Review Article: Investigating the Effect of Tranexamic Acid on Reducing Bleeding in Knee Arthroplasty and Improving Joint Function: A systematic review

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<u>ABSTRACT</u>

Knee arthroplasty is a type of surgery that replaces the joint surface of the femur and leg bones in the knee joint with an artificial surface. Tranexamic acid binds to the binding sites of lysine in plasmin and plasminogen and thereby displaces plasminogen from the surface of fibrin and thus inhibits fibrinolysis. Local use of tranexamic acid can reduce bleeding in gynecological and obstetric surgeries, especially after delivery, urological surgery, oral surgery in hemophilia patients, and brain and spinal cord surgeries. Tranexamic acid is a plasminogen inhibitor and also inhibits urokinase activators. Tranexamic acid can be used orally and intravenously. Urokinase is a physiological thrombolytic agent that is produced in the kidney parenchymal cells and found in the urine. Urokinase binds directly to plasminogen and produces plasmin. Tranexamic acid is a synthetic derivative of the amino acid lysine and an antifibrinolytic agent that binds to plasminogen and prevents the interaction of plasminogen with fibrin and prevents fibrin clot dissolution. Urine and urothelium contain high concentrations of plasminogen activators. Tranexamic acid is used to reduce bleeding in heart surgeries, liver transplants, orthopedic surgeries, as well as in cases of arthroplasty and knee joint replacement, and to reduce bleeding after prostatectomy or tooth extraction. Also, this drug is used to treat idiopathic menorrhagia (20-23). Although prostate surgery is a very common surgery, little study was done on strategies to reduce the amount of transfusion, and there is still no universally accepted method.

Introduction

he joint gets destroyed or damaged with age or for many other reasons. The most important goal of knee joint replacement is to eliminate the pain caused in the knee due to wear and tear, arthritis, rheumatism or destruction of the joint surface [1-3]. Currently, tranexamic acid is the only available drug that improves hemostatic function without increasing the risk of thromboembolic complications and is used in

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heart surgery to prevent fibrinolysis. Induced hypotension by means of neuraxial anesthesia is the only non-surgical and non-pharmacological strategy that reduces the rate of transpiration in prostatectomy [4-6].

Tranexamic acid reduces blood loss by inhibiting fibrinolysis. Damage to the normal function of the joint causes serious problems. If the treatment methods do not have an effect on improving the joint function, it will be necessary to perform arthroplasty surgery or joint replacement. This surgical method is highly sensitive, and pre- and post-surgery measures are more important. Joint repair, reconstruction and replacement surgery is called arthroplasty surgery. Depending on the severity of the damage, part or the whole joint can be destroyed and destroyed. To replace the destroyed joint, prostheses with different metal, ceramic, etc. materials are used. These prostheses have different durability depending on the patient's condition. Arthroplasty surgery is performed to replace the joints of various parts, including the knee, hip, shoulder, elbow, and ankle, but the most common surgeries are knee replacement and hip replacement. This surgery should be performed by an orthopedic specialist [7].

Many of your knee problems and pains can be improved with non-surgical procedures. These measures include: strengthening the muscles around the knee, weight control, taking painkillers and anti-inflammation, physiotherapy, injecting joint medicines. Knee joint replacement is recommended only when the joint is severely damaged and the pain and discomfort of the knee has not responded to other alternative methods, or the knee has a severe and progressive deviation and the knee arthritis is severe [8]. The main reason for knee joint replacement is arthritis. Although there are many types of arthritis, the most common types of arthritis are the following three types:

- ✓ Osteoarthritis of the bone.
- ✓ Rheumatism.

✓ Arthritis caused by damage [9].

A very important point is that before surgery, the patient should know what benefits this operation has for him and what problems it cannot solve and what problems it can create for him. More than 90% of people after knee joint replacement, their pain is significantly reduced and they can perform daily activities better [10]. Of course, this surgery can never make your knee completely like a healthy knee. After surgery, you can do activities such as walking, swimming, cycling, driving, climbing stairs or uphill. Activities such as fast walking, climbing hills and mountains, skiing, tennis, lifting objects weighing more than 25 kg are not suitable for the artificial joint, and activities such as running (Figure 1), jumping and impact sports are very dangerous for the artificial joint. Even if we follow all the tips for a good care of the artificial joint, after some time the plastic part of the joint wears down [11-13]. Of course, too much physical activity or too much weight accelerates this process. The goal of arthroplasty is to restore the function of the stiffened synovial joint and relieve pain [14].



Figure 1. Effect of Tranexamic Acid on Reducing Bleeding

As a surgery, it is usually performed when drug treatment has not improved the function of the affected joint. There are two types of arthroplasty surgery:

- ✓ Joint removal.
- ✓ Interspatial reconstruction.

Arthroplasty involves removing a portion of bone from a stiff joint, increasing the distance between the bone and socket to improve range of motion. Scar tissue eventually fills the gap and narrows the joint space again. Pain is relieved and movement is restored, but the joint is less stable.

Types of arthroplasty surgery

According to the type and severity of joint damage, two types of arthroplasty surgery are performed. In both types of arthroplasties, the surgeon uses artificial and special prostheses.

1- *Complete replacement of the joint:* If the joint damage is severe, both surfaces of the joint will be replaced with a suitable prosthesis. In this condition, all joint surfaces are destroyed and cannot be restored.

joint surface will be replaced with an artificial prosthesis. In this situation, part of the joint is healthy and the partial prosthesis is placed next to the healthy bone [15].

Reasons for performing arthroplasty surgery

For joint injuries, they first use non-invasive methods such as taking medicine, physiotherapy, direct injection of medicine into the joint, reconstructive surgery, etc. If these methods do not bring good results, the orthopedic specialist decides to replace the joint. Having pain and inflammation is one of the most important complications of joint injury [16-18]. Factors that can ultimately lead to joint replacement in patients include:

- ✓ Trauma or sudden impact (Figure2).
- ✓ Arthritis or osteoarthritis.
- ✓ Rheumatoid joint diseases such as rheumatoid arthritis.
- ✓ Dislocation and malunion of bones.
- ✓ Infection within the joint.
- ✓ Cartilaginous tumors within the joint.
- ✓ Synovitis disease.

2- *Replacement of a part of the joint:* If the damage to the joint is minor, only one side of the



Figure 2. Arthroplasty surgery

Necessary measures before performing arthroplasty surgery

Arthroplasty and joint replacement are among sensitive and important surgeries, and the patient must follow important points before performing the surgery. The procedures performed before the surgery will be explained to the patient by the relevant doctor or medical consultation team. In the following, we will refer to these important measures [19-21].

- ✓ Performing all tests such as blood test, electrocardiogram and chest X-ray.
- ✓ Presenting the results of diagnostic methods such as CT scan, MRI, etc.
- ✓ Consultation with the medical team regarding medical history and medications such as blood thinners.
- ✓ Avoid eating and drinking for at least 8 hours before surgery.

How to perform arthroplasty surgery

In most cases, arthroscopic surgery and joint replacement are performed under general anesthesia, unless the patient has special conditions and the anesthesiologist injects anesthesia. The surgical process is such that after the patient is admitted to the hospital and the anesthetic is injected, the surgery begins. First, they make an incision in the area of the joint, and then by pulling away the muscles and other parts of the joint, they remove the bone lesions [22-24].

Artificial prostheses are replaced in the place of the destroyed joint according to the type of arthroplasty. Next, orthopedic cement is used to keep the prosthesis firmly in place, and at the end, the incision is closed with sutures.

Care after arthroplasty surgery

The favorable and positive results of surgery depend a lot on post-surgery care. The care that is expressed under the title of medical advice is very important [25-27]. In this section, we explain care after arthroplasty surgery.

- ✓ Taking all medications prescribed by a specialist doctor.
- ✓ Avoiding heavy exercises and activities.
- ✓ Using assistive devices such as walkers and crutches depending on the type of joint replacement.
- ✓ Attending physiotherapy sessions.
- ✓ Having a healthy and nutritious diet.
- ✓ Regular dressing of wounds.

Benefits of arthroplasty surgery

Some patients are very concerned about the results of arthroplasty surgery [28-30]. Due to the advancement of surgical methods and the use of high-quality prostheses, these concerns are reduced to a great extent, so that the patient will see important benefits after the surgery. Among the benefits of arthroplasty surgery are:

- ✓ Reduce or eliminate pain and inflammation caused by injury.
- ✓ Extend the range of motion.
- ✓ Improve joint performance.
- ✓ Improving the quality of life.
- ✓ increasing the self-confidence.

Possible complications from arthroplasty surgery

Arthroplasty surgery, like other surgeries, has complications. The extent of these complications depends on the skill, knowledge and experience of the orthopedic surgeon and the post-surgery care. In this section, we mention the possible complications caused by arthroplasty surgery.

- ✓ feeling pain.
- ✓ Swelling and inflammation.
- ✓ Bleeding wound.
- ✓ Incidence of infection.
- ✓ Short-term side effects of anesthesia.
- ✓ Damage to nerve vessels.
- ✓ Allergic reaction of the body to artificial prosthesis.
- ✓ Need to replace the joint again.

Diagnosis of arthroplasty

Debilitating pain and reduced quality of life are the primary indications of arthroscopic procedures. Patients at this stage of discomfort and disability have most likely already been diagnosed with some form of arthritis. Pain and stiffness in weight-bearing joints are the main symptoms patients report, although some people also experience pain at night [31]. Other symptoms may include stiffness, swelling and locking of the joint, and even joint collapse, especially when the knee or hip is affected. To determine the degree of disability, the referring physician or surgeon will likely ask questions about walking, exercise ability, need for walking aids, and ability to perform self-care tasks such as dressing and bathing. In addition to assessing the joint itself and the level of mobility (Figure 3), the clinical examination includes an assessment of the patient's general health, the condition of the ligaments and muscles around the injured joint, as well as an assessment of the patient's mental outlook and social conditions to help develop the most effective post-operative rehabilitation program. Diagnostic tests usually include the following:

- ✓ X-rays of the affected joint and other joints to determine joint space loss.
- ✓ Imaging studies such as computed tomography, magnetic resonance imaging (MRI), and bone densitometry to evaluate bone loss or bone infection.
- ✓ Heart tests such as an electrocardiogram to evaluate the heart and circulatory system.
- ✓ Blood tests to rule out infection and possibly to confirm arthritis.

Things that are done before arthroplasty

Before arthroplasty, standard preoperative blood and urine tests are performed to rule out conditions such as anemia and infection. If the patient has a history of bleeding, the surgeon may ask you to perform clotting tests [32]. The patient meets with the anesthesiologist to discuss specific conditions that may affect anesthesia. Surgery is not performed if there is an infection anywhere in the body, or if the patient has certain heart or lung diseases. Smokers are asked to quit smoking.



Figure 3. Things that are done before arthroplasty

Also, weight loss is recommended for overweight patients. If the surgery involves deep tissue and muscle, such as a total hip arthroplasty, the surgeon may order blood units to be prepared. If a transfusion is needed to replace blood lost during the procedure, healthy patients may be asked to donate their own blood, which will be returned to them at the time of the procedure. Some pain medications may be discontinued weeks before surgery.

How do I prepare for arthroplasty?

- ✓ Your therapist will explain the arthroplasty procedure to you and give you the opportunity to ask any questions about the procedure.
- ✓ You will be asked to sign a consent form giving your permission for the procedure. Read the form carefully and ask questions if something is not clear.
- ✓ In addition to a complete medical history, your doctor may perform a complete physical exam before the procedure to ensure that you are in good health. You may have blood tests or other diagnostic tests.
- ✓ If you are allergic to any medicine, latex or anesthetics, inform your doctor.
- ✓ Tell your doctor about all prescription and over-the-counter medications and herbal supplements you are taking.
- Tell your doctor if you have a history of bleeding disorders, or are taking anticoagulants, aspirin, or other medications that affect blood clotting. It may be necessary to stop these medications before the procedure.
- ✓ If you are pregnant, or suspect that you are pregnant, you should tell your doctor.
- ✓ You will be asked to fast for 8 hours before the procedure, usually after midnight.
- ✓ You may receive sedation before the procedure to help you relax.
- ✓ You may meet with a physical therapist before surgery to discuss rehabilitation.
- ✓ Depending on your medical condition, your surgeon may request other specific medications.

How is arthroplasty surgery performed?

Arthroplasty requires hospitalization. This procedure may be done while the person is asleep under general anesthesia. The amount of anesthesia is something that should be determined based on the extent of the surgery and your healthcare provider's actions and specific recommendations. In knee arthroscopy, the prosthesis consists of three parts:

- ✓ A part of the tibia (lower part) that replaces the upper part of the lower bone (tibia).
- ✓ A femur (the upper part) that replaces the femur (the upper bone where the patella is located).
- ✓ A patellar part (knee cap) to replace the surface of the patella.

The thigh part is made of metal and the tibial part includes a metal tray and a plastic spacer. The patella is made of plastic, but it can be either plastic or metal [32]. If your surgeon performs a minimally invasive procedure, a smaller incision means less damage to muscles and tendons. Once the damaged joint is repaired, removed, or replaced, the incision is closed with surgical sutures and finally a dressing and bandage are applied.

Actions after recovery from surgery

After surgery, you will be monitored in the recovery room for several hours. Once your blood pressure, pulse and breathing have stabilized and you are awake, you will be transferred to a hospital room where you will stay for a few days. A physical therapist will meet with you shortly after surgery to discuss an exercise rehabilitation program. As your pain is controlled with various pain relief treatments, including pain relievers, you will be up and moving right away. You will follow a rehabilitation program in the hospital and after discharge. You'll either be discharged home, or you'll go to a rehabilitation center and continue

physical therapy to regain strength and range of motion. After returning home, the surgical site should be kept dry and clean. You will be given instructions about bathing. When you go for your next visit, the stitches will be removed [33]. Also watch for signs of infection, including:

- ✓ Ague.
- ✓ Redness or swelling.
- ✓ Bleeding at the surgical site.
- ✓ Increased pain at the surgical site.
- Numbness or tingling in the affected joint.

Diet Change

You do not need to change your diet unless your doctor tells you to. You will be notified of any activity restrictions, including driving. Your doctor may have additional recommendations and instructions based on your unique situation [34-36]. Depending on the type of arthroplasty, your full recovery can take up to four months. Your health care provider will evaluate you one week after surgery and determine the specifics of your physical therapy program. For the next two to six weeks after surgery, you will participate in physical therapy and work to resume your normal activities. Do not resume any sports until you have received clearance from your doctor to confirm your fitness. In the next three to four months, you will see an improvement in strength and range of motion in the repaired or replaced joint. By this point, the pain and swelling should be completely gone, and your doctor will approve your return to your favorite sports and high-intensity activities [37].

What are the risks of arthroplasty?

As with any surgery, complications can occur, including the risk of infection and blood clots. People who are at risk for complications are those who have heart problems. It can also cause side effects in people with diabetes whose diabetes is not well managed and who have a weak immune system. If the nerves around the replaced joint are damaged during surgery, the person will suffer nerve damage, which is usually rare [38]. Another common risk associated with arthroplasty is that the new joint does not function well and feels weak and stiff. There is also the possibility of loosening or dislocation of the implants. Replacement fittings may require replacement due to wear and tear. There may be other risks based on a person's overall health and any medical conditions. The surgeon may prescribe antibiotics and blood thinners in hopes of preventing complications. Be sure to discuss all concerns with your surgeon before the day of surgery.

Background research

In 2018, Mina et al conducted a meta-analysis study aimed at the effect of tranexamic acid to reduce bleeding in prostate surgery. They stated that tranexamic acid is effective in prostate surgery in the long term to reduce bleeding. In this study, tranexamic acid was given intravenously to patients before surgery. The results of their study were consistent with our study.

In 2018, Meng et al conducted a study with the aim of investigating the effect of tranexamic acid in reducing bleeding around prostate duct removal and stated that tranexamic acid can reduce bleeding without thrombolytic complications. The results of their study were in line with our study.

In 2016, Eti et al conducted a study aimed at the effect of oral tranexamic acid prophylaxis in prostate surgery. The use of oral tranexamic acid reduces bleeding in patients. In our study, intravenous tranexamic acid was more effective than other types of this drug. In any form of oral tranexamic acid, it also reduced bleeding in Maniez's study [38].

In 2016, Ali Mirman Soori and his colleagues conducted a study with the aim of investigating the effect of tranexamic acid on the amount of blood transfusion required in prostatectomy

surgery. Administering tranexamic acid before surgery reduces the amount of transfusion 24 hours after the end of surgery in patients undergoing TURP. The results of our study also indicated a reduction in bleeding in surgery by intravenous tragaxamic acid.

In 2016, Pour Fakher et al conducted a study with the aim of the effect of local tranexamic acid in prostate surgery to reduce bleeding. Bleeding was less in the tranexamic acid group. Platelet reduction in the intervention group was lower than the control group. In our study, oral tranexamic acid also reduced bleeding, but the effect of intravenous tranexamic acid in bleeding management and surgeon satisfaction was more than other types of this drug [39].

In 2011, Kumar et al conducted a study aimed at the effect of tranexamic acid on reducing bleeding during prostatectomy surgery. They stated that it was evident in the reduction of bleeding in the tranexamic acid group. The results of their study were consistent with our study [40-42].

Crescenti et al. conducted a study in 2011 with the aim of using tranexamic acid to reduce bleeding in patients with radical retropubic prostatectomy. They stated that the use of lowdose tranexamic acid in reducing the need for blood transfusion during surgery can be safe and suitable for patients [4]. The results of the study by Crescenti et al. were in line with our study.

Raniko et al. conducted a study aimed at the effect of tranexamic acid on primary bleeding during prostate surgery.

The effect of knee replacement surgery on the quality of life of patients with severe osteoarthritis.

The knee joint is one of the most important joints in the body, which is affected by various inflammatory and degenerative diseases that can cause the destruction of the articular cartilage and the loss of the proper function of the joint. Osteoarthritis causes significant clinical complaints in sufferers due to disability caused by symptoms such as pain, joint instability, reduction and limitation of joint range of motion. Knee, hip and hand joints are common places of osteoarthritis. Osteoarthritis becomes more common with age. This complication is a major problem for the elderly and a major cause of disability in these people. More than half of the world's people over the age of 65 experience changes in the knee joint that indicate the presence of osteoarthritis. Having severe osteoarthritis significantly affects a person's quality of life. The natural course of this condition leads to the disability of the patient and causes limitations in the physical activities and social life of the patients [47].

According to the definition of the world health organization, quality of life is not only the absence of disease or disability, but also the conditions in which a person feels satisfied in terms of emotional, social and physical functioning. The result that is finally achieved and remains for the patient after a medical or surgical treatment is the best and most basic criterion for judging the effectiveness of that treatment. Therefore, quality of life has always been considered as a final outcome in clinical trials, interventions and health care and is an indicator of treatment effectiveness.

The most important problem for patients with osteoarthritis is pain, which can negatively affect other aspects of life and have a profound effect on the quality of life of sufferers. Currently, there is no known treatment to stop or improve the process of osteoarthritis, and most of these methods are used to control symptoms. Most patients with knee osteoarthritis can control their disease with drug treatments and conservative methods, but these methods have a palliative effect and only delay the disease process, and finally with the progress of the disease, final treatment such as joint replacement is needed.

In general, studies have shown that knee joint replacement surgery in patients with severe osteoarthritis is very effective in improving the quality of life of these patients, especially by improving physical and social functioning, reducing mental problems. In most cases, knee joint replacement is known as an effective and cost-effective treatment model for severe osteoarthritis of the knee joint. When we compare knee replacement surgery with other treatment methods for osteoarthritis of the knee, the increase in quality of life and years of life that pass without symptoms of the disease. On the other hand, the cost of knee replacement surgery is significantly superior to other methods.

Conclusion

Tranexamic acid competitively inhibits the activation of plasminogen and thus reduces the conversion of plasminogen to plasmin. This drug also directly inhibits the activity of plasmin, but large amounts are required to produce this effect. The use of this drug in pregnant women is strictly prohibited and it is classified as group X, it may cause death or organ failure of the fetus. This medicine should not be used in patients with intravascular clot formation. Tranexamic acid is a drug known to help blood clots progress by preventing a natural process called fibrinolysis. This drug is currently used in cases where bleeding is a significant concern, such as after heart surgery or major trauma. This medicine can be used orally and directly on the bleeding site or injected into the vein. Interspace reconstruction is a place to change the shape of the joint and add an artificial disc between the two bones that make up the joint. Prosthesis can be made of plastic, metal, ceramic material or made of body tissue such as skin, muscle or fascia. When internal reconstruction fails, total joint replacement may be necessary. In recent years, joint replacement has become an option for most chronic knee and hip problems, especially due to improvements in the type and quality of prostheses. Elbow, shoulder, ankle,

and finger joints are most likely to be treated with joint removal or inter-articular reconstruction. Arthroplasty is performed on people who suffer from severe pain and stiffness in their joints.

Arthritis (OA) is the most common disease that causes joint destruction with pain and movement disorders. Other causes include rheumatoid arthritis (RA), hemophilia, synovitis, and rare bone diseases, all of which destroy cartilage. Arthroplasty rather than joint replacement is more often done in people with rheumatoid arthritis, especially when the elbow joint is involved. Joint replacement is usually reserved for elderly patients. Because the lifetime of its benefits is limited. The younger the patient, the more confidence in the treatment. Tranexamic acid or tranexamic acid is a tablet or capsule, white and oval in shape. Trangasmic acid capsule is used to improve blood clotting and is included in the category of blood clotting and anti-bleeding drugs. Tranxamic acid is not a hormone. Tranexamic acid is used to treat heavy menstrual bleeding in women. This medicine is used to reduce the amount of bleeding during your period, but it does not stop menstrual bleeding. Transid capsules are also used to treat vaginal bleeding or spotting.

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