Original article

Comparison between the Efficacy of prophylactic Cefazolin and the combination of Cefazolin and Cephalexin in open reduction and internal fixation of long bone fractures in lower extremities

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Abstract

Objective: Surgical site infection (SSI) is the second most common cause of hospital infections and is responsible for nearly 15% of these infections. Due to an increase in bacterial resistance, the lack of similar studies in our country, we conducted a study.

Methods: in this clinical trial, The patients were randomly divided into two groups: the case group that received intravenous antibiotics for 24 hours (2 gr cefazolin during induction of anesthesia and then 2 gr every 8 hours until 24 hours) and the control group which received standard antibiotic regimen (2 gr cefazolin during induction of anesthesia and then 1 gr every 6 hours until 48 hours, then 500 mg oral cephalexin for 48 hours up to one week.

Results: The number of patients participating in the study was 218, of which 167 were male (%76.6) and 51 female (% 23.4), respectively. The mean patient age 56.20 ± 13.40 years, respectively. Between two groups there was no significant difference in the frequency of fractures. In this study, there was no significant difference between age and gender of patients in the two groups. Finally, there was no statistically significant difference between the site and type of fractures.

Conclusion: This study showed that using a one-drug protocol is recommended for prevention of surgical site infection in internal fixation of closed fractures. In addition, using intravenous antibiotics reduces patient costs than those which is administered intravenous and oral together.

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Keywords: *Long bone fracture , Open reduction, Internal fixation , Prophylactic Cefazolin*

Introduction

Surgical site infection (SSI) is the second most common cause of hospital infections and is responsible for nearly 15% of these infections. Factors which contribute to infection include bacterial virulence, host immunity, the extent of damage, the type of fracture and post-operation care. However a large number of resistant pathogens such as methicillin-resistant Staphylococcus aureus (MRSA), and Candida species are commonly cause SSI [1]. Host factors involve age, drug allergies, pregnancy, hepatic and renal function, drug interactions, genetic factors and underlying diseases [2].

Open reduction and internal fixation of closed fractures is one of the most common orthopedic surgical procedures to treat fractures and has no

exception from mentioned condition. Preoperative antimicrobial prophylactic antibiotic is the basis of therapy in hospital. Many studies have shown that prophylactic antibiotics reduce the risk of infection in orthopedic surgeries [2-4], meanwhile some studies also stated that routine use of prophylactic antibiotics do not significantly reduce the risk of these infections.[5,6]

Studies suggested that prophylactic antibiotics for more than 24 hours have no benefit. However, in the case of prophylactic antibiotics after surgery (fractures of the long bones), there is no final decision [2, 5]. The indiscriminate use of antibiotics can cause antibiotic resistance in pathogenic organisms and the excessive economic burden for the patient and society can be a serious problem about this issue [6-8]. Most infections can be treated with an antimicrobial agent, but in some cases in order to obtain a wider coverage range of organisms we have to choose two or more antibiotics at the same time [9].

The principle of choosing the ideal antimicrobial therapy is to determine and identify the microorganism responsible and its sensitivity to existing drugs, But since there is an increase in level of bacterial resistance against antibiotic agents, especially in infections caused by Staphylococcus Aureus, antibiotic and antimicrobial susceptibility tests would be necessary [3,5,9].

In many cases, in the first hours, making a certain diagnosis and determining the etiology is not possible. So we have to use a wider treatment. This is especially important in patients with critically bad condition or immunocompromised individuals. In such cases, after determination of laboratory tests and cultures results, we continue one of medications and stop the rest [6,7,9].

Due to an increase in bacterial resistance because of using broad-spectrum antibiotics, the lack of similar studies in our country and the lack of sufficient consensus on the duration of antibiotic use after orthopedic surgeries, we conducted a study for comparing the effectiveness of prophylactic intravenous antibiotic therapy with cephalexin for 24 -48 hours plus oral cephalexin for a week in patients with long-bone fractures of the lower limb.

Method

This study was a clinical trial which was conducted in two groups of case and control. All patients aged 20 to 60 years with a diagnosis of lower extremity long bone close fractures who were referred to Imam Khomeini and Bou-Ali Sina hospitals of Sari in 2013 with a diagnosis of lower extremity long bone close fractures and open reduction and internal fixation with intra-medullary, plates, screws or pins were applied for them. Patients with significant underlying medical condition such as diabetes, rheumatic diseases, immunodeficiency and patients who needed to get antibiotic regimens for a reason other than fracture were excluded from the study.

The patients were randomly divided into two groups: the case group that received intravenous antibiotics for 24 hours (2 gr cefazolin during induction of anesthesia and then 2 gr every 8 hours until 24 hours) and the control group which received standard antibiotic regimen (2 gr cefazolin during induction of anesthesia and then 1 gr every 6 hours until 48 hours, then 500 mg oral cephalexin for 48 hours up to one week).

All patients were evaluated within 72 hours and then one week, two weeks, three months and six months after the operation in terms of superficial and deep, acute and chronic infections.

Symptoms include fever, chills , localized redness, warmth and swelling, drainage and laboratory investigation (if any clinical signs) include: CBC, ESR, CRP, culture and smears were checked. In case of detection of infection, it was recorded in the patient information form, and the patient was treated.

After collecting the data, it was analyzed by SPSS version 18 software and. In order to obtain the prevalence and frequency, descriptive tests were used. to compare quantitative variables t tests and to compare qualitative variables chi-square test (CHI-SQUARE)were used. $P>0.05$ value was considered statistically significant.

Results

The number of patients participating in the study was 218, of which 167 were male (%76.6) and 51 female (% 23.4), respectively. The mean patient age 56.20 ± 13.40 years (5.32 = Median), respectively.

130 patients with a mean age of 41.73 ± 21.49 years (34 = Median) were in group A including 31 (23.8) and 99 men (% 76.2). In Group B, 88 patients with a mean age of 78.37 years (31 = Median), which included 20 women (% 22.7) and 68 males (% 77.3), respectively. Between age ($P = 0.165$) and gender ($P = 0.848$) of patients in the two groups there was no significant difference.

Usage of antibiotics in Group A consists of 48 hours of intravenous antibiotics (cefazolin) and a week of oral antibiotics (cephalexin). However, patients in group B only received 24 hours of intravenous antibiotics (cefazolin). of 130 patients in group A 34 patients (% 6.38)had femoral fracture, 9 patients had both tibia and fibula fractures (% 2.10) In Group B, 66 patients (% 8.50) had femoral fracture, 58 patients had tibia fractures,

and 6 patients (% 6.4) had both tibia and fibula fracture.
Between two groups, there was no significant difference in the frequency of fractures (P = 0.101) (Table 1).

Table 1 : Frequency of fractured bone based on the fracture type in two groups

		Group A	Group B	P value
Fracture site	**Upper third**	42(32.3%)	29(33%)	0.612
	Mid third	52(40%)	30(34%)	
	Lower third	36(27.7%)	29(33%)	
Fracture type	**Transverse**	14(10.8%)	8(9.1%)	0.244
	oblique	63(48.5%)	38(43.2%)	
	Spiral	22(16.9%)	25(28.4%)	
	comminuted	31(23.8%)	17(19.3%)	

Between the site (P = 0.612) and type of fractures (P = 0.244) in the two study groups, there was no statistically significant difference (Table 2)

Table 2 : Procedure type in two groups

	Operation procedure			P value
	ORIF with IMN	**ORIF with plate and screw**	**ORIF with screw or pin**	
Group A	16(18.2%)	62(70.5%)	10(11.4%)	0.227
Group B	33(25.4%)	89(68.5%)	8(6.2%)	

In both groups there were 4 superficial infections after surgery which were found averagely after two weeks, so there was no statistically significant difference (P = 0.572). in terms of deep infection in patients in group A 6 patients and in group B 1 patient were affected which averagely about 5 weeks after surgery were diagnosed.Clinical sign and lab test results showed in the table 3.

Discussion

Infection is an unfortunate side effect of surgical site after surgery, especially orthopedic surgery, which can have very serious consequences for the patient and cause a burden to society. Several

Table 3: Clinical sign and lab test results in our patients

Variables	**Group A**	**Group B**	**P value**
fever	3(2.3%)	2(2.3%)	1
Erythema	2(1.5%)	4(4.5%)	0.183
Swelling	3(2.3%)	4(4.5%)	0.358
Tenderness	4(3.1%)	4(4.5%)	0.572
Discharge	7(5.4%)	1(1.1%)	0.102
Leukocytosis	4(3.1%)	4(4.5%)	0.572
ESR raising	5(3.8%)	2(2.3%)	0.518
CRP raising	7(5.4%)	5(5.7%)	0.925
Positive culture	6(4.6%)	1(1.1%)	0.153

studies have shown that the use of prophylactic antibiotic cause reduction in the post operative infection rate [2, 3, 10, 6, 11]. There are evidences on the effectiveness of antibiotic prophylaxis in orthopedic surgery with first and second-generation cephalosporin [12, 13]. In a study on the patients undergoing surgery for hip fracture and long bones there were still a need for antibiotic prophylaxis for surgery of closed fracture of long bones [14]. Guidelines suggest use of Cefazolin as first and Clindamycin as second drug of choice in antibiotic prophylaxis for surgery of closed fractures [15]. In the study of Slobogean et al to compare the use of single-dose and multi-dose antibiotic prophylaxis there was no difference in infection rates between the two groups and the single dose use was more cost-effective [16]. In a study designed by Mazza to evaluate the efficacy of ceftriaxone it was concluded that the use of a single dose of ceftriaxone economically is more effective than antibiotic prophylaxis protocols [2]. Also the study of MahmoudZadeh et al to compare the two prophylactic protocols with intravenous ceftriaxone for 24 hours and 48 hours showed no significant differences between the two groups [17]. All studies showed that the use of antibiotics at the accurate time and the right period had the desired efficacy for prevention of infection and there is no need for strict multi-drug protocols. In this study, there was no significant difference between the group that received prophylactic intravenous antibiotic and the group that received oral antibiotics as well as intravenous ones and the results were similar to other results observed in other studies.
Numerous studies have shown that short-term administration of prophylactic antibiotic up to 3

times is appropriate and the best time for administration of prophylaxis is during induction of anesthesia and 1-2 hours before the operation [8,18,19,20] it is similar to one-drug method which we used.

The most common mistake in antibiotic prophylaxis is prolonged antibiotic therapy [4, 21, 22], which has disastrous effects on the country's economic system. During receiving prophylactic antibiotic, the economic aspects and the development of drug resistance and adverse drug reactions should be noticed, which is considered as serious problems in the hospitals.

According to these hints and the results obtained in this study, using a one-drug protocol is recommended for prevention of surgical site infection in internal fixation of closed fractures. In addition, using intravenous antibiotics reduces patient costs than those which is administered intravenous and oral together.

Limitations and Suggestions

Since antibiotics are administered orally and are controlled by the patient, there is a possibility which they did not used properly as much as prescribe. We recommend that a study should be conducted to evaluate current protocols and their efficacy so the best method can be chosen. It is suggested that an acceptable standard protocol should be defined with cooperation and coordination of the different surgical units and those who are involved in these fields should be trained in terms of antibiotic prophylaxis indication, duration of therapy and choosing the best drug.

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