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Antibiotic prophylaxis in cesarean section- A review article

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Abstract

Good practice of prophylactic antibiotics is one of the safest ways to avoid post operative infection in class III and class IV Operative Wounds. This has been proven a safest method as chances of any adverse effect of the antibiotics in post operative phase is very less. In caesarean delivery, the use of antibiotics like cephalosporins is very common. Research shows, documented efficacy of cephalosporins in reducing occurrence of endometritis or wound infection to a significant extent. The practice doesn't cause any adverse effect in neonates as well. At the same time, use of prophylactic antibiotics also reduces hospital stay after operation. This review emphasizes on the time and type of prophylactic antibiotics use. From the analysis, efficacy of the drugs can be well established in cesarean delivery.

Keywords: Antibiotics, Prophylaxis, Infection.

1. Introduction

Antibiotic prophylaxis is a concept, used frequently in medical practices, which refers to the use of antibiotics before different surgery procedure. The main aim of this process is to control different types of bacterial infection which are highly probable in the course of a surgery. The practice of using antibiotic before operating any kind of surgery is performed under the supervision of the physicians and this practice is capable enough to save life of numerous patients.

Though it can be said that the practice should be incorporated in all kind of surgery where the patients are in risk of developing infection, but there are certain cases where the practice bears a lot of importance. These include, gastrointestinal surgeries, cesarean delivery, surgeries for implanting pacemaker or any other kind of medical devices inside the body, in case of cardiac procedures which may include coronary artery bypass grafts, replacement of valves, heart transplant etc. in this review article, the importance of using antibiotics in caesarean delivery will be discussed. Apart from that, different types of drugs which are frequently used during this course of action will be discussed in this topic.

Different types of infections are very common in cesarean delivery including development of wound, fever associated with the development of the wound, endometrititis or the inflammation of the inner layer of uterus or it can be UTI as well. In some serious cases incidents like pelvic abscess or accumulation of pus in the pelvic region may also occur.

There are instances of bacteremia or infection in blood cells or the destruction of the tissues in the inner area of the uterus may also occur. Apart from that there are instances like septic shock which happens because of reduction in the volume of blood caused by infection and septic pelvic vain thrombophlebitis or inflammation of the

veins at the pelvic region. Another incident called necrotizing fasciitis or the death of tissue in the inner layer of the uterine may also happen. All these factors may lead to death of the individuals. Therefore, cesarean infection is considered one of the leading causes of maternal mortality.

It is common to develop fever after any surgical procedure. But if the condition is associated with any kind of infection within the body, it requires special attention. It has been seen in research that if no antibiotics are applied, cases of infection in uterus may go up to 85% and among them 25% could be very serious in nature [1]. In this case, application of the antibiotics prior to the surgery has shown very promising result.

During cesarean delivery, genital tract gets ruptured and this site is often vulnerable to the infection by bacteria. In many cases, the infection may occur even when the membrane is not ruptured because of microbial invasion of the intrauterine cavity especially in case of preterm labor [2].

The most common micro organisms which cause infection are *Escherichia coli. Apart from that, other bacteria like Enterococcus faecalis, Staphylococcus aureus* and coagulase negative staphylococci, anaerobes (such as, *Peptostreptococcus* species and *Bacteroides* species), *Gardnerella vaginalis* and genital mycoplasmas etc. are also responsible for the infection. Among them *Staphylococcus aureus* and coagulase negative staphylococci may enter the body during the surgeries which are generally present at the endogenous flora of the skin [3].

There are several antibiotics present at the market but the most common ones which are used during prophylaxis are cephalosporins, such as cefazolin and cefuroxime. In case of allergy to Cephalosporin Clindamycin can be used. The antibiotics are generally administered 20 minutes to one hour before surgery intravenously. Generally a single does is administered before the surgery, but in case of operating procedures, multiple doses can be given as well.

The most effective of way of administration of antibiotics is either before or after the clamping of the cord; though the standard procedure is to administer it before the process of surgery take place. From observation of the cases, it can be concluded that incision of antibiotics before the surgery during Caesarean delivery has no effects on the infants and it can significantly reduce the chances of maternal infection. In this review article, different research work by the scholars related to the use of antibiotics prior to surgery in case of caesarean delivery will be reviewed and discussed. The main aim of the study is to find out correlation between different researches works and to understand the effectiveness of the whole concept.

2. Antibiotic prophylaxis in surgery

Antibiotic prophylaxis is extensively used in different types of surgical procedures since a very long time in order to prevent post operative infection at the site of the surgery and in other peripheral tissues. This process is known to have huge impact on the reduction of morbidity among the patients post surgical process. There are several micro organisms which may cause different types of infection in the patients and the main aim of antibiotic prophylaxis is to prevent those infections.

There are different types of antibiotics available in market and among them different types of antibiotics are used in different types of surgeries. Based on the nature of sites or type of operation, antibiotic spectrum is decided and proper investigation is required before ordering or administering any preoperative medication. There are surgical procedures which are generally considered clean (Class I) and in these cases use of prophylactic antibiotics are not required (except in case of setting of indwelling prosthetic placements or in case on incision of bones).

In case of class II surgical procedures, use of a single dose of antibiotic before the operation is recommended. In all types of abdominal surgery, including hepatobiliary, pancreatic, gastroduodenal surgery, most commonly used drug is cefazolin. A single dose of this drug is administered before the procedure. In case of Contaminated or class III, the most common practice involves mechanical preparation or parenteral antibiotics which can exhibits aerobic activity and anaerobic activity as well. For example, in case of emergency abdominal operation such as appendix or removal of inflammated gall bladder, this procedure is used. In trauma cases as well, this procedure is commonly used. In case of dirty or infected surgery, more steps need to be taken such as administration of antibiotics in pre and post operative period.

According to National Research Council, Operative Wounds and Rates of Wound Infection can be classified into following categories:

Table 1: Classification Wound Infection according to National Research Council

Clean(class I)	Non traumatic	2.1%
	No inflammation	
	No break in technique	
	Respiratory, alimentary, or genitourinary tract not entered	
Clean-contaminated (class II)	Gastrointestinal or respiratory tract entered without significant spillage	3.3%
Contaminated (class III)	Major break in technique	6.4%
	Gross spillage from the gastrointestinal tract	
	Traumatic wound, fresh	
	Entrance into the genitourinary or biliary tracts in the presence of infected urine or bile	
Dirty and infected (class IV)	Acute bacterial inflammation encountered, without pus	7.1%
	Transection of "clean" tissue for the purpose of surgical access to a collection of pus	
	Traumatic wound with retained devitalized tissue, foreign bodies, fecal contamination, or delayed treatment, or all of these, or from a dirty source	

(Source: Onyekwelu *et al* [4])

Table 2: Antimicrobial Prophylaxis for Surgery

Nature of operation of Operatiooperion	Common pathogens	Recommended antimicrobials	Adult dosage (before surgery)
Cardiac	*Staphylococcus aureus, S. epidermidis*	cefazolin or	1-2 g IV
		cefuroxime	1.5 g IV
		OR vancomycin	1 g IV
Esophageal, gastroduodenal	Enteric gram-negative bacilli, gram-positive cocci	High risk only: cefazolin	1-2 g IV
Biliary tract	Enteric gram-negative bacilli, enterococci, clostridia	High riskonly: cefazolin	1-2 g IV
Appendectomy, non-perforated	Enteric gram-negative bacilli, anaerobes, enterococci	cefoxitin	1-2 g IV
		OR cefazolin	1-2 g IV
		+ metronidazole	0.5 g IV
		OR ampicillin/sulbactam	3 g IV
Genitourinary	Enteric gram-negative bacilli, enterococci	High risk only: ciprofloxacin	500 mg PO or 400 mg IV
Vaginal, abdominal, or laparoscopic hysterectomy	Enteric gram-negative bacilli, anaerobes, Gp B strep, enterococci	cefoxitin or cefazolin	1-2 g IV
Caesarean section	same as for hysterectomy	cefazolin	1-2 g IV after cord clamping
Medical Termination	same as for hysterectomy	First trimester, high risk aqueous: peicillin G	2 mill units IV
		OR doxycycline	300 mg PO
		Second trimester: cefazolin	1-2 g IV
Incisions through oral or pharyngeal mucosa	Anaerobes, enteric gram-negative bacilli, *S. aureus*	clindamycin	600-900 mg IV
		+ gentamicin	1.5 mg/kg IV
		OR cefazolin	1-2 g IV
Neurosurgery	*S. aureus, S. epidermidis*	cefazolin	1-2 g IV
		OR vancomycin	1 g IV
Ophthalmic	*S. epidermidis, S. aureus, streptococci*, enteric gram-negative bacilli, *Pseudomonas* spp.	gentamicin, tobramycin, ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin, ofloxacin, or neomycin-gramicidin-polymyxin B	multiple drops topically over 2 to 24 hours
		cefazolin	100 mg subconjunctivally

(Source: Salkind *et al* [5], Manchi *et al* [6])

3. Literature review

A study conducted by Ronghua et al has shown the effects of antimicrobial prophylaxis in cesarean section of delivery [6]. The study was conducted among 100 women. Among them 87% belonged to age group 20 to 35, 21% belonged to age group to 20 to 25, 39% fall in the age group of 26 to 30 years. They study aimed to take patients from different age groups so that the result can be compared with one another groups. To conduct the study, the chosen combination of drugs was ceftriaxone and sulbactam. Among the whole group, in 38% of the cases, elective C-section had been carried out. Rests of the patients were inn

emergency c-section. In the second group, the drugs have been given for 7 days as intra and post operative antimicrobial prophylaxis. At the end of the study it has been seen that only 17% of the total women have diagnosed with infection post operative procedures. It means in most of the cases, the infection didn't occur and it has shown positive impact on the recovery of the infected women. Post-partum endometritis is very common in case of cesarean delivery in spite of giving antibiotics before the operative procedures. In this case as well, a few patients developed infection after delivery because of rupture of membrane in uterus. Among the total 17% of the women, 2% developed post-partum endometritis, 8% with wound infection and 7% with urinary tract infection. From the study it could be concluded that use of combination of ceftriaxone and sulbactam have significantly reduced the number of cases of Post-partum endometritis when applied in early rupture of the membrane. In this case the patients who have suffered from infections had been given more advanced regimen to follow up with that included amoxicillin and clavulanic acid, ciprofloxacin and tinidazole combination and the duration of treatment was prolonged. It had been seen in this study that after following the most common standard operating procedures of the use of antibiotics, post operative morbidity had significantly being reduced. This process had shown very positive impact on the overall success of the surgical procedure and also it has reduced the stay of the patients at hospital post operation. At the same time, the process is cost effective as well as it eliminates the complications which are generally highly anticipated and expected in cesarean section of delivery. After more analysis, it has been seen the infection in the women even after antibiotic prophylaxis was mainly due to pre occurred infection or any other disease or prolongation in the rupture of membrane. It means the percentage of infection could be reduced further if all these mentioned factors could be eliminated before the delivery procedures.

An investigation, conducted by Tita and colleagues [7], had shown positive results when broad-spectrum prophylaxis with adjunctive azithromycin was used in cesarean delivery. The study was conducted among 2000 women at 14 hospitals in US. These women were mostly in 24th week of their pregnancy or more weeks of gestation or some of them are already in their labor or some already has ruptured membrane. In some cases 500mg of azithomycin single dose was given intravenously and some were not given the drug. The procedure was conducted before cesarean incision. In addition to this antibiotic, intravenous dose of cefazolin was applied in all centres. It is well known that, within 6 weeks of cesarean delivery, most of the women develop different kind of infection including endometritis, wound infection, or other infections. But after antibiotic prophylaxis, it has been seen that the rate of infection significantly lower in the azithromycin group than placebo group. In azithromycin group infection rate was just 6.1% and in the placebo group it was 12%. At the same time, rate of endometritis in these two groups are respectively 3.8% and 6.1%. Wound infection rate was significantly less in the azithromycin group, which was 2.4% and in placebo group it was 6.6%. In both the cases, there was no impact on the health of the newborns as examined for next three months. Apart from that, members of the azithromycin groups have shown positive results in reduction in unscheduled hospital visits due to any health issues, hospital readmission or receipt of post-partum antibiotics. Overall it can be said that, for the members of this group overall cost has been reduced and their stay in hospital was shorter than the placebo group. From the investigation it has been very clear that introduction of azithromycin along with cefazolin has been proven a more potent combination than single use of cefazolin for prophylaxis of infectious complications in cesarean deliveries. From this study, it has been proved that a single adjunctive 500mg dose of azithromycin dose if applied intravenously, it will reduce the complexity of cases and chances of infection in most of women who are not having any preexisting infection or complexity and who are going through non-elective cesarean delivery. In the later phase of the trail, when routine phase of bacterial cultures conducted, it was found that it is much less frequently positive in azithromycin groups than the placebo group.

A study was conducted by Lomangisi *et al* (2015) at Mulago National Referral Hospital in Kampala, Uganda[8]. It was a randomized single blind clinical trial which included 493 women initially who were at their labor. Among them during the final trail, 464 participants were present till the final outcome received. The main criterion of inclusion as participants was that they all were at the emergency labor section. Those with pre-existing infection were kept out of the study. All patients were informed about the study before their inclusion as a common ethical practice. They all signed the consent form after being convinced about the efficacy of the study. Among the 464 patients, a clear division was done by creating four blocks with the help of computer generated digits. There was two groups, A and B. Patients, from group A, were given ceftriaxone 2 g intravenously 15 to 60 minutes prior to surgical procedures. Patients, from group B, were trailed with same drugs after the surgical procedure was over. In that case the patients were kept blinded but investigator was aware of the whole procedures and all details about the time of administration of drugs. After performing the procedures, the patients were kept under

check. Their conditions have been monitored till day 10 post operation. The main outcome of the trail was either infection (endometritris or wound infection or fever) or no infection throughout the observation phase till day 10. Also as a secondary outcome, neonatal were also kept under observation to find out if any of them got admitted to neonatal intensive care unit or if they are having any types of infection or not. Data regarding the trial was collected by following an interview method with the help of appropriate questionnaire. At the same time all assistant investigators were kept blind during the trail at the data collection phase to increase the efficacy of the trail. It was reported that infection rate was significantly low in group A than group B, as they received antibiotics before their surgery. Cases of endometritis were very low in group A compared to group B. in case of wound infection no significant difference was observed between two groups. Also it was another finding that not a single patient developed fever post cesarean delivery. There was doubt about this factor (no cases of fever) as all patients were given pain control drugs. So it was not clear whether it was because of antibiotics or pain control drug. In case of secondary outcome regarding infection among neonatal, the rate was 1.4% and 0.4% in group A and group B respectively. Infected neonates were treated with normal procedure in neonatal intensive care unit throughout the observation period. From the overall trail it could have been concluded that application of antibiotics within one hour prior to surgery had very positive impact in terms of reduction of post operative infection. Among different types of infection, the highest success rate was observed in case of endometritis. At the same time no significant adverse effect was observed in neonates during the observation period.

A study on the use of prophylactic antibiotics in case of cesarean section was conducted by Witt *et al* (2011)[9]. It is well researched and well trailed that use of prophylactic antibiotics reduces the chances of infection in post operative procedures. But the timing of administration of the drug may attract debate. The main aim of this research was to asses post operative infectious morbidity. In order to do that, antibiotic was given before operative procedures, after clamping of umbilical cord and in a placebo-controlled group. The chosen trail method in this case was 3-arm, double blind, prospective, randomized, placebo-controlled trial. Women, undergoing caesarean delivery in elective section, took part in the trail with their informed consent. In first two groups same antibiotic (cefazolin 2g) was used intravenously but the timing of administration was different. In first group it was given 20 to 30 minutes before the surgery and in second group, it was given within a few seconds after clamping of umbilical cord. In the third group, placebo was given before skin incision. The trail included a total number of 1112 women. Among them 370 women were in the first group, 371 women were in second group and 371 women were in placebo-controlled group. Among them 77 (6.9%) women had infection especially endometritis, wound infection, urinary tract infection. More specifically, 43 cases (3.9%) of wound infection, 9 cases (0.8%) of endometritis, 25 cases (2.2%) of urinary tract infection was observed. In group one primary outcome was observed in 18 out of 370 women (group 1; 4.9%), in group two primary outcome was observed in 14 out of 371 women (group 2; 3.8%), in group three primary outcome was observed in 45 out of 371 women(group 3; 12.1%). It shows that the placebo group has more number of women who experienced infection post surgical procedure. If first two antibiotic containing groups are compared with the placebo controlled group, the risk difference amounts to 7.8%. This is how the effectiveness of prophylactic cefazolin can be established in case of reducing the chance of post operative infection in case of cesarean delivery.

4. Conclusion

Prophylactic antibiotics are used in almost all cases where chances of post operative infection are high; cesarean section is one among them. In different studies it has been seen that use of antibiotics in pre or intra or post operative phase has reduced the occurrence of infection to a significant extent. But in most of the cases pre operative administration i.e. before skin incision has proven to be the most successful way of preventing infection. In most of the studies, pre operative administration has reduced the chances of endometritis to a great extent; though use of antibiotics in other types of infection may not be proven as useful especially if the wound or infection is preexisting. In such cases prolong treatment is required in post operative phase using amoxicillin and clavulanic acid, ciprofloxacin and tinidazole combination [10]. But in overall cases, use of prophylactic antibiotics can reduce maternal morbidity to a great extent. At the same time it reduces hospital stay after cesarean delivery. In case of neonates, no such major adverse effects of use of antibiotics have been found. So the procedure is considered safe in most of the cases. The most commonly used antibiotic in cesarean delivery is cefazolin, but use of other antibiotics in multiple researches has shown positive outcome as well. This technique is useful in both types of cesarean section, elective and in labor. In case of those who didn't respond well in prophylactic antibiotic treatment, they are generally recommended with antibiotic culture sensitivity tests. If the test results are found positive, then these cases can be eliminated and rate of efficacy of prophylactic antibiotics would be higher than present rate. During the process of surgery the most effective and

clinically proven safest drug used in third generation cephalosporins. But in some cases, it has been found that prophylactic antibiotics are used in clean surgery or class I surgery, which is considered unethical. Such unnecessary or unethical use prophylactic antibiotics may develop antibiotic resistance in the body of those individual.

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