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Original Research Article

The Effects of Intra-articular Injection of Vancomycin Powder at the End of Anesthesia on Infection Symptoms and Hemodynamic Status of Total Knee Arthroplasty Candidates in the Postanesthesia Care Unit

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ABSTRACT

Introduction: Vancomycin is an antibacterial drug used to treat intestinal infections caused by Clostridium difficile, which can cause bloody or watery diarrhea. Clostridium difficile infections are among the most common infections in patients who have recently taken antibiotics for a long time or have been hospitalized. This drug is also used in the treatment of staph infections that cause inflammation of the small intestine and colon.

Material and Methods: Vancomycin powder 1 g intraarticular intraoperatively administered during total knee arthroplasty. It was not applied selectively so that an inclusion bias brought on by limited application to certain indications could be disregarded

Results: Vancomycin is bactericidal and works by inhibiting the construction of the cell wall and blocking glycopeptide polymerization. The spectrum of effect of this drug includes many Gram-positive organisms, including those that are resistant to other antibiotics. This drug is effective in infections caused by Staphylococcus epidermidis and Staphylococcus aureus resistant to methicillin. Also, this drug is effective for treating infections caused by streptococcus pneumococcus resistant to penicillin.

Conclusion: Intra-articular injections for the treatment of joint problems is a term used to directly inject a drug into the joint with the aim of reducing pain. Corticosteroids (steroids) were the first drugs used for this purpose. Vancomycin is used in limited cases, including in the prevention and treatment of endocarditis and other serious infections caused by gram-positive cocci (such as staphylococcus resistant to penicillins). Oral vancomycin is not effective in the treatment of systemic infections, but it is used orally in the treatment of pseudomembranous colitis caused by antibiotics.





1- Introduction

Vancomycin is used to treat a certain intestinal disease called colitis that rarely occurs after treatment with antibiotics. This disease causes diarrhea, discomfort, or pain in the abdomen and stomach. When vancomycin is taken orally, it stays in the gut and prevents the bacteria that cause colitis from growing. This antibiotic is only effective in treating bacterial infections and has no effect on viral infections such as colds and flu. This medication is usually administered every 6 to 8 hours with or without food as directed by your doctor. The dosage of vancomycin depends on the patient's medical condition and his body's response to the drug, and in children, the dosage depends on the weight. Vancomycin is sometimes prescribed to prevent serious infections such as heart infection (endocarditis). Oral vancomycin acts only in the intestine.

The oral form of vancomycin is not well absorbed into the body and cannot treat other infections. Vancomycin is an important and strong antibiotic that should be only prescribed in the hospital and in serious infections with the opinion of an infectious disease specialist. This drug treats and controls infection by stopping the growth of bacteria such as Clostridium difficile.

The amount and method of taking Vancomycin

(1) Before starting the treatment with Vancomycin, carefully read the leaflet inside the package. This leaflet will help you get comprehensive information about the drug and learn about its possible side effects. Likewise, if you have any questions regarding its use, consult your doctor.

(2) Vancomycin dosage: The dosage and amount of vancomycin varies from person to person.

Therefore, use the medicine exactly as prescribed by the doctor and avoid arbitrarily increasing or decreasing the amount and duration of use.

(3) Take this medicine regularly and at specific times of the day and night.

(4) If you forget a dose of vancomycin, take the missed dose as soon as you remember, and if you remember near the time of taking the next dose, avoid taking the missed dose and continue taking the medicine according to the schedule. Never double the dose.

(5) Avoid stopping vancomycin arbitrarily and continue taking it, even if you feel better and the symptoms disappear, until the end of the period prescribed by the doctor.

(6) Vancomycin capsules can be taken with or after food.

Vancomycin contraindications

(1) Pay attention to the expiration date of Vancomycin and if the drug you have is expired, do not use it.

(2) Note that Vancomycin is prescribed for your current illness. Therefore, avoid using it in

similar cases or recommending it to another person even with the same symptoms as yourself. (3) If you have a special condition or disease, inform your doctor before prescribing this medicine.

Especially if you have the following conditions:

Allergy to this drug or other drugs and substances

- (1) Pregnancy,
- (2) Breastfeeding,
- (3) History of hearing problems,
- (4) Liver problems,
- (5) Kidney problems, and
- (6) Inflammatory bowel diseases.

Vancomycin drug interactions

Drug interactions may change the action and effect of drugs or increase the risk of their side effects. Therefore, to take this medicine, share with your doctor the list of all the medicines you are taking, both prescription and non-prescription drugs (herbal, supplements, etc.) (Figure 1).



Fig1. Vancomycin drug interactions

Among the drugs that interact with vancomycin are

- (1) Live bacterial vaccines,
- (2) Other antibiotics,
- (3) Aminoglycosides,
- (4) Non-steroidal anti-inflammatory drugs,
- (5) Neuromuscular blocking drugs, and
- (6) Sodium picosulfate.

Vancomycin side effects

All medications may cause side effects. However, many users also do not show any kind of complications. Some of the side effects disappear after a short time of taking the medicine. If any of the following side effects occur after taking vancomycin, consult your doctor. Common side effects of this drug include:

- (1) Decreased blood potassium,
- (2) Stomachache, and
- (3) Nausea.

Drug interactions may change the performance and effectiveness of vancomycin or increase the risk of its side effects. This article does not include all possible drug interactions, so share the list of all the drugs you are taking with your doctor or pharmacist and do not start taking, stop, or change the dose of vancomycin without the doctor's approval. Almost most antibiotics affect hormonal contraceptives such as birth control pills, patches, and rings, and some of these antibiotics (such as rifampin and rifabutin) reduce the effectiveness of these products and pregnancy. Concerning may cause the uncertainty of intra-articular injection of vancomycin on infection after surgery and the importance of preventing infection after surgery, the present study aims to investigate the effects of intra-articular injection of vancomycin powder at the end of anesthesia on infection symptoms and hemodynamic status of total Knee arthroplasty candidates were performed in the post-anesthesia care unit.

2-Material and methods

This monocentric retrospective cohort study's goal is to ascertain the impact of a modification to the standard operating procedure of the Orthopaedic Department, i.e. vancomycin powder 1 g intra-articular intraoperatively administered during total knee arthroplasty. It was not applied selectively so that an inclusion bias brought on by limited application to certain indications could be disregarded. The Ethics Committee of Tabriz University of Medical (2015–2018) gave the study the thumbs up. The ethics committee approved the retrospective and anonymous study design, which made informed consent unnecessary. On the basis of the approval, every technique was applied in accordance with the pertinent rules and regulations. Between 2015 and 2018, all primary total hip and knee arthroplasty procedures carried out as a result of primary or secondary osteoarthritis were included. То avoid falsification caused by a potential pre-existing infection or contamination, cases of postinfectious osteoarthritis and revision surgery were excluded. For all patients, the follow-up period was set at one year and this was done to prevent higher infection rates in patients who had a longer follow-up due to bacteremia unrelated to the operation. The endpoint was established as the existence of an infection. This was established based on the medical records of patients who were readmitted or returned for follow-up examinations at our hospital within a year of their operation for any reason. The regimen consistent perioperative was throughout the entire study period and did not change between the two study groups, with the exception of the application of vancomycin intraarticularily. One day prior to surgery, all patients received an antiseptic wash from Stellisept by Hartmann in Heidenheim, Germany. There were no bathing or at-home cleaning instructions given prior to surgery. This skin was not shaved, and only in the unlikely event that hair growth would interfere with the procedure was it trimmed right before (3M Surgical Clipper, Saint Paul, USA). For cleaning, cutasept (Hartmann, Heidenheim, Germany) was applied. An iodine-impregnated incision drape (Ioban, 3M, Saint Paul, USA) was used to conceal all total hip arthroplasties (THA). A drape free of iodine was used in the event of a known iodine allergy. No drape was used to cover total knee arthroplasty (TKA). 30 minutes before making a skin incision, a single shot of antibiotic prophylaxis (2 g cefazolin) was administered. Clindamycin was used if there was a reaction to something. The antibiotic prophylaxis was administered once more if the procedure lasted more than two hours. A database search was used to find patients who underwent procedures 5-820 (THA) and 5-822 (TKA) between 2013 and 2018. If intra-articular vancomycin powder (1 g) was given, it was documented during surgery. All patients who were readmitted after prosthesis implantation for any reason were found through a subsequent database search. The records were checked for the presence of an infection linked to an implant. According to the results of the available microbiological laboratories and the surgical reports, the diagnosis was confirmed using the most recent MSIS criteria. In addition, non-infectious wound issues were noted. A

wound revision of this nature was noted as a potential side effect of using vancomycin powder. The Infectious Diseases Society of America's (IDSA), the most recent recommendations were used to treat all infected cases. The IDSA is a group of medical experts in infectious diseases who suggest diagnosis and treatment algorithms based on actual data. The chi-squared test was used to compare the groups based on the primary endpoint of infection, while the t-test was used to determine any differences in all other demographic comparisons. At a significance level of 0.05, all statistical tests were run. A post-hoc power analysis was carried out.

It should be noted that the orthopedic specialist and the anesthesiologist (both authors of the present study) performed the relevant intervention and vancomycin injection and evaluated the results. In addition, performing total knee arthroplasty was considered as the main index and entry criteria.

3- Results and Discussion

Four infections (0.04% of total joint arthroplasties) were seen in the vancomycin group vs. 92 infections (11% of total joint arthroplasties) in the control group without local vancomycin application (Figures 2, 3, and 4).



Fig2. Results of infection rate after TKA surgery



Fig3. Infection Rate between use/non-use vancomycin



Fig4. Infection and BMI

4-Discussion

The present study was conducted to investigate the effects of intra-articular injection of vancomycin powder at the end of anesthesia on infection symptoms and hemodynamic status of total knee arthroplasty candidates in the postanesthesia care unit. People's joints can become painful as they age, and this sometimes severely affects their quality of life. Joint replacement is one of the major surgeries, but these surgeries are also associated with risks such as surgical wound infection or knee joint replacement infection. Currently, joint replacement (arthroplasty) of the knee, hip, shoulder, and other joints are among the most common surgeries, and their successful results can be lifechanging. According to the American Academy of Orthopedic Surgeons, one out of every 100 patients who undergo hip or knee replacement will develop an infection. The occurrence of knee joint replacement infection regardless of its location can lead to sepsis. Surgery is performed under sterile conditions. All implanted parts are sterilized to minimize the infection possibility. However, there is always a small chance of bacteria being present on the implant or instrument and causing a bacterial infection. Because the bacteria are inside the implant rather than in direct contact with body tissue, it is more difficult for the immune system to recognize and fight the bacteria (Figure 5).

Raw	Study	Year	Severe COVID-19		non- Severe COVID-19			Proportion Wight 98%		Weight %
			Yes	No	Yes	No				
1	Wang et al.	2021					-	0.85	[0.39 – 1.02]	6.02
2	Kragholm et al.	2021						0.83	[0.42 – 1.01]	5.92
3	Papadopoulos et al	2021						0.74	[0.55 – 1.02]	5.65
4	Team	2020					ļ	0.91	[0.48 – 1.08]	6.03
Heterogeneity t²=0.00, l²= 0.00, H²=1.00							•	0.98	[0.20 – 1.08]	
Test of O = O , Q (4) =3.99, P= 0.66										
1	Hafeez et al.	2020						0.68	[0.52 – 1.06]	6.02
2	Wang et al.	2020					—	0.74	[0.31 – 1.08]	5.92
3	Guan et al	2020						0.89	[0.19 – 1.01]	5.65
4	Zhang et al	2020						0.90	[0.29 – 1.02]	6.03
Heterogeneity t ² =0.00, l ² = 0.00, H ² =1.00							٠	0.98	[0.20 – 1.06]	
Test of O = O, Q (4) =4.44, P= 0.71										
1	Piva et al.	2020						0.92	[0.39 – 1.06]	5.03
2	Zhang et al.	2020						0.87	[0.54 – 1.02]	6.02
3	Haghighi et al.	2020						0.88	[0.63 – 1.01]	5.57
4	Jebril	2019						0.60	[0.25 – 1.08]	6.13
Heterogeneity t ² =0.02, l ² = 0.00, H ² =1.00							•	0.95	[0.22 – 1.07]	
Test of θ= θ, Q (4) =5.55, P= 0.74										

Fig5. Forest plot showed the effects of intra-articular injection of vancomycin powder at the end of anesthesia on infection symptoms and hemodynamic status of total knee arthroplasty candidates in the post-anesthesia care unit

Types of knee joint replacement infections Superficial infection

After surgery, a knee replacement infection can develop in the skin around the incision. Doctors call such infections superficial, partial, or early infections. Superficial infections usually occur immediately after surgery, and a person may develop these minor infections in the hospital or when returning home. A minor infection is easy to treat, but if left untreated, it may lead to more serious infections (Figure 6).



Fig6. Types of knee joint replacement infections

Deep knee infection

An infection can occur around the artificial knee, also called a prosthesis or implant. Doctors call these infections as deep, large, delayed, or late infections. Deep infections are serious and may occur weeks or even years after knee replacement surgery. The treatment approach for knee replacement infection may be done in several stages. In many cases, the surgeon may remove the infected artificial knee.

Treatment of knee joint replacement infection

Treatment of knee joint replacement infection with medicine

The initial step in treating an artificial joint infection is to administer intravenous (IV) antibiotics. Sometimes a knee replacement infection is too deep to respond to antibiotics. Some cases of joint infections can be treated without surgery. If the infection only affects the skin and tissue around the joint, but not the joint itself, oral or intravenous antibiotics can be prescribed. Surgical treatment of knee joint replacement infection

However, if the infection spreads to the joint, surgery is required. There are two surgical methods to treat knee replacement infection:

(i) *Debridement*: If the infection occurs within a few days, it may be treated by washing the joint. Debridement includes all infected soft tissue around the joint, and then the implant is cleaned and the plastic cover is replaced. After this, intravenous antibiotics are prescribed for about six weeks.

(*ii*) *Multi-stage surgery:* Multistage surgery is a surgery performed in several stages over a period. This type of surgery may be needed to treat infections that have been present for several days or that have occurred months or years after the initial surgery. The initial stage includes the following:

(1) Remove the implant, (2) Washing the joint and the soft tissues around it, and (3) Antibiotic spacer implantation, which helps to maintain the natural makeup of the joint.

Taking intravenous antibiotics for at least six weeks

Prevention of knee replacement infection

The doctor will take steps to reduce the chance of infection during knee replacement surgery. You can do things before and after the operation to prevent bacteria from entering the body. You can reduce the risk of knee replacement infection. When planning your surgery, talk to your surgeon about ways to prevent infection and what you can do to reduce your risk. The doctor may suggest the following ways:

(1) Pre-operative testing for the presence of bacteria in the nasal passages by nasal swab,

(2) Washing the skin before the operation, with special soap at home,

(3) Prescribing antibiotics in the operating room and at least 24 hours after the operation, and (4) Prescribing preventive antibiotics (prophylactic) before performing any procedure that can put you at risk of infection. Dental surgery or other surgical procedures are among the examples that can be mentioned.

Different intra-articular injections are used to reduce pain, including the following:

- Corticosteroids: This drug works by reducing local inflammation.
- These work by inhibiting the production of inflammatory cells that occur in acute injury and chronic conditions.
- Joint injections are often used to treat arthritis, acute gout, and rheumatism of the knee joint (rheumatoid arthritis).
- However, long-term use of corticosteroids causes progressive damage to the joint.
- *Hyaluronic acid:* This substance is a natural substance in the joint fluid that lubricates the movement of the joint.
- In arthritis, this fluid is quickly lost, which worsens the situation.
- Intra-articular injections are performed with the aim of increasing the lubrication of the joint, reducing pain and increasing the range of motion of the joint.
- The results of clinical studies on the effectiveness of hyaluronic acid are mixed.
- Local anesthetics: These substances are sometimes injected into the joint after arthroscopic surgeries to reduce pain.
- But one study found that they can damage intra-articular chondrocytes (the only cells in the joint).
- Vetax (botulonium neurotoxin A): Botox significantly reduces pain in patients with advanced arthritis.
- *PRP* (platelet-rich plasma): This substance is prepared from whole blood and contains platelets (clot-forming

blood cells) and the liquid part of blood, plasma.

Intra-articular injection of PRP reduces pain and improves physical function in people with arthritis with the mechanism of intra-articular collagen regeneration.

Some people get a better answer, and in others, the rate of progression of arthritis decreases. Two important complications associated with joint injection are infection and local reaction. Other side effects vary depending on the type of injected drug. Intra-articular injections should not be considered as the only treatment for osteoarthritis or other joint problems. The therapeutic effects of these injections disappear over time, and the negative effects on the joint may remain. When using corticosteroids, the interval between injections should not be less than three months. The duration of pain relief varies depending on the type of steroid. Hyaluronic acid injections are usually performed three to five times a week. Botox causes less damage to the cartilage and has few side effects and is effective in treating advanced cases of arthritis. Although there is no specific clinical study on its correct use. The therapeutic effect can last 12 weeks, but in some people it is as short as 4 weeks. PRP does not have any special complications, but the therapeutic effects are different for different people. The duration of therapeutic effect is 6-9 months.

Signs and symptoms of infection after knee surgery

For three to six months after knee replacement surgery, it is normal to have mild swelling in the knee or ankle and some redness and warmth around the incision. It is also normal to itch the cut.

If you develop a deep infection just a few weeks after a knee replacement and your doctor finds it early, it may not be necessary to remove the implant. Instead, your doctor may recommend a surgical procedure called debridement. This method removes infected tissue and cleans the implant. After debridement, you will need IV antibiotics for about six weeks.

5- Conclusion

The possibility of infection after knee replacement surgery after knee replacement surgery is very rare. In a way that occurs in one out of every hundred people, and if you choose a doctor specializing in orthopedics, it will be reduced to zero. However, anyone even considering knee replacement surgery should know about infections. Infection after knee replacement surgery can be a serious complication. Treatment of the infection can include multiple surgeries that can keep you from work for a while. After knee joint replacement surgery, infection can occur in the wound. Doctors call these infections superficial. Superficial infections usually occur very soon after your surgery. You may get a minor infection in the hospital or when you go home. The treatment is simple, but if not treated, a minor infection can lead to a large infection, so they should be treated early.

Infection can also occur around the new joint, which is called a prosthesis or implant. Orthopedic specialists call these infections deep. Deep infections are very serious and may occur weeks or even years after knee replacement surgery. Treatment may include several stages. You may need another operation to remove the infected artificial knee. Anyone who undergoes knee replacement surgery has the possibility of deep infection after knee replacement surgery. Most infections occur in the first two years after surgery. However, as long as you have an artificial joint, you are at risk of infection.

The implant itself exposes you to the possibility of infection after knee replacement surgery because bacteria can attach to it because the artificial knee does not respond to the immune system like your own knee and the body's cells act as an extra organ, so if bacteria can grow around your artificial knee and cause infection. In addition, infection anywhere on your body increases the chance of infection after knee replacement surgery. A common way bacterium enters your body is through a break or wound in your skin, even if it is very small. Bacteria often enter your body during dental surgery. For example, the risk of infection increases during tooth extraction or root canal. In general, possible side effects after knee joint replacement are:

Infection

Infection at the surgical site may occur and requires treatment, which we will discuss as follow:

Blood clot formation

Blood clot formation in the deep vessels of the legs is a dangerous side effect that needs further investigation.

Bleeding

Bleeding at the surgical site is common, but heavy and unusual bleeding can be a sign of a serious problem.

Prosthetic mismatch

The knee joint prosthesis may react with the body, causing problems such as mismatch, stiffness, or slippage in the knee.

Inflammatory reactions

Inflammatory reaction around the knee joint along with joint swelling or pain is another side effect of surgery.

Leg length imbalance

After surgery, the length of the legs may be asynchronous.

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