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One day versus three days' antibiotic prophylaxis in joint arthroplasty. A prospective randomized controlled trial

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ABSTRACT

Objectives: The objectives of the study was to compare the effectiveness of 1 day versus 3 days post-operative antibiotic prophylaxis in decreasing surgical site infection (SSI) rate after arthroplasty surgery.

Methods: A prospective, randomized controlled trial was conducted over 1 year, in Cairo University Hospitals. The study included adult patients, who were scheduled for arthroplasty. Sixty patients were divided into two groups, 30 patients in each. The first group of patients received cefazolin for 1 day postoperatively (1-day group) and the other group for 3 days postoperatively (3-days group). Patients were randomized using the sealed opaque envelope method.

Results: There were 32 females and 28 males. The mean patient age was 52 years (range 20–85 years). Wound infection developed in four cases (one case from the 1-day group and three cases from the 3-days group). All infections occurred within the early post-operative period, and completely resolved after proper management. Correlating the SSI to the type of surgery, operative time, the associated medical co-morbidities, and the duration of antimicrobial prophylaxis was not statistically significant.

Conclusion: This study suggests that there is no significant difference in the prevalence of SSI between 1 day and 3 days of antimicrobial prophylaxis after primary joint arthroplasty within the average post-operative follow-up period of 3 months.

Keywords: Antibiotic, Arthroplasty, Cefazolin, Infection, Prophylaxis

INTRODUCTION

The number of total joint arthroplasties performed in USA has increased over time, and the projected growth for total knee arthroplasty (TKA) and total hip arthroplasty (THA) from 2005 to 2030 is approximately 673% and 174%, respectively.[1] However, this growth in surgical procedures is associated with an increase in the number of surgical complications, such as periprosthetic joint infection.[1]

Joint replacement is safe and cost effective.[2] Prosthetic infection is a major, but infrequent, complication with a risk of between 0.54% and 0.63% in England.[2] Surgical site infections (SSI) represent a considerable burden for health-care systems. Guidelines for prophylaxis should be followed, especially in an era of multidrug-resistant strains of microorganisms.[3] Infection is

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one of the most devastating complications associated with arthroplasty and a common indication for revision surgery.[4]

Prophylactic antibiotics have been proven to be an effective measure for the prevention of post-operative infection. Optimal duration of prophylaxis is debatable. The standard practice is to administer prophylactic intravenous antibiotics only on the day of surgery in western countries and in some, a single dose prophylaxis is used.[5] However, in many countries in the Middle east including Egypt, prophylactic intravenous antibiotics are administered for several days postoperatively, and the 1-day antibiotic infusion is rarely used. To the best of our knowledge, data on appropriate regimen of antimicrobial prophylaxis in orthopedics are very limited in Egypt and the Middle East.

Prophylactic antibiotics have been described as antibiotics given to prevent infection when infection is not there, but the risk of infection is present.[6] The goal of antimicrobial prophylaxis is to achieve serum and tissue drug levels that exceed, the duration of the operation, the minimum inhibitory concentration for the organisms likely to be encountered during the operation.[7]

The current position of both the surgical care improvement project and the American Academy of Orthopaedic Surgeons is that post-operative administration of prophylactic antibiotics should not exceed 24 h regardless of the use of catheters and/or drains.[8] In developing countries (e.g., Egypt) post-operative wound infections had become a serious problem due to poor infection control programs, crowding hospital environment, and uncontrolled prescription of antimicrobial agents leading to multidrug-resistant strains of microorganisms. In Egypt, local protocols for prescribing antimicrobials in orthopedic surgery based on studies conducted in Egyptian hospitals are lacking.

The objective of this study was to investigate the optimum duration of post-operative antibiotic prophylaxis by comparing the incidence of infection after 1 day versus 3 days of antibiotic prophylaxis in primary joint arthroplasty. This study was conducted to assess the effectiveness and differences between 1 day and 3 days of antimicrobial prophylaxis after primary joint arthroplasty procedures.

MATERIALS AND METHODS

A prospective, randomized controlled trial (RCT) was conducted over a 12-month duration, during the period from December 2016 to December 2017 in the orthopedic and traumatology department, Cairo University Hospitals. The study included adult patients, (20 years of age and older), who were scheduled to have primary joint arthroplasty (including bipolar hemiarthroplasty [BHA], primary THA as well as primary TKA). The exclusion criteria were patients with history of prior antibiotic therapy within 72 h before surgery, those who had any symptoms or signs of pre-operative infection including chest or urinary tract infections, revision arthroplasty procedures as well as any patients with malignant tumors.

This study included 60 patients who were divided into two groups, 30 patients in each group. The first group of patients received cefazolin for 1 day postoperatively (1-day group) and the other group received cefazolin for 3 days postoperatively (3-days group). Patients were randomized using the sealed opaque envelope method.

One gram of cefazolin was given intravenously within 1 h before incision and at least 15 min before tourniquet inflation in cases of TKA. Moreover, 2 g of cefazolin were given to all patients who weighed more than 80 kg. Intraoperatively, cultures were obtained from the subcutaneous portion of the incision and from synovial fluid to exclude preexisting infection.

Postoperatively, cefazolin was given intravenously in a dose of 0.5 g every 8 h either for 1 day (1-day group) or 3 days (3-days group). Study patients did not receive any antimicrobial agents after discharge from the hospital. Patients were examined daily for any clinical signs of infection, including pain, tenderness, fever, localized swelling, and discharge from surgical site during their hospital stay and thereafter. Patients were reviewed in the outpatient department clinic at 2 weeks, 6 weeks, and 3 months after surgery for any clinical symptoms or signs of infection. In addition, laboratory investigations were requested for all patients, including complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), total leukocytic count beyond 11*103, ESR rising titer, CRP positive, and rising titer for the diagnosis of infection) (at 6 weeks and 3 months postoperatively), as well as culture and sensitivity in all cases of post-operative SSI.

RESULTS

A total of 60 patients were included in this study 30 patients in each group. There were 32 females and 28 males; (1-day group 16 males/14 females and 3-days group 12 males/18 females). The mean patient age was 52 years (range 20–85 years); with the 1-day group: 55.3 years (range 20–85 years), and 3-days group 48.7 years (range 20–80 years). In addition, there were 14 smokers (5 in 1 day group and 9 in 3 days group) among the study patients [Table 1].

Primary THA was performed in 41 patients, BHA in 14 patients, and TKA in five patients. Duration of surgery ranged from 1 to 3 h with a mean of 1.98 h. Wound infection developed in four cases (one case from the 1-day group and three cases from the 3-days group, none of them was a smoker). All infections occurred within the early

post-operative period, that is, within 3 weeks postoperatively and completely resolved after proper management. Out of the four infected cases, three cases were superficial SSI (one case from the 1-day group and two cases from the 3-days group) and were managed by oral linezolid 600 mg twice daily empirically after taking the cultures from SSI and continued for 2 weeks thereafter. Cultures were negative, and complete resolution occurred. The case that developed deep SSI (from the 3-days group) had a fever and purulent discharge, and its culture and sensitivity result showed methicillin-resistant *Staphylococcus aureus* (MRSA). This case was managed by thorough debridement and irrigation then linezolid 600 mg (according to culture and sensitivity results) every 12 h for 6 weeks. Complete resolution occurred without the need for further intervention [Table 2].

Correlating the SSI to the type of surgery was not statistically significant (P = 0.439). Correlating the SSI to operative time, associated medical co-morbidities, the duration of antimicrobial prophylaxis was not statistically significant [Table 3].

Table 1: Co-morbidities among patients included in the study.

Disease	Number (percentage)		
	1-day	3-days	Total
DM	4 (13.3)	7 (23.3)	11 (18.33)
HTN	7 (23.3)	2 (6.7)	9 (15)
RA	2 (6.7)	4 (13.3)	6 (10)
SLE	0 (0)	2 (6.7)	2 (3.3)
AS	0 (0)	1 (3.3)	1 (1.7)
SCA	0 (0)	1 (3.3)	1 (1.7)
Epilepsy	0 (0)	1 (3.3)	1 (1.7)
Obesity	7 (23.3)	9 (30)	16 (26.7)
Smoking	5 (16.7)	9 (30)	14 (23.3)

N.B. Six out of 27 affected cases with comorbidity had multiple co-morbidities. DM: Diabetes mellitus, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, AS: Ankylosing spondylitis, SCA: Sickle cell anemia, HTN: Hypertension

DISCUSSION

In this study, deep infection occurred in one case from the 3-days group (3.3%), there were no cases of deep infection within the 1-day group and the rate of superficial infection in the 1-day group was 3.3%, while in the 3-days group was double (6.6 %). Mauerhan *et al.*[9] compared the effect of duration of antimicrobial prophylaxis on post-operative infection rate in 834 patients undergoing primary THA and TKA. Using cefuroxime (second-generation cephalosporin) for 1 day, the rate of deep infection was 0.7% (three cases out of 410) and the rate of superficial infection was 2.1% (nine cases out of 410) that was similar when they used cefazolin for 3 days (out of 424 cases, deep infection occurred in six cases with a percentage of 1.4%, and superficial infection occurred in eight cases with a percentage of 1.9%).

Differences in rates between both studies may be due to the sample size, but the correlation of duration of antimicrobial prophylaxis and infection rate was not statistically significant P = 0.539 [Table 4].

In this study, only one case had a deep infection with MRSA in 3-days group, while there was no deep infection in 1-day group. In Mauerhan *et al.*[9] study, *Staphylococcus epidermidis* and *S. aureus* were the most common organisms isolated from infected cases of the cefuroxime group. Other organisms such as MRSA, Proteus, and Group G *Streptococcus* were also isolated in the cefazolin group. In Nelson *et al.*[10] study: *S. aureus*, Proteus, and Pseudomonas were the most common organisms isolated from infected cases. In addition, *Escherichia coli* was isolated from one case who had received cefazolin for 7-days, while no deep infection occurred in patients who had received cefazolin for 1-day [Table 5].

Table 2: Data of infected cases.

	1-day		3-days	
	Case 1	Case 2	Case 3	Case-4
Gender	Female	Female	Female	Male
Operation done	BHA	TKR	THA	THA
Co-morbidities	DM	SLE	RA	AS
Operative time	1.5 h	2.5 h	2 h	2 h
Type of infection	Superficial SSI	Superficial SSI	Superficial SSI	Deep SSI
Time of infection	20th Post-operative day	10th Post-operative day	15th Post-operative day	10th Post-operative day
Organism/s isolated	No	No	No	MRSA
Antimicrobial sensitivity				Ciprofloxacin, levofloxacin, linezolid, co-trimoxazole, cefepime and vancomycin

BHA: Bipolar hemiarthroplasty, TKR: Total knee replacement, THA: Total hip arthroplasty, DM: Diabetes mellitus, SLE: Systemic lupus erythromatosus, RA: Rheumatoid arthritis, AS; Ankylosing spondylitis, SSI; Surgical site infection, MRSA; Methicillin-resistant *Staphylococcus aureus*

Table 3: Correlating the SSI to different variables.

Correlating the SSI to	*P*-value
Type of surgery	0.439
Operative time	0.362
Medical co-morbidities	0.127
Duration of antimicrobial prophylaxis	0.539

SSI; Surgical site infection

There was no statistically significant correlation between the prevalence of SSI with time of surgery, operative time, medical comorbidity, and duration of antibiotic prophylaxis.

To the best of our knowledge, this study is one of the very first Egyptian orthopedic studies addressing the post-operative antimicrobial prophylaxis following primary arthroplasty in addition to its design (RCT). However,

Table 4: Antimicrobial regimen and infection rates of different studies.

Study	Operation performed	Antimicrobial regimen	Number of cases	Deep infections	Superficial infections
Mauerhan *et al*. 1991[9]	THA	Cefuroxime for 1 day	410	3 cases (0.7%)	9 cases (2.1%)
	TKA	Cefazolin for 3 days	424	6 cases (1.4%)	8 cases (1.9%)
Niimi *et al*. 2011[4]	THA	Antibiotics for 1 day	223	0–1.6%	Not assessed
	TKA	Antibiotics for 3 days	104	No	
Nelson *et al*. 1983[10]	THA	1-day Nafcillin	147	3 cases (2%)	Not assessed
	TKA	7-days Nafcillin	136	2 cases (1.5%)	
	Hip fractures	1-day Cefazolin	39	0	
		7-days Cefazolin	36	2 cases (5.5%)	
Evrard *et al*. 1988[11]	THA	Cefamandole for 2 days	488	3 cases (0.7%)	Not assessed
		Cefazolin for 5 days	477	2 cases (0.5%)	
Tany *et al*. 2003[12]	THA	Cefazolin Single doze	1152	THA 1.1% TKA 1%	Not assessed
	TKA	Cefuroxime 3 doses	215	THA 1.1% TKA 1.6%	
The current study	THA TKA	Cefazolin for 1 day	30	No	1 case (3.3%)
	BHA	Cefazolin for 3 days	30	1 case (3.3%)	2 cases (6.6%)

THA: Total hip arthroplasty, TKA: Total knee arthroplasty

Table 5: Bacterial isolates from infected cases.

Study	Antimicrobial regimen	Isolates	Number
Mauerhan *et al*. 1991[9]	1-day cefuroxime	*Staphylococcus epidermidis*	2
		Staphylococcus aureus	1
	3-days cefazolin	*Staphylococcus epidermidis*	1
		Staphylococcus aureus	2
		MRSA (Methicillin-resistant *Staphylococcus aureus*)	1
		Proteus	1
		Group G *Streptococcus*	1
Nelson *et al*. 1983[10]	1-day nafcillin	*Staphylococcus aureus*	1
		Proteus	1
	7-days nafcillin	Pseudomonas	1
		Staphylococcus aureus	1
	1-day cefazolin	No isolate	
	7-days cefazolin	Proteus	1
		Escherichia coli	1
		Pseudomonas	1
Everard *et al*. 1988[11]	2-days cefamandole	No isolate	
	5-days cefazolin	Proteus	1
		Staphylococcus aureus	1
The current study	1-day cefazolin	No isolate	1
	3-day cefazolin	MRSA (Methicillin-resistant *Staphylococcus aureus*)	

there are quite few limitations to this study, including the small sample size as well as the short follow-up period. In addition, different types of arthroplasties have been included in this study.

CONCLUSION

This study suggested that there is no significant difference in the prevalence of deep wound infection regardless different associated co morbidities between 1 day and 3 days of antimicrobial prophylaxis after primary joint arthroplasty within the average post-operative follow-up period of 3 months.

RECOMMENDATIONS

This study could possibly be considered a kind of a pilot study and we would recommend a larger sample size, with possibly a multicenter study including different hospitals or medical institutions in Egypt with a longer follow-up duration. This would be integral to developing the national guidelines of antibiotic prophylaxis in orthopedic surgery based on our own local characteristics and practice setup. We would also recommend another large sample trial comparing one dose versus multiple doses of antibiotics prophylaxis in joint arthroplasty as a suggestion for further research.

AUTHORS' CONTRIBUTIONS

ME conducted the research, collected and organized data, analyzed and interpreted data. MAK, WE, and MY analyzed and interpreted data, and wrote the manuscript. All authors have critically reviewed and approved the final draft and are responsible for the manuscript's content and similarity index.

ETHICAL APPROVAL

This study was approved by Trauma and Orthopaedic Department, Cairo University on the February 14, 2017.

Declaration of patient consent

The authors certify that they have obtained all appropriate patients consent forms for the study. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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