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A STUDY ON PATTERN OF USING ANTIMICROBIAL PROPHYLAXIS IN CESAREAN SECTION

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Caesarean section is a major operation, with great potential benefit, but also with substantial risks for both mother and baby.[1] Maternal mortality and morbidity are higher than for vaginal delivery, although rates are becoming lower with advances in technology.[2] Infectious morbidity remains a leading cause of postoperative complications following caesarean delivery.[3] The major infectious complications of caesarean delivery are Fever, wound infection, endometritis and UTI(Urinary Tract Infection).[4]

Pathogenesis of post-cesarean infection

Postoperative endometritis is a polymicrobial infection caused by bacteria normally present in the host's lower genital tract. The major microorganisms responsible for endometritis are aerobic gram-negative bacilli, principally E.coli; anaerobic gram-negative bacilli, principally *Bacteroides species* and *gardnerella vaginalis*; aerobic gram-positive cocci, primarily Group B and Group D streptococci; and anaerobic gram-positive cocci, specifically *peptococcus* species and *peptostreptococcus* species.[5]

The development of clinical infection is dependent on a complex balance between host defence mechanisms and bacterial virulence factors.

Cesarean delivery alters this balance so as to predispose the patient to infection. During labor and abdominal delivery, the endometrium and peritoneal cavity invariably are contaminated with large numbers of highly pathogenic aerobic and anaerobic bacteria. The serosanguineous fluid that collects in the abdomen after surgery and the injured uterine tissue at the site of the incision provide excellent culture media for microbial growth. The bacterial inoculum is particularly large when cesarean section is performed after multiple vaginal examinations and extended duration of labor and ruptured membranes.[5]

Postoperative surgical site infection (SSI) remains a major source of illness and a less frequent cause of death in the surgical patient.[6] Surgical site infection (SSI) is a common post operative complication and causes significant morbidity and mortality, increased antibiotic usage, prolonged hospital stay, adds cost and decreases patients quality of life. An estimated 40-60% of SSI are preventable with appropriate use of prophylactic antibiotics. However overuse, under use, improper use and misuse of antibiotics occurs in 25%-50% of operations.[7] Patients who develop SSI's are up to 60% more likely to spend time in an ICU, 5 times more likely to be readmitted to the hospital, and 2 times more likely to die than are patients without an SSI.

Antibiotics administered prior to the contamination of previously sterile tissues or fluids are deemed '*prophylactic antibiotics*'. Prevention of surgical site infection is the major goal of antibiotic prophylaxis.[1]

Rationale for using prophylactic antibiotics steps from very old familiar saying "*prevention is better than cure*". For optimal prevention of postoperative wound infection, it is necessary to follow a series of general principles. This includes the type of surgical intervention, class and character of antibiotic used, its time and route of administration.[8]

Since infection by gram positive or negative organisms is possible hence antibiotic cover will be sufficiently comprehensive and effective if antimicrobial agent chosen has a wide spectrum of action.[8]

The use of antibacterial prophylaxis of postoperative infection is firmly established within clean contaminated procedures. For clean procedures, prophylaxis has traditionally been reversed for operation involving foreign body implantation.[9]

The administration of prophylactic antibiotics with in specific interval has been shown to reduce the burden of SSI, but adherence to proper timing guidelines remains problematic.[10]

The review of trials found evidence that prophylactic antibiotic in women undergoing caesarean section substantially reduced the incidence of episodes of fever, endometritis, wound infection, urinary tract infection and serious infection after caesarean section.[11]

Prophylaxis is indicated for operations in which bacterial contamination is encountered or expected.[12] The therapeutic tissue levels of antibiotics should exist before the incision is made and the only exception is caesarean section where a special foetal consideration exists as the prophylactic drug masks neonatal sepsis.[13]

Preoperative antimicrobials can prevent infection when gives after cord clamping in emergency caesarean section, in high risk situation such as active labour or premature rupture of membranes.[14] Obesity appears to a risk factor of particular importance for wound infection.[15] Prophylaxis in low risk patients remains controversial. It increases adverse effects and costs.

The drug remains effective for 3-4 hours. Depending on the agent selected, 1-3 doses are required i.e. coverage for first 24 hours. Overuse of prophylactic antibiotics lead to the development of resistance.[1]

The ideal prophylactic antibiotic should be inexpensive, nontoxic, and active against some pathogens known to be involved and proven effective in clinical trials. It should not be a drug ordinarily used for therapy of an established infection.[13]

Approximately 30-50% of antibiotic use in hospitals is now for surgical prophylaxis. However 30-90% of this prophylaxis is inappropriate that increases the selective pressure favoring the emergence of antimicrobial resistance. Judicious use of antibiotics in the hospital through effective antibiotic policy and guideline development is then essential.[16]

FORMATION OF A HOSPITAL ANTIBIOTIC COMMITTEE

Hospital antibiotic committee (one representative of infectious diseases, one representative of Clinical Pharmacy, one representative from surgery, one representative from general medicine) has the responsibility for the formulation and supervision of an *antibiotic policy.*

Function of the antibiotic committee

- To consult widely with the clinical staff to get agreement on antibiotic usage in different specialities.
- To then establish an antibiotic formulary, which may prevent the use of some drugs and restrict the use of others.
- To formulate guidelines for antibiotic prescribing, including indication for prophylaxis and therapy of infection, the optimum dosages, timings and duration of therapy and policies for minimizing the risk of toxicity.
- To review the appropriateness of antibiotic use and emergence of antimicrobial resistance and provide feedback on this to clinicians.
- To be responsible for education and dissemination of information.
- To work closely with the Infection Control Team and the Microbiology Department.[27]

The key members of antibiotic committee are the pharmacist, the microbiologist, clinical doctors and nurses, reciprocal membership between the infection control committee and the drugs committee and other members can be co-opted as necessary.

Good practices

-Consider whether or not the patient actually requires an antibiotic.
-Avoid treating colonized patients who are not actually infected.
-In general do not change antibiotic therapy if the clinical condition is improving.
-If there is no clinical response within 72 hrs, the clinical diagnosis, the choice of antibiotic or the possibility of secondary infection should be reconsidered.
-Give an antibiotic for the minimum length of time that is effective.
-Review the duration of antibiotic therapy after 5 days.
-Consider the use of pharmacy ‘stop’ policies, where drugs are written up for a specified period and are then only continued if a new prescription is issued.
-For surgical prophylaxis start the antibiotic with an induction of anaesthesia and continue for a maximum of 24 hrs only.[27]

PRINCIPLES OF ANTIBIOTIC PROPHYLAXIS

- Decide if prophylaxis is appropriate.[28]
- Choose an antibiotic effective against the pathogens most likely to be encountered.
- Choose an antibiotic with low toxicity.
- Administer a single, fully therapeutic dose intravenously 30 to 60 minutes preoperatively.
- Administer a second dose of antibiotic if the operation lasts longer than 4hr or twice the half-life of the antibiotic.
- Give 2 or 3 doses post-operatively. There is no need to extend administration beyond 24 hrs.

- Use of antibiotic is appropriate when infection is frequent or when consequences of infection would be unusually severe.
- Avoid antibiotics likely to be of use in the treatment of serious sepsis.
- Do not use antibiotic prophylaxis to overcome poor surgical technique.
- Review antibiotic prophylaxis protocols regularly as both cost and hospital antibiotic resistance patterns may change.[29]

ANTIMICROBIAL RESISTANCE- AN ALARMING HEALTH CARE ISSUE

Antimicrobial resistance is a major public health problem worldwide, and international efforts are needed to counteract its emergence.[36] Although it is widely accepted that the control of antibiotic prescribing is essential for the control of antibiotic resistance. Antibiotic misuse is common. Studies have suggested that up to 70% of treatment courses are ‘unnecessary’ and ‘inappropriate’. Therapy is often unnecessarily prolonged and prophylaxis is often inappropriate or given at wrong time.[37]

The frequency with which MRSA has been recovered from various infection sites has increased steadily throughout the United States. The frequency of methicillin resistance among staphylococcal strains change from 2.4% in 1975 to 29% in 1991. CDC’s National Nosocomial Infections Surveillance identified a rapid increase in vancomycin- resistant enterococci (VRE) from 0.3% in 1989 to 7.9% in 1993. The rate of high-level enterococcal resistance to penicillin and aminoglycosides increased simultaneously. The use of vancomycin has been reported consistently as a risk factor for infection and colonization with VRE and may increase the possibility of the emergence of vancomycin-resistant *S. aureus* or vancomycin-resistant *Staphylococcus epidermidis.*[4]

RATIONAL USE OF ANTIBIOTICS

Infections are the major cause of morbidity and mortality in developing countries. Almost one third of drug use is for antibiotics. The following guidelines will ensure that antibiotics are used in a way which minimizes the *emergence and spread of resistant organisms*, and which maximizes their efficacy and safety.

- ✓ Use antibiotics only when indicated.
- ✓ Where appropriate, specimens for gram stain, culture and sensitivity testing should be obtained before commencing antibiotic therapy.
- ✓ The choice of agent should be based on factors such as spectrum of activity in relation to the known or suspected causative organism, safety, previous clinical response, cost, ease of use and potential for selection of resistant organisms.
- ✓ An adequate dose and duration is essential.
- ✓ A history of allergy or other adverse effect to the drug under consideration should always be sought.
- ✓ Prophylactic use of antibiotics should be restricted to situations where it has been shown to be effective or where the consequences of infection are disastrous.
- ✓ Empirical antibiotic therapy should be based, where possible, on local epidemiological data on potential pathogens and their patterns of sensitivity.
- ✓ Antibiotic therapy directed at specific organisms should include the most effective, least toxic and narrowest spectrum agent available.
- ✓ Oral therapy should be used in preference to parenteral therapy whenever clinically possible.
- ✓ Antimicrobial combinations should only be used where indicated.
- ✓ Topical antibiotics should be restricted to a few proven indications. Eg:-eye infections.
- ✓ Reserve new antibiotics for situations where serious infections have not or are unlikely to respond to conventional agents.[38]

Antimicrobial use is very high and in many cases irrational. Apart from unnecessary cost this can increase chances of antimicrobial resistance.

OBJECTIVES OF THE STUDY

- ❖ To compare the incidence of maternal and neonatal infectious complications between two groups, in which Group I received both preoperative and postoperative prophylaxis & Group II postoperative only.
- ❖ To evaluate the cost of therapy.

Considering the aims, the study was structured in the following manner

1. Design of a structured data collection form.
2. Getting Ethical Committee clearance to conduct this study.
3. Screening of patients admitted to the Hospital, using the selection criteria.
4. Recording the relevant demographic, socioeconomic and clinical data along with prophylactic antibiotic therapy of the patients selected.
5. Evaluating the effect of antibiotic prophylaxis on maternal and neonatal infectious complications by comparing the preoperative along with postoperative group & postoperative only group, monitoring of adverse drug reaction and cost evaluation.
6. Recording the data associated with cesarean delivery and prophylactic therapy.
7. Statistical analysis of data.
8. Interpretation of results.

RESEARCH DESIGN

A. Study Setting

The study was conducted in the inpatient department of a Hospital.

B. Period of study

6 Months (From July 2006 to December 2006).

C. Design of study

Prospective observational study.

D. Study population

200 patients admitted and delivered by cesarean section, In which 100 of them received pre- operative & post-operative prophylactic antibiotics(Group I); The next 100 of them received only postoperative antibiotics (Group II) & Meeting all the inclusion criteria during the study period.

E. Selection Criteria

INCLUSION CRITERIA

- Patients who are in the age group of 18-40 years.
- Patients who are admitted for cesarean deliveries.

EXCLUSION CRITERIA

- Patients who are already on antibiotic therapy for any infections.
- Patients whose data is insufficient.

F. RESEARCH STUDY APPROVAL AND CONSENT

The study was approved by the Human Ethical Committee, of the selected hospital. All patients participating in the study provided consent (Appendix II). Confidentiality of all patient information was strictly maintained.

G. STATISTICAL ANALYSIS

The data were entered in Microsoft Excel format and the statistical analysis were done using SPSS for Windows version 14.0. For the comparison of groups the Chi-square test for categorical variables and the student t test for continuous variables were used.

METHODOLOGY

Data Collection

Those cases which met study criteria were identified. Information on patients admitted for cesarean delivery was collected and recorded in a standard proforma by reviewing their medical records after getting a written consent from the patient. Additional information was collected by interviewing the patient or the bystanders. The patients condition was monitored daily till the day of discharge from the hospital. Confidentiality of the patient information was maintained strictly. Institutional ethical committee clearance was obtained for the study.

Total of 200 patients between age group 18 to 40 were considered for the study. From this 100 of them are coming under group I receiving pre-operative and postoperative prophylaxis and the remaining 100 under group II receiving post operative antibiotic only.

AGE DISTRIBUTION OF PATIENTS

The analysis shows that 34.5% patients within the age group of 18-25 years,44% patients were between 25-29 years, 17.5% patients were between 30-34 years and 4% patients were between 35-40 years of age.

Mean age of group I is 26.85 (3.780) and for the group II is 25.68(4.017). P-value is 0.035. So the mean difference between these two groups is statistically significant.

PRE OPERATIVE STAY

The mean days of preoperative stay of group I is 8.09 and that of group II is 4.84(6.273). P-value is 0.003. so the mean difference between two groups is statistically significant.

Most of the patients under group I came for safe confinement. So these patients were admitted several days before the surgery compared to group II majority of which included emergency cases.

LENGTH OF STAY

The mean days of length of stay of group I is 14.25 (8.854) and of group II is 11.68 (6.336). P value is 0.019 so it is statistically significant.

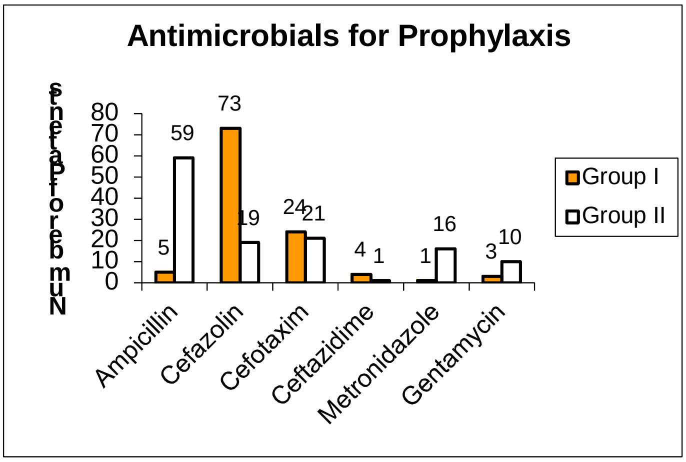
The patients under group I had more days of pre-operative stay compared to group II.

COMMONLY USED ANTIBIOTICS FOR PROPHYLAXIS

In group I cefazolin is the commonly used antibiotic (73%) & in group II ampicillin is commonly used and its percentage is 59. The secondmost drug in both groups were cefotaxime.

The Cochrane Database Systematic review of “Antibiotic prophylactic regimens and drugs for cesarean section” found that both ampicillin and first generation cephalosporins have similar efficacy in reducing postoperative endometritis.[41]

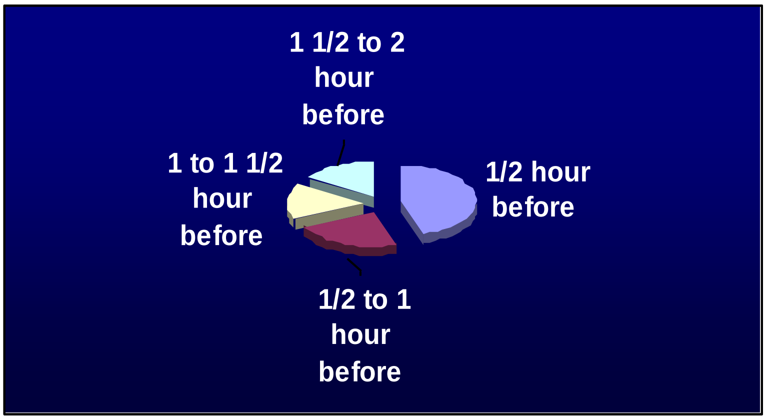
Categorization of patients based on usage of antibiotics (Graph – 10)



TIMING OF PROPHYLAXIS

From total of 200 patients only 100 (group I) receives antibiotic prophylaxis (before surgery). Majority of patients receives ½ hour before surgery (45 patients).

Categorization of patients based on timing of prophylaxis: (Graph – 11)

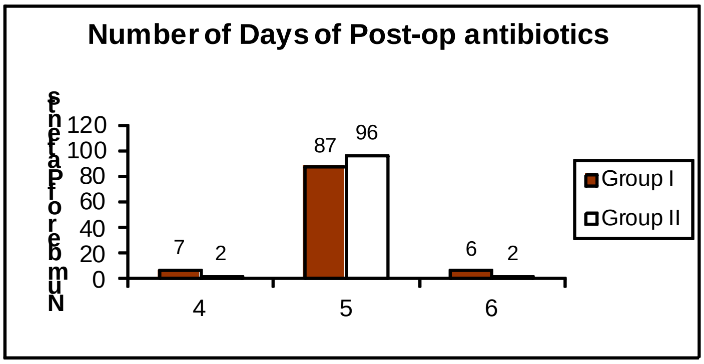


Thigpen E tals "Timing of prophylactic antibiotic administration in the uninfected laboring gravida" found that there was no difference in maternal infectious morbidity whether antibiotics were given before skin incision or at cord clamping.[3]

DATA ON NO OF DAYS OF POST OP ANTIBIOTICS

From analysis 87% of patients in the group I & 96% of patients in the group II receives therapy for 5 days.

Categorization of patients based on no of days of post op antibiotics (Graph – 12)

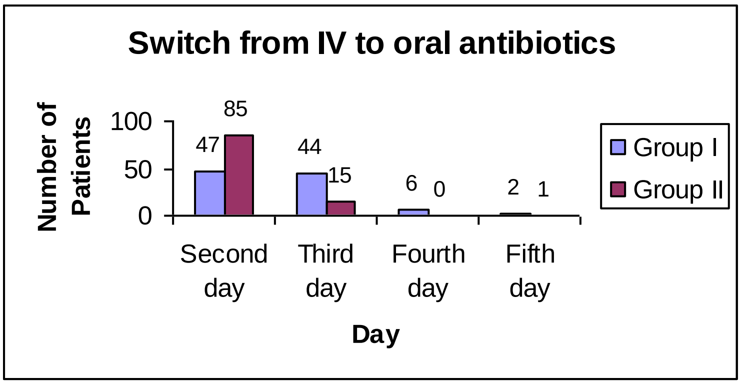


Increased duration and unnecessary antibiotic use causes resistance and unnecessary costs.

DATA ON EARLY SWITCH FROM IV TO ORAL ANTIBIOTICS

Majority of patients in groupI receives oral therapy in 2nd (47.0%) and 3rd (44.0%) day and in group II it is 2nd day (85.0%).

Categorization of patients based on early switch therapy (Graph – 13)



Early switch therapy causes decreased cost because oral drugs are less expensive than their parenteral counterparts.

MATERNAL COMPLICATIONS

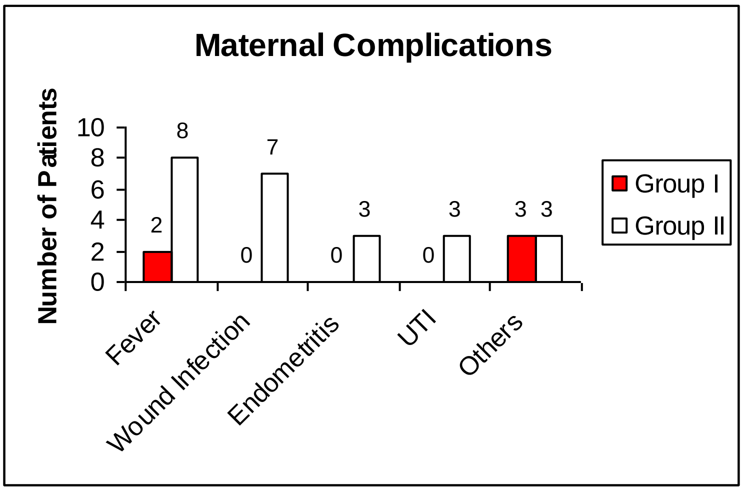
In the analysis prophylactic group shows 2 percentage of fever cases and it is 8 percentage in post-operative prophylactic group. P value is 0.101 so it is not statistically significant.

Wound infection cases are not there in prophylactic group and it is 7 percentage in post-operative prophylactic group. P value is 0.014 and it is statistically significant.

Endometritis and uti cases are only in the nonprophylactic group. The rate is 3 percentage. P value is 0.246 and therefore the difference in the rate is not statistically significant between two groups.

Other complications are 3 percentage in each group. P value 1 and not statistical significance.

Categorization of patients based on maternal complications (Graph – 15)

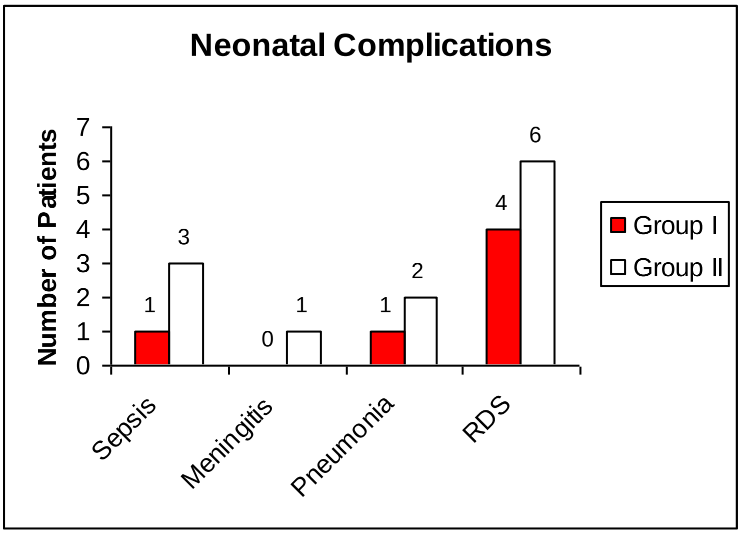


The results of a study done by Di LietoA et al conducted a ***retrospective analysis concerning the incidence of cesarean section*** **(CS),** showed that the administration of antibiotics as cefazolin and ampicillin is able to reduce in a significant way the incidence of postoperative infective morbidity.[39]

NEONATAL COMPLICATIONS

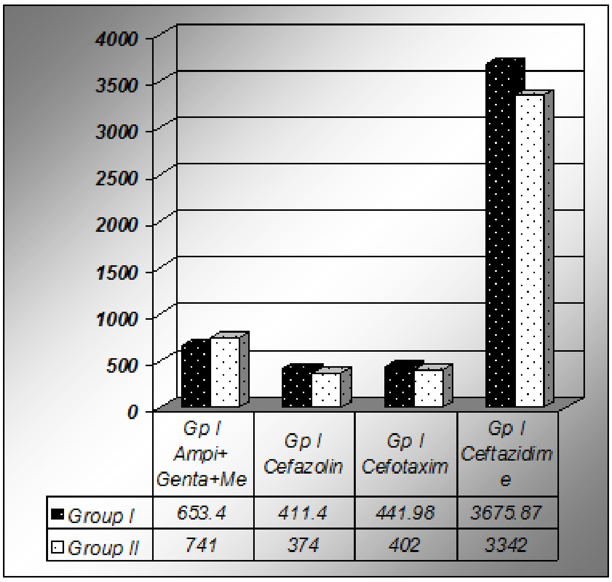
In the neonatal analysis the complication rate is high in the group II compared to group II. But the P value not less than 0.05. So it is not statistically significant.

Categorization of patients based on neonatal complications (Graph-16)



COST EVALUATION

Categorization of antibiotics based on cost (Graph – 19)



Mean cost of prophylactic group is 584.3133 and of nonprophylactic group is 426.3062 P value is 0.001. Difference between two groups are statistically significant.

CONCLUSION

Study shows the pre-operative antibiotic prophylaxis significantly reduces the postoperative wound infection($P<0.05$) and reduces the rate of fever, endometritis, urinary tract infection etc. The pre-operative prophylaxis also reduces neonatal infection rate and complications Cefazolin is seem to be the most cost effective antibiotic in our study.

The antimicrobial should be safe for the patient and economical for the hospital. The concept of clinical pharmacy is being advocated in health care practice to promote rational drug use. Clinical pharmacists will have to consider the clinician's choice of drugs to provide the most cost effective therapy. A concentrated effort should be made in areas of clinical surgery where the value of antibiotic prophylaxis has not been proven.

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