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### **Original Research Article**

# Investigating the Effectiveness of Prophylactic Cefazolin Injection before Spinal Anesthesia on Hemodynamic and Clinical Symptoms of Infection in Total Hip Arthroplasty

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#### K E Y W O R D S

Antibiotic Prophylaxis Preoperative THA

#### ABSTRACT

**Introduction:** Cefazolin injection at home is usually prescribed by specialists in hospital or clinical settings to treat bacterial infections. Cefazolin may be prescribed to people who have a bacterial infection whose body does not respond to other antibiotics or to people who are at risk of infection after surgery.

**Material and Methods:** The main result was the emergence of any SSI within a year of surgery. The surgical information recording system had records for every patient who underwent THA. The attending surgeon examined the surgical site daily while the patient was admitted, and the clinical data was documented on a standardized record form. Patients were scheduled for follow-up appointments in the outpatient clinic at 2 & 6 weeks, 3 & 6 months, and 1 year after surgery following discharge.

**Results:** Simple dressings, superficial wound revision, and short-term oral antibiotics were used to treat cases of superficial incisional SSIs. Deep incisional and organ-space SSI cases underwent open or arthroscopic debridement while keeping the prosthesis in place, either with or without subsequent oral medications.

**Conclusion:** In case of infection in the artificial joint, the most important point is timely diagnosis. Symptoms can be swelling, redness and pain in the affected joint. It is important not to start antibiotics for the patient before a definitive diagnosis because it not only makes the diagnosis difficult, but also interferes with proper and effective treatment. For diagnosis, it is necessary, if necessary, draw joint fluid and send it to the laboratory. In cases where the infection was detected in time in the first four weeks from the beginning, the treatment can be done by keeping the prosthesis. In these cases, washing the joint completely and prescribing appropriate antibiotics based on culture results controls the infection in 80% of cases.





#### **1. Introduction**

Cefazolin is an antibiotic of the first generation cephalosporins and is mainly used in hospitals and is used in moderate to severe infections [1-<u>3</u>]. This drug is used in the treatment of bacterial infections of lungs, skin, soft tissue, bones and joints, blood, heart valves, and urinary tract, especially during pregnancy. This drug is also used to prevent infection after surgery. Cefazolin is a bacteriocide that prevents the formation of the bacterial cell wall and thus causes the death of growing and dividing bacteria [4]. Cefazolin drug is used by infusion or injection. Patients who have never had a beta-lactam allergy or an MRSA infection are most frequently given cefazolin for surgical prophylaxis [5-7]. Cefazolin is not used for surgical sites when the most likely organisms cannot be eradicated by the drug alone [8], for patients who only need cefazolin for preoperative surgical prophylaxis, those or who have severe adverse reactions to it frequently use

clindamycin or vancomycin as a substitute [9], and patients with beta-lactam allergies can typically tolerate cefazolin [10,11], if MRSA has been colonized, or in patients who are particularly vulnerable to MRSA (i. e. in the absence of the need for additional antibiotics to treat potential gram-negative or anaerobic organisms (e.g., patients in nursing homes, people who have previously contracted MRSA, or people who have recently had a positive MRSA colonization test) [12], patients who require antimicrobial additional protection (e.g., cefoxitin, ertapenem, or cefazolin combined with metronidazole), for colorectal cancer. Additional antibiotics are available based on particular surgical sites besides hospital- and patientspecific antibiotic resistance [13]. Cefazolin ampoule is a bacteriocide that prevents the construction of bacterial cell wall and, in this way, causes the death of growing and dividing bacteria (<u>Figure 1</u>).



Fig1. Prophylactic cefazolin injection before spinal anesthesia

# Antibacterial effect

Cefazolin is mainly a bactericidal drug, but it may also have bacteriostatic effects [14]. The level of activity of this drug depends on the type of organism, the amount of penetration in the tissue, the amount of drug used, and the rate of reproduction of the organism. Cefazolin binds to the proteins that bind penicillin, and thus inhibits the construction of the bacterial cell wall. Cefazolin is effective against *Escherichia coli*, *Enterobacteriaceae*, *Haemophilus influenzae*, *Klebsiella, Proteus mirabilis, Staphylococcus*, *Streptococcus pneumoniae*, and *Streptococcus* [15].

# Drug absorption

It is not well absorbed from the digestive tract and should be administered by injection  $[\underline{16}]$ .

# Distribution

In most body tissues and fluids, such as gall bladder, liver, kidneys, bone, and phlegm, Bile, synovial fluid, and peritoneum are widely distributed. The penetration of this drug into the cerebrospinal fluid (CSF) is very low. It passes through the placenta. About 74-86% of it is bound to protein [<u>17</u>].

#### *Metabolism* Not metabolized.

Cefazolin injection and things you should know about it:

# Excretion

It is mainly excreted unchanged through urine and through renal tubular secretion and glomerular filtration. A small amount of it is secreted in breast milk. Its elimination half-life is about 1-2 hours in patients with normal renal function, and 12-50 hours in patients with very advanced kidney diseases. Cefazolin can be removed from the body with hemodialysis or peritoneal dialysis [<u>18</u>].

# The amount and method of taking cefazolin

Before starting the treatment with cefazolin drug, carefully read the drug leaflet inside the package. This leaflet will help you get comprehensive information about the drug and learn about its possible side effects. Furthermore, if you have any questions regarding its use, consult your doctor [19]. The dose and amount of cefazolin varies from person to person; use the medicine exactly as prescribed by your doctor. Do not take

this medicine in more or less amounts than prescribed by the doctor. Take this medication exactly as directed by your doctor and complete the course of treatment even if you feel better and your symptoms are gone. Stopping the drug early may lead to a return of the infection [20-22]. The best effectiveness of cefazolin is achieved when you inject the medicine every day at certain times of the day and do not miss doses. During treatment with this medicine, drink enough fluids unless you are restricted by your doctor [23].

If your condition does not improve or even worsens after taking the medicine for a while, inform your doctor. If you inject this medicine at home, get all the instructions related to preparation, see the doctor, and ask about the proper storage of the medicine. In adults, it can be taken from 250 mg intramuscularly or intravenously every 8 hours to 1 gram every 6 hours and in children, 8 to 12 mg per kilogram of child's weight can be used intramuscularly or intravenously every 8 hours, or 6 to 12 mg per kilogram of child's weight every 6 hours. More precisely, cefazolin injection is as follows:

#### Adults

The usual dose of cefazolin in adults is 250 mg to 1.5 g by infusion every 6 to 8 hours. The maximum daily dose of cefazolin is 6 grams, which can be increased to 12 grams in rare cases [24].

#### Babies and children

In babies up to one month old or children who weigh less than 2 kg or in children who weigh more than 2 kg but 7 days or less have passed since their birth, cefazolin dose as intravenous infusion, 20 mg per kg body weight every 12 hours, in babies older than 7 days or heavier than 2 kg, 20 mg for each kilogram of body weight every 8 to 12 hours, and in children between 6.25 and 25 mg for each kilogram of body weight every 6 hours or it is 3.8 to 3.33 mg every 8 hours. In adults and children with kidney failure, the dose of the drug should be adjusted by the doctor [25].

#### Intravenous infusion

The contents of the vials of 250 mg in 5 ml, 500 mg, and 1 g were dissolved in 10 ml of injectable sterile water and the obtained solutions were mixed again with 50 to 100 ml of infusion liquid such as sodium chloride solution. For injection, 5 or 10% dextrose injection solution was diluted and 0.9% sodium chloride injection, Ringer's injection solution was diluted and infused according to the prescribed dose within 30 minutes (Figure 2) [26]. Since proper antibiotic administration during anesthesia and total hip surgery is very important, the present study was conducted to investigate the effectiveness of prophylactic cefazolin injection before spinal anesthesia on hemodynamic and clinical symptoms of infection in total hip arthroplasty.



Fig 2. Cefazolin injection for spinal anesthesia

#### 2. Material and methods

#### 2.1. Patients and study environment

The present study is a randomized clinical trial, double-blind (the main researcher and the person analyzing the results), and with parallel groups and with the participation of patients who are candidates for hip joint replacement (unilateral) in Shohada and Imam Reza hospitals (Tabriz University of Medical Sciences-Iran) in 2016. The care bundle entails:

(1) The use of an appropriate antiseptic agent for surgical scrub and skin preparation. Aqueous solutions of 10% povidone-iodine and 2% chlorhexidine-alcohol are both considered appropriate; we used an aqueous solution of 10% povidone-iodine.

(2) The appropriate use of antimicrobial prophylaxis: Timing (1 h before). A retrospective cohort study was conducted among THA patients from the start of the care bundle to September 30, 2017. All patients receiving THA during that period were included. These patients were located using a system for recording surgical information that prospectively records information on every surgical case performed in both inpatient and outpatient settings. Since elective THA is not appropriate for patients with type II wound classifications, we only included the type I surgical wound classification in our analysis. (3) The main inclusion criterion for entering the study was performing hip joint replacement surgery, and the main criterion for exiting the study was sensitivity to antibiotics, especially cefazolin.

#### **3. Results and Discussion**

Antibacterial effect: Cefazolin is mainly a bactericidal drug, but it may also have bacteriostatic effects. The level of activity of this drug depends on the type of organism, the amount of drug penetration in the tissue, the amount of drug consumption, and the rate of reproduction of the organism. Cefazolin binds to the proteins that are the binding site of penicillin, and in this way, it inhibits the construction of the bacterial cell wall. Cefazolin is effective against Escherichia coli. Enterobacteriaceae, Haemophilus influenzae, Klebsiella, Proteus Staphylococcus, mirabilis, *Streptococcus* pneumoniae, and Streptococcus (group A betahemolytic). 14 (11.06%) cases had SSIs, eight (00.60%) of which had infections in the prosthetic joints. In risk categories 0, 1, and 2, respectively, the SSI rates were 0.86 percent (8/926), 1.30 percent (5/384), and 7.69 percent (1/13) when stratified by the NNIS risk index.

Of the 14 procedures that led to infection diagnoses, four (29%) had superficial incisional SSIs, two (14%) had deep incisional SSIs, and eight (57%) had organ-space SSIs. The majority of the SSIs (11/14, or 79%) was developed within three months of surgery (Figure 3).



Fig 3. Infection rate After THA in deference BMI

Fever, chills, lethargy, sweating, and weight loss are possible symptoms of infection. The occurrence of these symptoms during treatment with cefazolin may indicate the exacerbation of your disease or the addition of a new infection to the previous disease. Cefazolin can cause a false positive response in the urine sugar test. If cefazolin is injected into your vein, it is better to be familiar with the symptoms of skin infection caused by angioket. In case of pain, warmth, redness, swelling, and irritation in the injection area, inform the medical staff. The effectiveness of birth control pills may decrease when using cefazolin. Cefazolin was used as antimicrobial prophylaxis, given less than an hour before incision, and discontinued within 24 hours in all of the SSI cases. Eight cases (57%) had pathogens identified: two cases (25%) each of methicillincoagulase-negative staphylococci, resistant methicillin-sensitive S. aureus (MSSA), two cases (25%) each of MRSA (Figure 4).



Fig 4. Time to reinfection rate

Simple dressings, superficial wound revision, and short-term (2 weeks) oral antibiotics were used to treat cases of superficial incisional SSIs.

Deep incisional and organ-space SSI cases underwent open or arthroscopic debridement while keeping the prosthesis in place, and then underwent a lengthy course of intravenous antibiotics lasting at least three months, either with or without subsequent oral medications. There were no cases of relapse within at least a year of treatment for any of the 14 patients with SSI who overcame their infections without removing their prostheses.

#### Respect for the care package

In every instance, the preoperative antiseptic agents used in the surgical scrub and skin preparations were appropriate. In addition, using HEPA filters, laminar air flow, and traffic control, all THAs were carried out in the same operating room with sufficient ventilation (about 15 times per hour). One hour prior to the incision, a prophylactic antimicrobial agent was given in 98.7% (1306/1 323) of the procedures. Ninetynine percent (1315/1323) of the cases involved the use of cefazolin, and 95 percent (1260/1323) of all THAs involved the use of an antibiotic within 24 hours of the procedure (Figure 5).



Fig 5. Respect for the care package

#### Factors that could lead to surgical site infections

The only preoperative infection that was not at the surgical site was the only statistically significant risk factor for SSI. Cefazolin ampoule is sometimes injected together with serum, although injecting this ampoule with serum is not contraindicated, but the instructions of the product manufacturer and expert opinion should always be prioritized in this regard. On the other hand, if there is a sign of sensitivity to any type of injection in the past, you should definitely inform the specialist about this issue. The pain caused by the injection of many antibiotics is normal, this pain can be accompanied by burning; however, the duration of this burning and pain is important.

#### Discussion

The present study was conducted to investigate the effectiveness of prophylactic cefazolin injection before spinal anesthesia on hemodynamic and clinical symptoms of infection in total hip arthroplasty. Infection in the artificial hip joint after joint replacement surgery is an important issue in medicine, which has adverse consequences for the patient and the medical team. In general, in cases where an open fracture has occurred, there is a possibility of infection. In open fractures with a wound, it becomes easier for microbes to enter the body [27]. If the environment is clear, the microbes will start to cause infection. In closed fractures, the probability of infection is much lower, unless the surgeon has used open surgery to treat the fracture. In cases where only the skin is infected, the treatment is easy. However, in some cases when the infection penetrates the bone, the treatment will face certain problems [28].

# Factors related to joint surgery that increase the risk of infection

The risk of infection after joint replacement surgery is higher in the following groups:

(1) Patients who have undergone revision surgery (joint replacement surgery) are 8 times more at risk than patients who undergo joint replacement surgery for the first time.

(2) In the case of knee replacement surgery, it has been proven that the use of metal-on-metal prostheses causes 20 times more infections after joint replacement surgery than metal-on-plastic prostheses [29].

(3) Patients with rheumatoid arthritis are 2.6 times more likely to get infections after joint replacement surgery than other patients with arthritis [30].

Infection treatment techniques after joint replacement surgery

#### Non-surgical methods

If the infection has not penetrated deep into the joint and only the skin and soft tissue around the joint is infected (superficial infections), oral, or intravenous antibiotics are used to treat the infection [31].

#### Surgical procedures

The standard technique for the treatment of infections after arthroplasty includes complete debridement, removal of dead tissue, and complete replacement of the joint prosthesis. Complete debridement of deep infections that develop shortly after joint replacement surgery, with joint washing surgery [32], are treated. In this procedure, which is called debridement, the surgeon removes all infected soft tissues [33], and then the joint prosthesis is completely disinfected and the plastic part of the spacer is placed [34]. It is necessary to take intravenous antibiotics for six weeks after surgery. Staged surgery-re-replacement, the more time that has

passed since the infection started, the more difficult it is to treat the infection and it requires the removal of the joint prosthesis [35]. Once the orthopedist confirms complete healing of the infection (typically six weeks after removal of the infected prosthesis), the patient can undergo joint replacement surgery. Replacement surgery is the second step in the treatment of infection. In replacement surgery, the orthopedist removes the spacer containing the antibiotic, washes the joint, and reinserts the perfect artificial joint into the patient's body [36].

Treatment of infected hip joint after arthroplasty surgery with a new prosthetic system

#### Part I-Treatment of joint infection

Prosthesis of antibiotic-loaded acrylic cement (PROSTALAC) is designed to treat joint infection while maintaining joint function [37]. The use of this type of prosthesis instead of conventional space-creating cement brings acceptable results in the treatment of artificial joint infection after arthroplasty surgery. In a study, it was shown that the use of conventional spacer cement increases the risk of joint loosening after joint replacement surgery [38] while the risk of joint loosening was significantly reduced in patients whose infection was treated with PROSTALAC (Figure 6). The reason for this is to maintain the stretching of tissues when using PROSTALAC; which allows the tissue to adapt better to the prosthesis after the replacement surgery [39].



Fig 6. Treatment of joint infection

# Part II-Maintaining efficiency and health and improving the patient's quality of life

Infection of the replaced joint has adverse effects on the life and health of patients. PROSTALAC prosthesis increases joint function and quality of life of patients treated for joint infection. By creating a temporary prosthesis surrounded by antibiotic-containing cement, the PROSTALAC prosthesis allows the patient to move the hip joint during treatment. Patients who are treated for deep joint infections with PROSTALAC prosthesis, their hip joint will have less pain and, at the same time, better function in the future. In this way, it can be mentioned that PROSTALAC prostheses are an excellent alternative to the conventional cement spacers and maintain function and reduce joint pain during the treatment period of infections around the prosthesis [40].

#### 4. Conclusion

Cefazolin falsely increases urinary or serum creatinine concentrations (when measured by the Jaffe reaction). Cefazolin also makes the result of the Coombs test positive and may cause falsely positive results of the urine sugar test by the copper sulfate method (Benedict's reagent or Clinitest). AST, ALT, ALP, bilirubin, GGT, and LDH levels may increase. The number of eosinophils may increase and the number of neutrophils, white blood cells, and platelets may decrease. Probenecid competes with cephalosporins for tubular secretion in the kidneys and therefore inhibits the renal excretion of these drugs. As a result, the simultaneous use of probenecid with this drug may increase the concentration and prolong the presence of the drug in the serum. The simultaneous use of this drug with medicines that cause kidney toxicity (vancomycin, cleistin, polymyxin B, and aminoglycosides), or diuretics that act on the arch of Henle, increases the risk of kidney toxicity. Simultaneous use with drugs with a bacteriostatic effect (tetracyclines, erythromycin, or chloramphenicol) may prevent the bactericidal activity of the drug and avoid simultaneous use.

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