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# A prospective blinded randomized controlled trial of use of preoperative antibiotics in routine abdominal surgery: A comparison between single dose versus three doses between Ofloxacin + Metronidazole and Cefotaxime + Sulbactum

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**Introduction:** Anti microbial prophylaxis before any elective surgery is preferred deterrent post operative surgical site infection now. Many regimes with different antimicrobial agents are tried and most institutions have developed their own regime or philosophy to address postoperative surgical site infection. We have also our own antibiotic prophylaxis and protocol. **Method:** A total of 138 patients (above 16 years) were taken for study. It was randomized and blind study. Patients were prospectively analysed. First, patients were divided into two groups. Those who have received single dose antibiotic at incision and those who received two more doses after first dose. Open elective as well as laparoscopic elective procedures have included study. Routine practice of preoperative bath, preoperative preparations of the area with iodophores and spirit, operating under normothermia and hydration were as per institutional philosophy and common to all the patients. Two combinations compared: Cefotaxime+ Sulbactum & Ofloxacin + Metronidazole. Keeping outcome of study in mind all materials were analysed and statistical analysis done and confidence intervals were noted. **Results:** Study revealed interesting observations. Single dose pre operative prophylaxis scored over three doses regime in all cases for lap surgery. **Conclusion:** Multiday and antibiotics use for prolonged period is not advisable these days after a routine elective abdominal surgery.

**Keywords:** Postoperative, Surgical site infections, Antibiotics

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# Introduction

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

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

01. 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.
02. To select an agent which is safe, inexpensive, and preferably bactericidal and most narrowly covers the anticipated SSI in that particular procedure.
03. Time the administration so that it reaches the maximum serum and tissue concentration at the time of incision.
04. 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]. Most of the countries have reported SSI as one of the major problems. As antibiotics prophylaxis depends on the local microbiological flora as well as the Involvement of the microbiologists, the antibiotics and agents differ from area to area. However any third generation cephalosporins are mentioned as prophylactic antibiotics in standard text book of surgery, especially in colorectal surgery. We have chosen a combination of fourth gen cephalosporins along with a beta lactamase inhibitors in one arm and Ofloxacin, a fluoroxoquinolone combined with Metronidazole. Both the regimens give wider gram positive as well as gram negative cover. Bacteroides Anaeroids are also covered. Most of the countries reported their experience in SSI. We use routine antibiotics coverage which lasts for five days after surgery. It is shown that a single dose of Injectable antibiotic in appropriate time is what is actually needed to prevent SSI.

Below is given worldwide experience in a table on SSI to give an idea. It proves that it is a global problem.

**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(18) | 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 prophylactic antibiotics regime between these two. Both laparoscopic as well as open elective cases were considered to 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 cephalosporin's, imidazoline derivatives, beta lactamase inhibitors, fluoroquinolones 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-

01. **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.

02. **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 blactamase-producing strains. A subset of thirdgeneration agents (ceftazidime and cefoperazone) also is active against P. aeruginosa but less active than other third-generation agents against gram-positive cocci.

03. **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.

01. 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].

02. **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 (MIC90) usually are less than 0.2 mg/ml. [22]. Ofloxacin and metronidazole were used in
combination, whereas the cefotaxime was combined with sulbactum. 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 or 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. 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 cholecystectomy fulfilled 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

As the number of operations increase the rate of SSI also does. Operation theatres are complex and different environment now. Especially the sepsis and antisepsis concepts have taken strong roots presently. Operation Theater are specialized zone with HEPA filters laminar air flow and modular concept. But Antibiotics prophylaxis has become ever more important as the surgeries are complicated, use of prosthesis have become routine. Single dose antibiotic prophylaxis holds merit as in our works as well as longer duration therapy. It also reduces the chance of increasing resistance to antibiotics.

In two studies [8, 9], one involving the United Kingdom and the other in the US of A the usefulness of prophylactic antibiotics is found to the standard of choice. In both the studies the authors have found strong recommendation for use of preoperative prophylaxis to prevent SSI. The present study too showed the same outcome. In laparoscopic surgery a single dose antibiotic prophylactic injected at the induction of anesthesia helped in reducing the SSI rates in our cases. We strongly recommend single dose prophylaxis in laparoscopic surgery [20, 21, 22].

In open surgery, we had some SSI in patients. What would be the approach to these cases is debatable and needs study. In this regard we have differences of experiences from the developed world. Allthough not a statistically significant finding, it needs to be addressed too in future studies.

# Conclusion

The study conclusively states that single dose of prophylactic antibiotics is good enough for laparoscopic as well as open surgeries.

All the regimens, used properly, are equally efficacious in preventing SSI.

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