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Original Research Article

PHARMACOECONOMIC USE OF 750 MG CEFUROXIME INTRAVENOUSLY FOR INGUINAL HERNIA MESH REPAIR SURGERY ASSOCIATED INFECTIONS.

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ABSTRACT

Main delineative of the present study was to ascertain the effectiveness of cefuroxime prophylaxis in restraining the postoperative wound infection during scavenging inguinal hernia mesh after furbish up surgery and also to equate single day with multiple day antibiotic prophylaxis during hospital stay and for monetary appraise. 326 patients with inguinal hernia were investigated and divided into two groups with 171 patients in group A and 155 in group B. Group A was treated with three intravenous doses just half an hour before surgery followed by two more doses with 8 hours interval and oral therapy of 500 mg of cefuroxime divided into two doses. Group B received six intravenous doses and followed by same oral therapy as of group A. Total therapy was carried out uninterrupted for 4 days in both groups. The outcomes of study indicated that 4.7% and 6.45% of the patients of group A and B explicated surgical site infections respectively, while the hospital detention of group A and B was 2.15 and 3.27 days respectively. Overall, the cost effectiveness of group A was 33% more frugal than Group B. It is concluded that there was no significant differences in one day and two days prophylaxis with cefuroxime in patients with inguinal hernia mesh repair surgery relative to post-operative surgical site infection. The risk of post-operative wound infection could therefore be efficaciously be contended by one day t.i.d treatment, eventually had salutary consequences on the hospital stay and cost obligingness of patient.

Keywords: Antibiotic cost, surgery, antibiotic prophylaxis, intravenous cefuroxime.

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INTRODUCTION

Hernia is an excrescence of a viscous or a part of a viscous through an abnormal opening in wall of its containing cavity and it is a defect in innermost layer of abdomen where hernia sac became an out pouch of peritoneum¹. Abdominal hernias only occur in areas where aponeurosis and fascia are devoid of striated muscle². A number of such cosmos areas are present in normal individuals but others might be initiated through muscular atrophy, surgery or trauma³. The common sites of hernia are groin, umbilicus and linea alba⁴. Abdominal wall hernia are much more common in males than females⁵. In diseased considerations the relative incidences of hernia is about 3%⁶. Their treatment is only the surgery⁷. Hernia furbish up is one of the most general surgeries today⁸. An average annual

hernial surgical cases, in major cities of Pakistan have been estimated as 9.5-15% of the total hospital admitted cases⁹.

Infection is an impingement of the body by various agents such as viruses, bacteria, fungi, protozoan, worms, and their toxins¹⁰. Infection might be local e.g., an abscess; or confined to one body system e.g., pneumonia in lungs; or generalized e.g., septicemia¹¹. Infecting daemon usually inscribe the body by inhalation, ingestion, sexual transmission, passage to a fetus during pregnancy, at birth, wound contamination, animal bites, or by insect bites¹². In spite of significant progress in precluding and handling infectious diseases, they remained a major causation of illness and death, particularly in poor sanitation, poor nutritional and over-crowded regions of the world¹³.

Antimicrobial prophylaxis is used to reduce the incidence of postoperative wound infections¹⁴. Patients concomitant with high infection, often require preoperative antibiotics¹⁵. Treatment, rather than prophylaxis is frequently suggested for procedures concerted with preexisting infection (i.e. abscess, pus, or necrotic tissue)¹⁶. In 2010, an estimated 16 million operative procedures were performed in the United States¹⁷. A recent prevalence study stated that SSIs were the most common healthcare-associated infection, accounting for 31% of all HAIs among hospitalized patients.¹⁸

Patients expected to experience surgical procedures associated with high infection rates or in which the consequences of infection are serious like implantation of prosthetic material should receive preoperative antibiotics.¹⁹ Such treatment rather than prophylaxis, is indicated for procedures associated with obvious preexisting infection (i.e. abscess, pus, or necrotic tissue).

Cephalosporins are suitable first line agents for such procedures, affecting the most likely organisms. Eluding the use of broad-spectrum antibiotics that may develop antimicrobial resistance.²⁰

Elements inducing the progress of SSI's include bacterial inoculums and virulence, host defenses, preoperative care, and intraoperative management²¹. Common Pathogens likely to cause the post-operative infections at surgical site are given in Table 1²²⁻⁴⁰.

Table 1: Common Pathogens likely to cause the post-operative infections at surgical site.

Disease/Indication	Number of Patients	Percentage	Remarks for inclusion/exclusion
Hernia	469	100%	--
Paraumbilical hernia	51	10.87 ~ 11	Excluded
Epigastric hernia	28	5.79 ~ 6	Excluded
Incisional hernia	19	4.05 ~ 4	Excluded
Inguinal Hernia	371	79.10 ~79	Considered for further selection

Random sampling of different SSI of the patients of the hospital showed some of the very common pathogenic strains including *Staphylococcal species*, *Coagulase negative Staphylococci*, *Streptococcus pneumonia*, *Streptococcal spp.*, *Moraxella catarrhalis*, *Enterobacteriaceae*, *Haemophilus Influenzae*. Some strains of *Salmonella*, *Klebsiella*, *Proteus mirabilis*, and very uncommon *Citrobacter* and *Shigella species*

The best available and logical choice which is also clinically proved could be a broad spectrum second generation cephalosporin.⁴¹ As for as bacterial spectrum of SSI is concern, Cefuroxime which is a broad spectrum 2nd generation cephalosporin is one of the best fit antibiotic.^{42,43}

Aims of the study: To reduce the cost of therapy for the patients in terms of less hospital stay, reduced I.V dose and more patient compliance.

MATERIAL and METHOD:

The quasi-experiments were acquitted in the surgical unit of Shalamar hospital located at Lahore from 1st July 2010 to 31st March 2013. 326 comprehensive patients with inguinal hernia were selected from a lot of 469 patients. Since 20.89% patients were not exhibited inguinal hernia yet possessed other types of hernia, were not included in this study. 45 patients were also not included in this study due to the reasons mentioned in exclusion criteria.

Inclusion criteria:

Inclusion criteria included the patients with age limit range over 16 to 65 years with both genders for elective surgery of inguinal hernia.

Exclusion criteria:

Patients with COPD, diabetes, hypertension, hepatitis and jaundice were not included in the study. It also included smokers, patients with the histories of fungal skin infection, drug toxicity, drug allergy, chronic renal failure and pancreatitis. Similarly non elective surgeries, para umbilical hernia, epigastric hernia and incision hernia were also excluded (Table 2).

Table 2: Reported patients and their inclusion/exclusion status.

Type Of Infection	Observation
Grade I infection	Slight reddening and induration of wound edges requiring no intervention
Grade II infection	Slight serous discharge from wound requiring no intervention
Grade III infection	Obvious infection or purulent discharge from wound requiring repeated change of dressings and antibiotic therapy

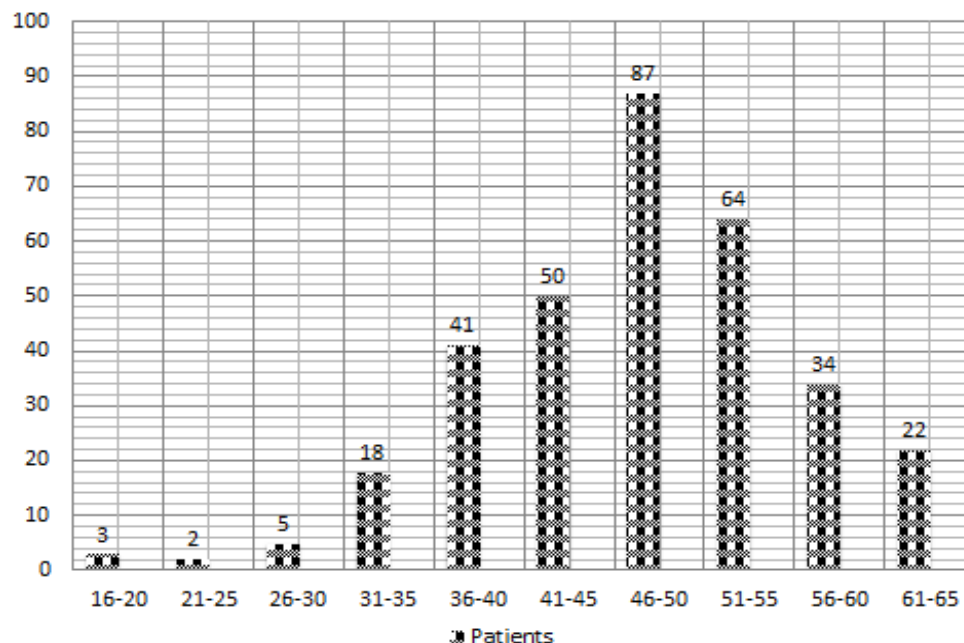
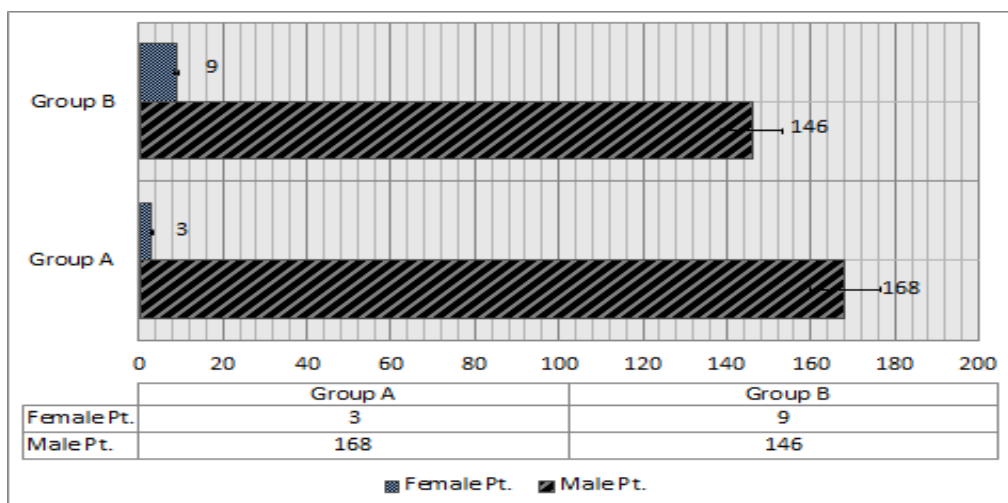


Figure 1. Frequency of occurrence of inguinal hernia in different age groups.



Male to Female patient ratio in both groups

Figure 2. Frequency of male and female patients reported.

Ethical committee permission:

Permission was apprehended from the hospital's ethical committee for the study.

Procedure of admission:

The patients were admitted through the OPD in the surgical ward for Hernial repair mesh surgery.

Patient's consent from:

Specific information consent was also apprehended from the experimental patients.

Diagnosis confirmation:

The experimental patients were extensively examined in the wards for mundane and precise investigations to sustain the diagnosis.

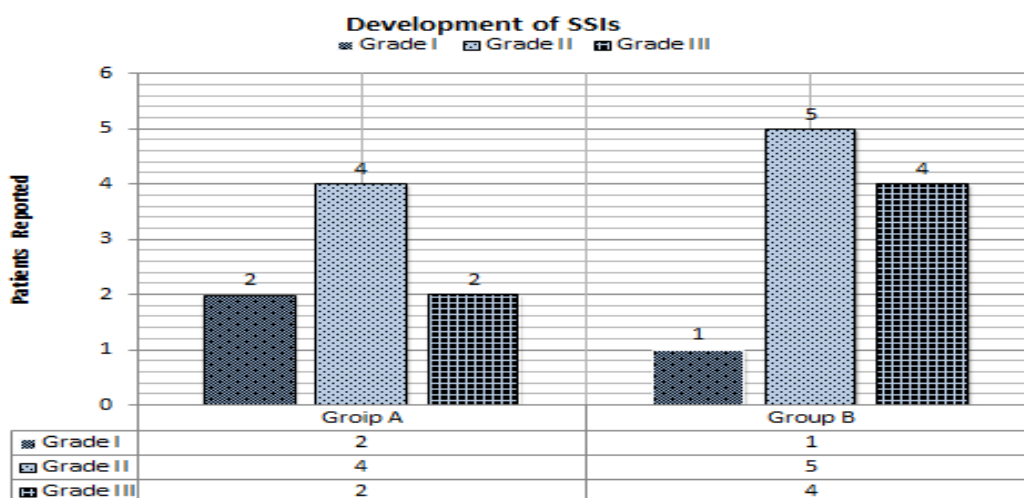


Figure 3. Frequency of grades of wound infection in both groups.

Experimental Protocol:

The experimental patients were divided randomly irrespective to the gender and age into two groups i.e., Group “A” and “B”. Group “A” of 171 patients were treated with three I.V. doses 30 min before surgery, followed by two more doses in 8 hour intervals and oral therapy dose of 250 mg BD cefuroxime for 4 days. Group “B” of 155 patients received 6 I.V. doses of cefuroxime in 8 hour intervals, starting from first dose 30 min before surgery. The patients in this group were dislodged to an oral therapy of cefuroxime 250 mg BD for 3 days. Patients of both the groups were kept ascertained for 48 hours in ward to find any postoperative sepsis or SSI.

Observational parameters:

Diurnal record of pulse, temperature, respiratory rate, abdominal affection and bowel sounds of each patient was maintained. Complete blood profile was executed on 2nd post-operative day while the wounds were examined prior to discharging the patient from the hospital. Subsequently the patients were also perceived on the 5th, 7th, 15th and 30th day in surgical OPD for any wound contagion and feverishness. The wound contagion was categorized into three grades depending upon the inclemency (Table 3).

Table 3: grades of wound infection

Procedure	Likely pathogens
Cardiothoracic	<i>Staph epi, Staph aureus, Streptococcus, Corynebacteria, enteric-Gram-negative bacilli</i>
General Surgery	
1. Appendectomy (non-perforated)	1. Enteric Gram(-) bacilli
2. Colorectal Surgery	2. Enteric Gram(-) bacilli, Enterococcus, anaerobes
3. High-risk esophageal, gastro-duodenal, or biliary surgery	3. Enteric Gram(-) bacilli, Gram(+) cocci
4. Penetrating abdominal trauma	4. Enteric Gram(-) bacilli, Enterococcus, anaerobes
Gynecologic Surgery	
1. C-section (after cord-clamping)	1. Staph epi, Staph aureus, Group B Strep, Enterococcus
2. Hysterectomy	2. Enteric Gram(-) bacilli, Group B Strep, Enterococcus
Head and Neck Surgery	<i>Anaerobes, Staph aureus, Gram(-) bacilli</i>
Neurosurgery	
1. Clean	1. Staph aureus, Staph epi
2. Skull fracture, CSF leak	2. Anaerobes, Staph epi, Staph aureus
3. Penetrating trauma	3. Staph, strep, Gram(-) bacilli, anaerobes
4. Spine	4. Staph aureus, Staph epi
Orthopedic Surgery	
1. Closed fracture	1. Staph epi, Staph aureus
2. Open fracture	2. Staph, strep, Gram(-) bacilli, anaerobes
Urologic(Genitourinary) Surgery	<i>Staph epi, Staph aureus, Gram(-) bacilli, Enterococcus</i>

Statistical Analysis:

Observations of every parameter in each group for age and hospital stay were recorded and the data were presented as Mean $\pm$ Standard errors. Data was congregated on a pre-constituted Performa and analyzed by applying SPSS software ver. 16. Furthermore frequencies and percentages for gender and wound infection in both groups were also computed. Chi square test was also used to compare the frequency of wound infection in group A and Group B patients.

Table 4: Reported wound infections at surgical site and mean hospital stay of both groups.

Group	Total patients	SSI reported	G. I Inf.	G.II Inf.	G. III Inf.	Hospital Stay (Days)
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A	171		4.67%	8 Pt.	2	4	2	2.15 ± 0.13
	M	F						
	168	03						
B	155		6.45%	10 Pt.	1	5	4	3.27 ± 0.19
	M	F						
	146	09						

RESULTS:

Total 326 patients were included in the study in a range of 16 to 65 years with a mean age of 47.45 ± 8.79 years. Maximum number of patients was in the age group of 46 to 50 years (**figure 1**). There were 314 (96.31 %) male and 12 (3.68%) female patients (**figure 2**). In group A, 8 patients (4.7 %) developed SSI while 163 patients had normal wound healing. 2 patients developed grade I infection, 5 patients developed grade II infection while two patients developed grade III infection. In group B, 10 patients (6.45 %) developed out of which 1 patients developed grade I infection, 5 patients developed grade II infection and 4 patients developed grade III infection. On comparing the results of both groups by applying Chi Square test a value 0.990 was obtained which was insignificant. Mean hospital Stay in Group A patients was 2.15 ± 0.13 while mean hospital stay in group B patients was 3.27 ± 0.19 (Figure 3, Table 4).

In terms of cost effectiveness, the cost of antibiotics and others medications of group A patient is almost 700 Pak rupees with the use of research/mother brand for complete 5 days therapy. While the same therapy with two days IV use of cefuroxime and subsequent oral therapy of 250 mg b.i.d for a total of 5 days costs 1008 Pak rupees. In terms of total cost of the therapy including patient's hospital stay, medication and other charges, group A has almost 33 % less expenditures than Group B.

DISCUSSION:

Inguinal hernia is one of the common distresses in every part of the world.⁴⁴ External hernias exhibit differently and required treatment through surgery⁴⁵. Hernia bushel is one of the most common elective procedures in general surgery nowadays⁴⁶. Average annual hospital admission of the patients with hernia in major cities of Pakistan enumerate from 9.5 to 15% of the total patient population in hospital that were recommended for surgery⁴⁷. In Pakistan, it has also been estimated that incidents of inguinal hernia among males is 26 times more as compared to females. It has been investigated that cephalosporins were the most harmonious agents for many surgical operations. These antibiotics often target the precise microorganisms, obviating the broad-spectrum antimicrobial therapy that might lead to ontogenesis of antimicrobial resistance²⁰. An investigation apprized that the 2nd generation cephalosporins prophylaxis in surgical operations is of ultra-short period. Bowater and his colleagues also attained a similar conclusion⁴⁸.

Results demonstrated that nearly 96.31% of males were affected by inguinal hernial disease, compared with 3.68% of females. The outcomes of this investigation are assanant with Rutkow⁴⁹ and Memon's⁵⁰ findings. The results of present study pointed out that 4.8% of the patients (i.e., 8 patients) from group "A" acquired wound infection. Further, 2 of the patients, evolved grade-I infection, 4 patients produced grade-II infection while 2 patients acquired grade-III infection. 6.45% of Patients (i.e., 10 patients) among the group "B" explicated wound infection. In this group one patients suffered from grade-I infection, 5 patients endured distress of grade-II infection and 4 patients erupted the grade-III wound infections. In 2003 Zahid *et al.*, arrived at similar conclusion⁵¹. On the other hand, Rashid *et al.*, in an alike fashion demonstrated the effects of prophylactic use of cefuroxime for clean

contaminated surgical procedures⁵². P value indicated insignificant results among both of the groups.

CONCLUSION:

It was concluded that there was no significant difference among one day (with 3 I.V doses) and 2 days prophylaxis with 6 I.V doses of cefuroxime in patients with elective inguinal hernia mesh repair surgery during post-operative surgical site infection. The risk of post-operative wound infection could effectively be sustained by one day t.i.d prophylactic treatment with cefuroxime. It could also be salutary to the cost, abidance and hospital stay. Furthermore, this study be amplified in Pakistan on a large scale.

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