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Postoperative Outcome of Single Dose Vs Multiple Doses of Prophylactic Antibiotics in Major Elective Obstetric and Gynecological Surgeries: A Prospective Observational Study

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Abstract: ***Antibiotic prophylaxis is a well established entity in current medical practice for prevention of SSI, urinary tract infection (UTI), endometritis and other complications related to surgery, developing as a result of invasion by bacteria or other pathogens. Patterns of use of antibiotic prophylaxis in pioneer health care institutes have been studied and it has been found that about 30-90% of total use of antibiotics in hospitals is inappropriate in terms of choice of antibiotic, dose and timing.[1] Many studies support the use of single dose of prophylactic antibiotics over multiple doses. [2-5] But in practice multiple dose regimens are being frequently used. Major complication arising out of the situation is antimicrobial resistance. Ineffective older antibiotics leading to the need for newer and stronger antibiotics pose a huge financial as well as pathological burden on society. Our study aimed at comparing the effect of single dose with that of multiple doses of prophylactic antibiotics in major elective obstetric and gynaecological surgery. This prospective observational study was conducted at department of obstetrics and gynecology at Indraprastha Apollo Hospitals, New Delhi, India from August 2015 till December 2016. A total of 400 patients (200 in each group) admitted for major obstetric and gynecological surgeries were studied at the time of discharge, 1week and 1month after the surgery. No significant difference was found in rates of surgical site infections (SSI), febrile illness, urinary tract infection(UTI), and chest infection, while a significant increase was found in rate of injection site inflammation in those receiving multiple dose regime of prophylactic antibiotics.***

1. Introduction

Surgical site infections (SSIs) are second commonest nosocomial infection accounting for approximately one quarter of 2 million hospital acquired infections in United States of America annually.[6,7] Among an estimated 27 million surgical procedures, surgical site infections are reported in up to 500,000 cases each year [8] . It has been estimated that 2-5% of patients undergoing clean extra abdominal surgeries and up to 15-20% of patients undergoing intra abdominal procedures will develop a SSI [9-14] . A study done by Nisa M showed wound infection rate of 5%.[15] Nelson et al [16] compared one day of antibiotic prophylaxis with seven days of antibiotic prophylaxis and found no statistically significant difference between the two groups in terms of wound infection. Moreover shortening the duration of therapy reduces the medical cost and prevents development of resistance of the microorganism to antibiotics. A study done by Her young [17] has shown that the single dose of antibiotic prophylaxis can reduce the antibiotic cost by 75-80%. Other studies have also shown that considerable cost effectiveness can be achieved with a single dose.[18-20] Tchabo JG also reported non significant difference in incidence of postoperative infection and mean duration of hospital stay when comparing single dose antibiotic Vs multiple doses.[22] The American college of obstetricians and gynecologists published guidelines in 2006 which was revised in 2009 regarding prophylactic antibiotic use in gynecological and obstetric procedures. They stated that single dose of 1g or 2g IV cephazolin is drug of choice for all major gynecologic and obstetric procedures including cesarean sections and hysterectomies.[23] Patterns of use of antibiotic prophylaxis in Indian pioneer institutes have been studied and have been found that about 30-90% of total use of antibiotics in hospitals is inappropriate in terms of choice of antibiotic, dose and timing.[24] Despite available guidelines[23,25-27], most practitioners still prescribe multiple dose regimens for antibiotic prophylaxis. Thus there is need of reinforcement of proper usage of antibiotics in hospitals.

2. Aims and objectives

Aim: To observe and study the effect of single dose of prophylactic antibiotics to that of multiple dose regimen administered for preventing Surgical Site Infections (SSI) during major elective Obstetric and Gynecological surgeries.

Primary Objective: To compare the rates of SSI with single and multiple dose regimen of prophylactic antibiotics given during major elective Obstetric and Gynaecological surgeries.

Secondary Objective: 1.To observe the occurrence of common infections i.e. febrile illness, Urinary tract infections, injection site inflammations, and chest infection in the two groups. 2. To observe the impact of other factors such as history of previous surgery and postoperative blood transfusion on the occurrence of SSI in the two groups i.e., one with single dose of prophylactic antibiotics and the other with multiple dose regimens .

3. Materials and Methods

Study setting

The present single centered Prospective observational study was conducted at Department of Obstetrics & gynecology, Indraprastha Apollo Hospitals, New Delhi, after taking approval from Ethics committee of the hospital. The period of study was from August 2015 to December 2016. Study population consisted of patients admitted at Indraprastha Apollo Hospitals for major gynecologic and obstetric surgeries from August 2015 till December 2016. Sample size estimation was done as per following formula: $n = 4pq/L^2$ Where n = sample size per group, p = the minimum known overall prevalence of the disease under consideration, q = 1-p, L = allowable error/precision/variability (5-20%). As per the previous studies, the prevalence of surgical site infection in intra-abdominal surgeries is approximately 15-20%[54-58] and allowable error is fixed at 0.05 $n = 4p(1-p)/L^2 = 4\times 0.15(1-1.0.15)/(0.05)^2 = 204$ Thus 200 cases were taken in each group in our study.

Group Allocation

Patients were divided in two groups on basis of treatment they received. Group A consists of cases that were administered single dose of prophylactic antibiotic and Group B of those who were administered multiple doses.

Inclusion criteria: All non infected, elective major Obstetric and Gynaecological surgical cases.

Exclusion criteria:

1) Cases with pre existing infection including asymptomatic bactiruria
2) Uncontrolled Diabetes
3) Carcinomas
4) BMI >30
5) Hemoglobin concentration < 8g/dl (severe anemia)
6) Immunosuppressed individuals

Procedure Methodology

A written and informed consent was taken from patients who were included in study. Baseline assessment was done before surgery. Routine preoperative were performed on each patient. Pre-anaesthetic checkup was done and physician's clearance was obtained. Preoperative shaving was avoided and if required clipping was done in immediate preoperative period. First dose of antibiotic prophylaxis was aimed to be given within an hour of the incision in gynecologic cases and after cord clamping in cesarean sections. First group consisting of patients receiving single dose were administered Injection Co-amoxyclav in single dose intravenously. Second group consisting of patients receiving multiple doses were administered injection Co-amoxyclav, amikacin, and metronidazole intravenously in multiple doses. The choice of antibiotic was as per practice of operating surgeon. Hand washing was done as per standards of WHO guidelines on hand hygiene in health care (2009) with iodine based liquid soap preparations.[28] Standard suture materials used for approximating skin during surgery were either number 3-0 polyglecaprone 25(monocryl) or number 3-0 prolene. Sterile dressing was done and was either changed on postoperative day 3 and then removed at follow up visit at 1 week or was removed directly at follow up visit at 1 week as per choice of the surgeon. Postoperatively, record of 4 hourly vital signs and temperature was taken. Abdominal and perineal examinations were performed at least twice daily. Following parameters were studied at the time of discharge, and follow up visits after 1 week and after 1 month: 1. Surgical site infection (wound necessitating antibiotic usage or drainage, 2. Any febrile illness (any clinically relevant fever for unknown reason with axillary temperature >38°C (100° F) on two consecutive postoperative days, or >39°C (102.2°F) on any one postoperative day after 48 hrs of surgery) 3. UTI (single bacterial growth exceeding 10^5 bacteria/ml), 4. Chest infection (any upper or lower respiratory tract infection necessitating administration of antibiotics.) 5. Injection siteinflammations including pain, swelling and thrombophlebitis. Data was collected on a prescribed proforma.

Statistical methods: Based on the above study means were calculated as mean± 2 standard deviations (SD). Statistical analysis to determine the significance of outcome measures in two groups was carried out by applying Chi- Square test. Odds ratio with Spearman's correlation test was applied for risk stratification.

4. Results

Baseline variables in our study in both groups were comparable.

Table 1: Means of baseline study variables in Group A (Single dose) and Group B (multiple dose).

Variables	Group B (multiple dose)	Group A (single dose)	p value
Age	34.7 ± 9.554	35.2 ± 9.58	-
Hospital stay (days)	4.46 ± 4.04	3.41 ± 0.62	.094
Duration of surgery (hours)	1.62 ± .70357	1.32 ± 0.67	.909
Duration of catheterization (hours)	16.55 ± 6.084	15.13 ± 6.3	.811
Duration of IV cannulation	54.96±13.41	16.66±4.25	0.001*

p value ≤ 0.05 – significant

The mean duration of IV cannulation in single dose group was 16.66±4.25 and that in multiple dose group was 54.96±13.41 hrs which was significantly higher (p value 0.001).

Table 2: Incidence and statistical significance of SSI and Febrile illness in two groups in our study

	SSI				Febrile illness			
No. of cases	Group A	Group B	Odds ratio	P value	Group A	Group B	Odds ratio	p value
At discharge	1	1	1	1.00	3	5	0.59	0.48
1 week	2	3	0.66	0.65	2	3	0.66	0.65
1 month	0	0	1	1.00	0	0	1	1.00

*p value ≤ 0.05 – significant

In our study the overall rate of surgical site infections was 1.25% in both groups combined. In Group A the rate of SSI was 0.5% before discharge and 1% at follow up at 1week, and in Group B the rate was 0.5% before discharge and 1.5% at follow up at 1 week. This was statistically insignificant. In our study the mean number of doses of prophylactic antibiotics in group B was approximately 5 doses. When we compared the cost of antibiotics in 200 patients, the average cost of antibiotic in those receiving multiple dose regimen was approximately 7 times higher than those receiving single dose regimen, with no added benefit of decrease in rate of SSIs and other infections.

The rate of febrile illness in our study in Group A was 1.5% before discharge and 1% at follow up visit at one week. In Group B 2.5% patients developed febrile illness before discharge and 1.5% patients at first follow up visit at 1 week. This was statistically insignificant.

Table 3: Incidence and statistical significance of chest infection and UTI in two groups in our study

	Chest infection				UTI			
No. of cases	Group A	Group B	Odds ratio	P value	Group A	Group B	Odds ratio	P value
At discharge	1	1	1	1.00	2	2	1	1.00
1 week	1	0	3.03	0.49	1	1	1	1.00
1 month	0	0	1	1.00	0	0	1	1.00

*p value <0.05= significant

Rate of UTI in our study in group A was 1% before discharge and 0.5% at 1 week follow up, and in group B it was similar 1% before discharge and 0.5% at follow up at 1 week.

Rate of chest infection in our study in group A was 0.5% before discharge and same at 1 week follow up, while in group B it was 0.5% before discharge and none at 1 week follow up and was statistically insignificant.

A significant difference was found in rates of swelling at injection site in those receiving multiple dose regimen compared to those receiving single dose regimen(p value – 0.03). Rates of pain and thrombophlebitis were also higher in those receiving multiple dose regimen, but were statistically non significant.

Table 4: Incidence and statistical significance of Injection site inflammations in two groups in our study

Injection site inflammations	Group A	Group B	Odds ratio	p value
Pain	4	10	0.3878	0.11
Swelling	6	16	0.3557	0.03*
Thrombophlebitis	1	2	1	0.5

*p value <0.05= significant

In those who received single dose regimen, only 5 patients out of 200 i.e. 2.5% of sample size were administered further dose of antibiotics as treatment, while in those who received multiple dose regimens further doses of antibiotics were given to 6 patients as treatment, which justifies our study that single dose of prophylactic antibiotics is as effective as multiple doses.

Table 5: Comparison of prevalence of surgical site infection in Group A (single dose) and Group B (multiple dose) among those who had history of previous surgery and those who did not have history of previous surgery

	Group A							Group B						
		At discharge		At 1 week		At 1 month			At discharge		At 1 week		At 1 month	
	Total No. of cases	SSI	No SSI	SSI	No SSI	SSI	No SSI	Total No. of cases	SSI	No SSI	SSI	No SSI	SSI	No SSI
History of previous surgery	21	0	21	1	21	0	21	12	0	12	0	12	0	12
No history of previous surgery	179	1	178	1	178	0	179	188	1	187	3	185	0	188
Relative risk(RR)		0		8.52		0			0		0		0	
P value		N/A		0.12		N/A			N/A		N/A		N/A	

*p value <0.05= significant

A rise in relative risk of SSI with history of previous surgery was seen in Group A at follow up visit at 1(RR 8.52) week but this was statistically not significant(p value 0.12).

Table 6: Comparison of prevalence of surgical site infection in Group A(single dose) and group B(multiple dose) among those who received blood transfusion and those who did not receive blood transfusion

	Group A							Group B						
		At discharge		At 1 week		At 1 month			At discharge		At 1 week		At 1 month	
	Total No. of cases	SSI	No SSI	SSI	No SSI	SSI	No SSI	Total No. of cases	SSI	No SSI	SSI	No SSI	SSI	No SSI
History of blood transfusion	18	0	18	1	17	0	18	15	0	15	1	14	0	15
No history of blood transfusion	182	1	181	1	181	0	182	185	1	184	2	183	0	185
Relative risk(RR)		0		10.11		0			0		6.17		0	
p value		N/A		0.09		N/A			N/A		0.12		N/A	

*p value <0.05= significant

In our study a rise in relative risk of SSI was seen with postoperative blood transfusion at the time of follow up at 1 week in both groups(RR 10.11 in Group A and RR 6.17 in Group B) but this was statistically not significant(p value 0.09 in Group A and 0.12 in Group B).

5. Discussion

Our study was a single centered observational study conducted at a tertiary care private sector based institution. Thus there was a limitation in sample size. Randomization was at the level when a patient reached our health facility and visited a surgeon of their choice. Randomization beyond this was not feasible. Blinding was single sided as patients did not know what treatment they received, but not on side of researcher as it was an observational study and we knew the nature of treatment being administered. Confounders like pre-existing skin infection, febrile illnesses, severe anemia, asymptomatic bactiruria, uncontrolled diabetes etc. were taken as exclusion criteria. In our study we found that there was no significant difference in rates of SSI, febrile illness, chest infections and UTI between single dose of antibiotic prophylaxis and multiple dose regimen, instead a rise in injection site inflammation was seen in those receiving multiple dose regime. Single dose regimen is also more cost effective than multiple dose regimen. There is a need for implementation of available guidelines by practitioners in their day to day practice. No significant relationship was found between rates of SSI to history of previous surgery and blood transfusions during hospital stay in our study.

6. Conclusion

Single dose antibiotic prophylaxis in major gynaecological and obstetric surgeries is as effective as multiple dose regimen.

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