Research Article

A prospective, randomized, double blind controlled trial of the use of preoperative antibiotics in routine abdominal surgery: A comparative analysis between Ofloxacin + Metronidazole, Cefotaxime + Sulbactum and Cefepime +Tazobactum (Single does vs. Three doses) and their effects.

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Abstract

Introduction: Anti microbial prophylaxis before any elective surgery is a preferred deterrent to post operative surgical site infection now. We have used different antibiotics, two being from the cephalosporin class, one from the fluoroxoqiuinolones and anti beta lactamases in combination along with metronidazole. The aim was to find out the best and most economical pre operative prophylaxis in our surgical practice. Three antibiotics regimens were studied. Patients were divided into two groups against each agent of Ofloxacin +Metronidazole, Cefotaxime + Sulbactum and Cefepime +Tazobactum. They were again subdivided into two groups one receiving single dose and another three doses of the antibiotics regimens. **Methods:** A total of 138 patients (above 16 years) were taken for the study. It was a randomized and blind study. Patients were prospectively analysed. First, the patients were divided into two groups. First group received a single dose of antibiotic at incision and those who received two more doses at eight hours interval after the dose at incision. **Discussion:** The single dose pre operative prophylaxis scored over three doses regime in all the cases for lap surgery irrespective of OT condition. Three doses regime worked better in combined OT condition for the open elective procedures. The study also revealed the most economic choice for routine elective abdominal surgery. **Conclusion:** Multiday and antibiotics use for a prolonged period is not advisable these days after a routine elective abdominal surgery. Single dose injection of antibiotics at a proper time is good enough for preventing postoperative surgical site infection after a routine Laparoscopic surgery. Three doses regime is better in open surgical cases performed in OTs where emergency procedures are undertaken. It is advisable to use the most cost effective regime to reduce the healthcare cost in the country.

Key words: Postoperative, Surgical site infections, Antibiotics

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Introduction

All though modern surgery started in the seventeenth century, it really progressed after the advent of anesthesia and the concept of sepsis. It was Joseph Lister who revolutionized the infection free practice of surgery by his understanding of “germs” and spraying Phenol in and around the operating environment. The days of “Laudable Pus” was finally over. He is aptly recognized as the father of modern surgery [1]. However surgical site infections still worry the surgeons and many methods are in place to prevent it. The rate is stabilized at 2% foe extra abdominal surgeries and over 20% for intra abdominal procedures [2].

Surgical site infection or SSI is defined by the centre for disease control and prevention, Atlanta, as a

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proliferation of micro-organism in the incision site either within the skin ad subcutaneous tissue, muskulo-fascial layers,or in an organ and a cavity[3].

The CDC also has a recommended guideline for antimicrobial prophylaxis [4,5].

1. To use AMP inthose procedures, which carry a risk of infection,when the consequences of such infection is great and have evidence that using AMP reducing the incidence of SSIs.
2. To select an agent which is safe, inexpensive, preferably bactericidal and most narrowly covers the anticipated SSI in that particular procedure.
3. Time the administration so that it reaches the maximum serum and tissue concentration at the time of incision.
4. Maintain adequate level/ therapeutic level of the antibiotics at the closure of the incision.

There is widespread evidence of using AMP before all surgical procedures that is it is beneficial and prevent SSIs [6,7].

A meta-analysis on AMP in biliary surgery suggests that increase of SSIs over 9 times if compared to those cases where no AMP was use with 95% confidence Interval.[8].

Single dose cephalosporins was found to be effective in Biliary, genitor-urinary and gynaecological procedures was found to be efficacious in preventing SSIs in these procedures.[9]

A sudy was undertaken in Germany to find out the efficacy of AMP in both open and laparoscopic cholecystectomies. It was found to be beneficial equally in both the open and laparoscopic groups over no AMP group and was found to be statistically significant (p=<05). [10]

Development of SSI leads to increase in hospital stay, Expenditures, Morbidity as well as deaths. [11,12].

Basing on NNIS report it can be sayed that SSI is an important nosocomial problem in all the countries. The world wide experience suggests that SSI is a major health care as well financial problems in all the countries [13,14].

Table 1 World wide experience of SSI

Country	Setting	Period	Design	SSI No.	SSI (%)
Australia[15]	28 Hospitals	1992	Retrospective	5432	8
France[16]	University Hospital	1993-1998	Retrospective	9422	7
US of A[17]	NNIS Hospitals	1992-1998	Prospective	738398	3
Thailand[18]	University Hospital	2003-2004	Prospective	4764	1
Vietnam[17]	Tertiary care Hospitals	1992-1998	Prospective	697	11
Italy[8]	Public Hospitals(31)	1 month	Prospective	617	3

SSI can be caused by two different kinds of spreads. Exogenous and endogenous. Most common cause of exogenous route is the Operating environment and the most common endogenous route is from the GIT or Genital in females .

It is well established that Prophylactic antibiotics must be injected at anaesthesia and it has been shown that multiple doses regime is redundant for preventing SSI. It is also shown that antibiotics given over two hours preoperatively failed to initiate desired effect and action.

Keeping these factors in mind the study was undertaken to evaluate the best and most economic prophylactic antibiotics regime in two different environments. One, in which both emergency as well as elective abdominal cases are undertaken, the second is where only elective cases are undertaken. The reason being, such conditions exist in the state of Assam. Both laparoscopic as well as open elective cases were considered t find out if any difference would come out after the study.

Materials and Methods

A total of 138 patients were taken for the study. Inclusion criteria were above 16 years of age and no history of allergy to cephalosporins, imidazoline derivatives, beta lactamase inhibitors, fluoroxoquinolones and history of seizures. Excluded are the emergency procedures and history of seizures and hypersensitivity towards the chemicals to be used.

The patients were divided into the study groups in a randomized and blinded method. Cheat picking was applied to select patients in the various groups.

Antimicrobial agents used-

1. **Metronidazole**-Metronidazole and related nitroimidazoles are active *in vitro* against a wide variety of anaerobic protozoal parasites and anaerobic bacteria (19). Metronidazole is clinically effective in trichomoniasis, amebiasis, and giardiasis, as well as in a variety of infections caused by obligate anaerobic bacteria, including *Bacteroides, Clostridium,* and microaerophilic bacteria such as *Helicobacter* and *Campylobacter* spp.

2. Cefotaxime-Cephalosporins and cephamycins inhibit bacterial cell wall synthesis in a manner similar to that of penicillin. Cefotaxime, a Third generation cephalosporin is less active than first-generation agents against gram-positive cocci, but this is much more active against the Enterobacteriaceae, including b-lactamase-producing strains. A subset of third-generation agents (*ceftazidime* and *cefoperazone*) also is active against *P. aeruginosa* but less active than other third-generation agents against gram-positive cocci.

3. Cefipime-*Fourth-generation* cephalosporins, such as *cefepime*, have an extended spectrum of activity compared with the third generation and have increased stability from hydrolysis by plasmid and chromosomally mediated b-lactamases. Fourth-generation agents are particularly useful for the empirical treatment of serious infections in hospitalized patients when gram-positive microorganisms, Enterobacteriaceae, and *Pseudomonas* all are potential etiologies [20]

4. Sulbactum-Sulbactam is a b-lactamase inhibitor similar in structure to clavulanic acid. It may be given orally or parenterally along with a b-lactam antibiotic. It is available for intravenous or intramuscular use combined with Cephalosporins. Dosage must be adjusted for patients with impaired renal function. The combination has good activity against gram-positive cocci, including b-lactamase-producing strains of *S. aureus,* gram-negative aerobes (but not *Pseudomonas*), and anaerobes; it also has been used effectively for the treatment of mixed intra-abdominal and pelvic infections [21].

5. Tazobactum-Tazobactam is a penicillanic acid sulfone b-lactamase inhibitor. In common with the other available inhibitors, it has poor activity against the inducible chromosomal b-lactamases of Enterobacteriaceae but has good activity against many of the plasmid b-lactamases, including some of the extended-spectrum class. It has been combined with piperacillin and Cefepime as a parenteral preparation [*21*].

6. Ofloxacin- It is a quinolone antibiotic. The quinolone antibiotics target bacterial DNA gyrase and topoisomerase IV . For many gram-positive bacteria (such as *S. aureus*), topoisomerase IV is the primary activity inhibited by the quinolones. In contrast, for many gram-negative bacteria (such as *E. coli*), DNA gyrase is the primary quinolone target.

The fluoroquinolones are potent bactericidal agents against *E. coli* and various species of *Salmonella, Shigella, Enterobacter, Campylobacter,* and *Neisseria*. Minimal inhibitory concentrations of the fluoroquinolones for 90% of these strains (MIC_{90}) usually are less than 0.2 mg/ml. [22] Ofloxacin and metronidazole were used in combination, whereas the cefotaxime was combined with sulbactum and cefepime was combined with tazobactum as the agents to be studied.

The operation time and other details were noted. Most of the surgeries were done by a particular surgeon. Group 1 patients received a single dose of either Ofloxacin and Metronidazole at incision, and the group 2 patients received two more doses 8 hours apart. This policy was followed in open and laparoscopic groups separately.

A separate group received a fourth generation cephalosporin and tazobactum as a single dose prophylaxis only and the results were analysed.

While analysing the data information were segregated for cases undergoing in a combined Operation theatre where emergency cases are also undertaken and in operation theatres where only clean and elective cases are undertaken. Data were analysed by SPSS 16.5 Statistical package.

Graph and prism version 5.04 and excel 2007. RATES OF ssiwere extracted, 2x2 tables were prepared and odds ratio(OR),relative risk (RR)with 95% confidence interval(95% CI) calculated. All categories were verified by chi-square test with Y ates correction (with 95% CI).

Results

Over the period from sept 2010 to May 2011 39 patients of lap chole fitted with the inclusion criteria and taken for the study in two groups.

Table 1: Study groups for lap chole

Treatment group	Nos. of Pts.	Median age	Males	Females
Group1	20	35(29-62)	9	11
Group 2	19	33(18-53)	11	8
Total	39	34	20	19

The two groups behave equally well and there were no SSI.

Table 2: Wound infection rate in Lap chole in two groups.

Treatment group	Nos. of Pts.	Nos. of SSI
Group 1	20	0
Group 2	19	0
Total	**39**	**0**

In the second arm of open surgery 46 patients underwent elective abdominal surgeries (September 201-December 2010, by a single surgeon).

Table 3: Open surgery in two groups

Groups (Open)	Nos. of Pts.	Median age	Males	Females
Group 1	24	25	10	14
Group 2	22	45	9	11
Total	**46**	**35**	**19**	**25**

The rates of SSI is given in the table. No significant difference was noted statistically.

Table 4: SSI rate in Open surgery

Treatment groups	Nos. Of Pts.	SSI
Group 1	24	5(20%)
Group 2	22	3(14%)
Total	**46**	**8 (17%)**

In the other group single dose versus three doses of Ofloxacin and Metronidazole was studied. We had 32 patient. Here also no significant difference in SSI was noted.

Table 5: Single vs. Three doses of Ofloxacin+ Metronidazole groups

Groups	Nos. Of Pts.	Median age	Males	Females
Group 1	15	37	4	11
Group 2	17	35	3	14
Total	**32**	**36**	**7**	**25**

Table 6: Single versus multiple doses of Cefotaxime+Sulbactum.

Treatment groups	Total pts.	SSI	Total Pts.
Single dose	15	4	19
Three doses	17	3	20
Total	**32**	**7**	**39 (18%)**

No significant difference of SSI rate between the two groups. Now while comparing the rates of infection within these two combination regimes, no significant difference in SSI were noted.

Table 7: No significant difference between the two groups.

Treatment groups	Total Patients	SSI
Cefotaxime+Sulbactum	47	8
Ofloxacin+Metronidazole	32	7
Total	**79**	**15**

Rates of SSI in both the arms showed no significant differences.

Discussion

Preoperative antibiotics prophylaxis is a standard procedure in today's operation theatres [4,5]. It saves multiple regular doses of antibiotics as well as offer better prevention of nosocomial Soft tissue infection post operatively[7,8]. Post operative SSI can be life threatening too. Many studies are there to prove the merit of preoperative prophylaxis in surgery[6,7]. In biliary surgery, there are reports, which categorically proves that pre-operative prophylaxis prevents post operative SSI [8]. We studied different antibiotics regimens with single and three doses schedule in our routine elective abdominal surgeries to see the efficacies of each arms of the study. The Antibiotics used belong to Cephalosporin, Fluoroxoquinolones, Imidazolines derivative as well as Beta lactamase inhibitors [19,20,21,22].

All of these are in common use in the operation theatres worldwide. The study revealed that. Preoperative prophylactic antibiotics prevent post operative SSI s. It was also revealed that single dosing of preoperative antibiotics at the indication of anaesthesia or within half an hour of incision works as good as, if not better, when compared with three doses regimens of the antibiotics under evaluation. We have also found that the cost also varies depending on the regimens, which also bring benefits to the patients.

Conclusion

The study conclusively states that single dose of prophylactic antibiotics is good enough for laparoscopic as well as open surgeries when done in elective only operation theatres. Open abdominal elective surgeries performed in a combined operation theatres, where both emergency and elective cases are undertaken need three doses.

Laparoscopic surgeries done in combined operation theatres do not need more than single dose prophylaxis. All the regimens, used properly, are equally efficacious in preventing SSI.

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