during operation is achieved by employing tourniquets to obstruct the uterine blood supply. A randomized study noted the advantages of artery tourniquets. The application of a tourniquet to the uterine artery, as opposed to the absence of a tourniquet, led to a substantial reduction in the loss of blood, with an average of 1870 milliliters less (31)**.**

Clamps:

The utilization of a traumatic clamp, which restricts the uterine vessels and reduces uterine blood flow, was first explained by Bonney. The Bonney clamp is placed from the public end of the abdominal wound; it has to keep the round ligament in its grasp to prevent it from slipping below the uterine vessels. Ring forceps are utilized for compressing the blood flow from the infundibulo-pelvic ligament, effectively halting the flow of uterine blood. Before utilizing rubber-shod clamps, bulldog clamps, or tourniquets, it is essential to ascertain the ureter's location. The tourniquet's disadvantage is which it frequently necessitates the creation of a small incision in the broad ligament or an avascular region (though this isn't necessary) (32)**.**

Operative techniques:

if heavy bleeding is anticipated or happens during myomectomy, uterine artery ligation, embolization, or internal iliac artery ligation can additionally be performed to prevent hysterectomy.

In theory, fertility in the future must be maintained, as the uterine vessels are going to re-cannulate. Nevertheless, the extent to which uterine artery embolization as a primary technique affects fertility and obstetric results remains unclear. This is the cause why this method is utilized in cases where other measures have been unsuccessful and extra hemostasis is required to prevent hysterectomy (33)**.**

Tranexamic acid

Tranexamic acid:

It is Antifibrinolytic Agent, Antihemophilic Agent, Hemostatic Agent

Formulation:

Chemical Name: Trans-4 (aminomethyl) cyclohexane-carboxylic acid. The structural formula is C8H15NO2. The molecular weight is 157.2. Tranexamic acid is a white, crystalline powder. The pH of the aqueous solution for injection ranges from 6.5 to 8. Protein binding is extremely less (less than three), with plasminogen being the primary target at therapeutic plasma levels. Tranexamic acid doesn't attach to serum albumin.

Biotransformation:

fewer than five percent of a dosage is metabolized**.**

Duration of half-life: Removal occurs within around 2 hours of the IV injection of a 1 -gram dosage (34)**.**

Therapeutic plasma level:

10 mcg per milliliter (63.6 micromoles per litter). after the injection of the last of the four dosages of ten milligrams per kilogram of body weight (mg per kilogram) IV or twenty milligrams per kilogram orally, the therapeutic levels remain in serum for between seven and eight hours and in multiple different tissues for a maximum of seventeen hours**.**

Dosing: Adult

For elective cesarean sections, the blood loss decrease intravenous is as follows: 1000 milligrams administered over a period of five min a minimum of ten min before the skin incision.

Side Potential negative consequences include blurred vision or other visual alterations • Hypotension. • Vomiting. • Thrombo-embolism or thrombosis. • Nausea. • Diarrhea. • Menstrual discomfort that is unusual in nature -caused by clotting of menstrual fluid (35)**.**

Mechanism of action:

Tranexamic acid is a synthetic analog of the amino acid lysine. TXA functions as an antifibrinolytic by reversibly binding 4 to 5 lysine receptor locations on plasminogen or plasmin. This stops plasmin from binding to and degrading fibrin, thus preserving the matrix structure of fibrin. Tranexamic acid provides an antifibrinolytic effect that is approximately 8 times greater than that of heparin (36)**.**

Contraindications:

Hypersensitivity, active intravascular clotting, subarachnoid hemorrhage,may cause CNS depression, visual defects, Ureteral obstruction: Exercise caution when administering the administration of cases with upper urinary tract hemorrhage; obstruction of the ureter as a result of formation of clots is currently documented.

Storage and packaging: Unless otherwise specified by the manufacturer, store at a temperature between fifteen and thirty degrees Celsius (59 and 86°F). Preserve from freezing temperatures (37).

IV infusion solutions, such as those having carbohydrates, electrolytes, dextran, or amino acids, can be combined with tranexamic acid administration. The administration of tranexamic acid can be supplemented with heparin.

Stability: Intravenous infusion mixtures must be made on the same day as they will be needed to be administered (38). Tranexamic acid must not be combined with blood or added to any solution having penicillin.

Role of Tranexamic Acid in Bleeding:

Tranexamic acid is commonly utilized in operations that pose an elevated probability of bleeding, including those that involve the heart, liver, vascular system, and large orthopedic surgeries. In outpatient disorders that involve prolonged hemorrhage, its oral form is currently being assessed for possible application. The risk of death in individuals who have experienced significant bleeding as a result of trauma was reduced by tranexamic acid. Nevertheless, the probability for mortality may be elevated when the medication is administered above three hours following the injury. Tranexamic acid is frequently utilized in cardiac operations, whether with or without cardiopulmonary bypass (39)**.**

Tranexamic acid is utilized in orthopedic operations to decrease blood loss. TXA has been demonstrated to be beneficial in the prevention of blood loss before and after surgery and the clearing of the surgical field**.**

Tranexamic acid and menorrhagia, Tranexamic acid significantly decreases uterine bleeding in females with menorrhagia. 1st -line nonhormonal management for dysfunctional uterine bleeding and excessive hemorrhage correlated with uterine fibroids. On November 13, 2009, the United States Food and Drug Administration accepted tranexamic acid oral tablets for the management of excessive bleeding during menstruation. The United Kingdom altered the status of tranexamic acid from PoM (Prescription only Medicines) to P (Pharmacy Medicines) in March 2011. The modification has been made to provide management for excessive hemorrhage during menstruation.

Other clinical indications include postpartum hemorrhage (PPH). Tranexamic acid is additionally beneficial in the management of hemorrhage in hemophilia as a 2nd -line treatment following factor VIII in cases with hereditary angioedema (40)**.**

References

1. Petermans S, Ameye L, Timmerman D, Verguts J. Ultrasonography in the prediction of complications during and after uterine myomectomy. Gynecol Surg. 2016;13:507–14.
2. Picetti R, Shakur-Still H, Medcalf RL, Standing JF, Roberts I. What concentration of tranexamic acid is needed to inhibit fibrinolysis? A systematic review of pharmacodynamics studies. Blood Coagul fibrinolysis. 2019;30(1):1–10.
3. Bradley LD, Gueye NA. The medical management of abnormal uterine bleeding in reproductive-aged women. Am J Obstet Gynecol. 2016;214(1):31–44.
4. Sparic R, Mirkovic L, Malvasi A, Tinelli A. Epidemiology of uterine myomas: a review. Int J Fertil Steril. 2016;9(4):424.
5. Dvorská D, Braný D, Danková Z, Halašová E, Višňovský J. Molecular and clinical

attributes of uterine leiomyomas. Tumor Biol. 2017;39(6):1010428317710226.

6. Florence AM, Fatehi M. Leiomyoma.[Updated 2023 Jul 17]. StatPearls [Internet] Treasure Isl StatPearls Publ. 2024;
7. Valentine LN, Bradley LD. Hysteroscopy for abnormal uterine bleeding and fibroids. Clin Obstet Gynecol. 2017;60(2):231–44.
8. Paul PG, Shintre H, Mehta S, Gulati G, Paul G, Mannur S. Parasitic myomas: an unusual risk after morcellation. Gynecol Minim Invasive Ther. 2018;7(3):124–6.
9. Kaganov H, Ades A. Uterine fibroids: investigation and current management trends. Aust Fam Physician. 2016;45(10):722–5.
10. Zhang F, Liu Y, Quan Q, Meng Y, Mu X. Diagnostic value of preoperative CA125, LDH and HE4 for leiomyosarcoma of the female reproductive system. Cancer Manag Res. 2021;4657–64.
11. Laganà AS, Pacheco LA, Tinelli A, Haimovich S, Carugno J, Ghezzi F, et al. Management of asymptomatic submucous myomas in women of reproductive age: a consensus statement from the global congress on hysteroscopy scientific committee. J Minim Invasive Gynecol. 2019;26(3):381–3.
12. Brooks JP, Edwards DJ, Blithe DL, Fettweis JM, Serrano MG, Sheth NU, et al. Effects of combined oral contraceptives, depot medroxyprogesterone acetate and the levonorgestrel-releasing intrauterine system on the vaginal microbiome. Contraception. 2017;95(4):405–13.
13. El-Balat A, DeWilde RL, Schmeil I, Tahmasbi-Rad M, Bogdanyova S, Fathi A, et al. Modern myoma treatment in the last 20 years: a review of the literature. Biomed Res Int. 2018;2018(1):4593875.
14. Chabbert-Buffet N, Kolanska K, Darai E, Bouchard P. Selective progesterone receptor modulators: current applications and perspectives. Climacteric. 2018;21(4):375–9.
15. Hodgson R, Chittawar PB, Farquhar C. GnRH agonists for uterine fibroids. Cochrane Database Syst Rev. 2017;2017(10).
16. Bartels CB, Cayton KC, Chuong FS, Holthouser K, Mehr SA, Abraham T, et al. An evidence-based approach to the medical management of fibroids: a systematic review. Clin Obstet Gynecol. 2016;59(1):30–52.
17. Saharan S, Khajotia S, Falodia S, Budania S, Prakash P. Effect of Mifepristone on Uterine

Fibroid with special reference to Symptoms and its Size. Int multispeciality J Heal. 2016;

18. Garg D, Segars JH. Treatment modalities for fibroids, indications, risks, and benefits. Uterine Fibroids A Clin Caseb. 2018;87–106.
19. Yang W, Luo N, Ma L, Dai H, Cheng Z. The changes of surgical treatment for symptomatic uterine myomas in the past 15 years. Gynecol Minim Invasive Ther. 2018;7(1):10–5.
20. Milazzo GN, Catalano A, Badia V, Mallozzi M, Caserta D. Myoma and myomectomy: Poor evidence concern in pregnancy. J Obstet Gynaecol Res. 2017;43(12):1789–804.
21. Ierardi AM, Savasi V, Angileri SA, Petrillo M, Sbaraini S, Pinto A, et al. Percutaneous high frequency microwave ablation of uterine fibroids: systematic review. Biomed Res Int. 2018;2018(1):2360107.
22. Spies JB. Current role of uterine artery embolization in the management of uterine fibroids. Clin Obstet Gynecol. 2016;59(1):93–102.
23. Ferrari F, Arrigoni F, Miccoli A, Mascaretti S, Fascetti E, Mascaretti G, et al. Effectiveness of Magnetic Resonance-guided Focused Ultrasound Surgery (MRgFUS) in the uterine adenomyosis treatment: technical approach and MRI evaluation. Radiol Med. 2016;121:153–61.
24. Lynnerup N. Mummies and paleopathology. In: Ortner's Identification of Pathological Conditions in Human Skeletal Remains. Elsevier; 2019. p. 799–807.
25. Camilli S, Conway F, Di Giovanni A, Lazzeri L, Zupi E, Piccione E, et al. OP24. 05: Highly vascularised uterine myomas at ultrasound and correlation to histopathology. Ultrasound Obstet Gynecol. 2017;50:126–7.
26. Tsujioka H, Matsuoka S, Sorano S, Yamamoto H, Nakamura S, Tohyama A, et al. Follow-up study of symptomatic submucous fibroids after hysteroscopic myomectomy. Clin Exp Obstet Gynecol. 2017;44(1):61–4.
27. Bhagavath B, Lindheim SR. Options for controlling blood loss during myomectomy. Fertil Steril. 2019;111(5):894.
28. Nassif J, Nahouli H, Khalil A, Mikhael E, Gharzeddine W, Ghaziri G. Epinephrine-induced Takotsubo cardiomyopathy during laparoscopic myomectomy: case report and review of the literature. J Minim Invasive Gynecol. 2017;24(6):1037–9.
29. Atashkhoei S, Fakhari S, Pourfathi H, Bilehjani E, Garabaghi PM, Asiaei A. Effect of

oxytocin infusion on reducing the blood loss during abdominal myomectomy: a double-blind randomised controlled trial. BJOG An Int J Obstet Gynaecol. 2017;124(2):292–8.

30. Kathopoulis N, Prodromidou A, Zacharakis D, Chatzipapas I, Diakosavvas M, Kypriotis K, et al. The effect of intravenous tranexamic acid on myomectomy: a systematic review and meta-analysis of randomized controlled trials. J Pers Med. 2022;12(9):1492.
31. Al RA, Yapca OE, Gumusburun N. A randomized trial comparing triple versus single uterine tourniquet in open myomectomy. Gynecol Obstet Invest. 2017;82(6):547–52.
32. Afolabi MA, Ezeoke GG, Saidu R, Ijaiya MA, Adeniran AS. Comparing perioperative vaginal misoprostol with intraoperative pericervical hemostatic tourniquet in reducing blood loss during abdominal myomectomy: A randomized controlled trial. J Turkish Ger Gynecol Assoc. 2019;20(1):23.
33. Karlsen K, Hrobjartsson A, Korsholm M, Mogensen O, Humaidan P, Ravn P. Fertility after uterine artery embolization of fibroids: a systematic review. Arch Gynecol Obstet. 2018;297:13–25.
34. Rong G xiang, Shen C lin, Gui B jie, Yin H, Tang Z. Comparison of tranexamic acid pharmacokinetics after intra-articular and intravenous administration in rabbits. Pak J Pharm Sci. 2017;30(4).
35. Goobie SM. Tranexamic acid: still far to go. Vol. 118, BJA: British Journal of Anaesthesia. Oxford University Press; 2017. p. 293–5.
36. Diebel ME, Martin J V, Liberati DM, Diebel LN. The temporal response and mechanism of action of tranexamic acid in endothelial glycocalyx degradation. J Trauma Acute Care Surg. 2018;84(1):75–80.
37. Ziu E, MZ KS, Mesfin FB. Subarachnoid hemorrhage. 2017;
38. Donnelly RF. Stability of Tranexamic Acid Mouth Rinse. Int J Pharm Compd. 2018;22(5):412–6.
39. Myles PS, Smith JA, Forbes A, Silbert B, Jayarajah M, Painter T, et al. Tranexamic acid in patients undergoing coronary-artery surgery. N Engl J Med. 2017;376(2):136–48.
40. Janbain M, Enjolras N, Bordet JC, Bolbos R, Leissinger CA, Dargaud Y. Hemostatic Effect of the Combination of Factor VIII Concentrate with Tranexamic Acid (TXA) in the Prophylactic Setting in Severe Hemophilia a. Blood. 2018;132:2490.