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EFFECT OF GENTAMICIN TO PREVENT OF INFECTION IN SURGICAL SITE; A RANDOMIZED CLINICAL TRAI (RCT)

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ABSTRACT

Background: The purpose of this study was to investigate whether gentamicins and normal saline after cesarean delivery and before closing surgical wound reduce the incidence of post-cesarean infection within 1 month follow-up. **Methods:** We conducted a randomized clinical trial at two university-affiliated hospitals including Imam Khomeini hospital and Razi Hospital, at Ahwaz Jundishapur University of Medical Sciences in 2013. Pregnant women who underwent cesarean delivery were assigned into two groups to receive either 80 mg gentamicinsplus 300 cc normal saline (intervention) (n= 180 cases) or 300 cc normal saline alone (control) (n= 180 cases) (Gentamicine, Sobhan Co, Rasht, Iran; 0.9% Sodium Chloride Injection, Iran Pharmaceutical and Parenteral Co., IPPC, Tehran, Iran). The clinical trial registration code is IRCT2015021221048N1. Inclusion criteria were maximum operation time of 40 minutes and Pfannenstiel incision. Women were excluded if they had weight over 100 kg, immune deficiency, diabetes or high blood pressure. **Results:** A total of 360 women were included in the final analysis. Surgical wound infection occurred in 7 women in intervention group and 8 women in control group. There was no significant difference in the rate of post-cesarean infection between intervention and control group, respectively 3.9% and 4.4%,p value = 0.5. In addition. **Conclusion:** Finally we concluded that Gentamicinsplus normal saline in compare with normal saline alone does not reduce the rate of post cesarean wound infection.

KEYWORDS: Cesarean Section, Surgical wound infection, normal saline, Gentamicins.

INTRODUCTION

Surgical site infection after the surgery is a major cause of illness and sometimes death due to surgery, including Caesarean section. In addition, it is the second common problem in infectious diseases of women.[1, 2] Surgical site infection after cesarean section is defined as infections related to abdominal or uterine cut.[3] Subcutaneous abdominal wound disorders may occur hours or days after abdominal delivery. The number of reported surgical site infection after cesarean section is different in different countries[3], but the average rate of surgical site infection after cesarean section is 7 to 20 percent, and it is related to demographic factors and delivery factors[4,5] There are ways to reduce infection, including the use of antibiotic prophylaxis, methods of preparing the skin, subcutaneous suture and subcutaneous drainage. These methods are based on this premise that they reduce bacteria and reduce the amount of dead space of subcutaneous tissue. This space could potentially be a place of serous fluid or blood to become infected and lead to open wound.[6] In addition to the above-mentioned methods, antibiotic prophylaxis can reduce the rate of infectious complications after cesarean section up to 75 percent. In addition to the above-mentioned methods, antibiotic prophylaxis can reduce the rate of infectious complications after cesarean section up to 75 percent. First generation of cephalosporin antibiotics are most commonly used to prevent infection after cesarean section and are usually prescribed after the birth of baby and cutting the umbilical cord.[5] In this study, subcutaneous infection rate following cesarean section has been investigated in two groups. In one group, subcutaneous wash has been done by normal saline and in another group by normal saline and gentamicin.

METHOD

It was a randomized clinical trial which has done on 360 patients undergone to Caesarean section in Imam Khomeini and Razi hospital in Ahvaz University of Medical Sciences were studied in 1392. In this randomized, double-blind clinical trial, the patients were divided into intervention group with 180 patients and control patients also with 180 patients. In the intervention group, before closing the wound, 300cc normal saline and 80mg gentamicin were used and in the control group the wound was also washed with 300cc normal saline.

Then these two groups were followed-up for a month in the terms of incidence of wound infection and rehospitalization due to wound infection. Dividing people into two groups were done based on the table of random numbers. In addition to this, patients and evaluators of wound infection status were not aware of the type of washing solution. That's why this study

is considered as a double-blind study. The Saline solution with the concentration of 0.9 percent was prepared from the products of Daroo Pakhsh Chemical-Pharmaceutical Co. (9% Sodium Chloride Injection, Iran Pharmaceutical and Parenteral Co., IPPC, Tehran, Iran) and gentamicin from products of Sobhan pharmaceutical Co. in Rasht.

Exclusion criteria were the underlying problems such as obesity (more than 100 kilograms), immunodeficiency, diabetes and hypertension.

Inclusion criteria were also a maximum of 40 minutes surgery and incision fanestil. Evaluated variables are the rate of infection incidence within a month after the operation and need to be re-admitted. If any of the symptoms of fever, redness, tenderness or open sores in wound are observed infection was confirmed. In addition to variables such as age (years), gravid, gestational age (weeks), weight (kg), previous cesarean section (has / doesn't have), duration of surgery (minutes), the number of days of hospitalization were recorded for each patient.

Patients' consent for participating in the study was consciously obtained. This study was approved by the ethics Committee of Ahvaz University of Medical Sciences and the code of ethics is AJUMF.REC.1393.315. The registration code of clinical trial is IRCT2015021221048N1.

Statistical analysis was performed by SPSS software, version 19. To compare the incidence of infection rate between the two groups, Chi-Square test was used. Quantitative amounts in terms of mean and standard deviation and qualitative amounts in terms of the number and relative percentage were used for each group.

RESULTS

Totally, 360 patients in two groups of intervention group (180 patients) and control group (180 patients) were statistically analyzed. Basic variables between two groups were similar (Table 1). Basic and clinical data in Table 1 show that two groups are similar in terms of gravid variables, gestational age, maternal weight and history of cesarean section. 70.6 percent of patients in the intervention group and 72.2 percent of patients in the control group had a cesarean section previously (P value =0.4).

Table 1: Demographic and clinical information in intervention group and in control group

Variable	intervention(n=180)	Control (n=180)	P value
Age	25 ±4.4	26 ± 4.9	0.05
Gravid	2±0.6	2 ±0.5	0.2
Gestational age	38 ±0.4	38 ±0.3	0.07
Maternal weight	74 ± 3.7	73 ±2.4	0.06
History of cesarean section	127(70.6)	130(72.2)	0.4
P value amounts are based on Independent Samples Test results. Significant level was considered less than 0.05.			

Evaluated variables results after the study have been shown in Table 2. The incidence of infection in the intervention group and control group, respectively 4.4% and 3.9% was reported that the difference between them was not significant (P value = 0.5). One, two or three days hospitalization rate between two groups was almost identical (P value = 0.4). Re-hospitalization rate were observed in just two patients from the control group.

Table 2: Studied variables in both intervention and control groups

Variable	Details	Intervention (n=180)	Control (n=180)	P value
Duration of Surgery (minutes)		37 ± 1/4	37 ± 0.9	0.4
Macrosomia or CPD †		27(15%)	20(11.1%)	0.1
Noncephalic show		21(11/7%)	18(10%)	0.3
Defecation by the fetus		13(7/2%)	12(6.7%)	0.5
The number of hospitalization days	1 day 2 days 3 days	1(0/6%) 155(86/1%) 24(13/3%)	4(2.2%) 153(85%) 23(12.8%)	0.4
Infection		7(3/9%)	8(4.4%)	0.5
†CPD: Cephalopelvic disproportion P value amounts were calculated based on Chi square test. Significant level was considered less than 0.05.				

DISCUSSION

In this study, the incidence of infection rate after using a combination of gentamicin and normal saline and normal saline alone as the abstergents before closing the cesarean delivery wound in both intervention and control groups in a double-blind clinical trial were evaluated. The results of this study showed that there wasn't any significant difference between the incidence of infections rate in the combination of gentamicin and normal saline group (intervention group) and normal saline group (control group) (P value = 0.5).

According to this issue that there was not any statistically significant difference in terms of demographic and clinical data (P = 0.04 age, p = 0.2 gravid, p = 0.07 gestational age, p = 0.06 maternal weight and p = 0.4 history of cesarean section) between the intervention and control groups, it can be inferred that the results of the study are not influenced by demographic and clinical differences between intervention and control groups.

Duration of surgery in the intervention group was 37 ± 1.4 minutes and in the control group was 37 ± 0.9 minutes that doesn't show any statistically significant difference (P = 0.4) between two groups. In total, there were 47 cases of macrosomia or CPD that 27 cases were in the intervention group and 20 cases were in control group that doesn't show any significant difference (p = 0.1) between two groups. There were 25 cases of defecation by the fetus that 13 cases were in the intervention group and 12 cases in the control group that it shows that two groups didn't have any statistically significant difference (P = 0.5) in terms of defecation by the fetus.

The results of previous studies were different from the findings of the present study. The studies have generally examined the effect of antibiotic prophylaxis, the administration time and the manner of administration on the incidence of infection rate after cesarean section.

In some studies in line with current studies, Sekhavat and colleagues examined the effect of antibiotic prophylaxis (Ampicillin and Kflyn) on reduction of fever and infectious complications after elective cesarean. In their studies like the current study, any statistically significant differences were not observed between the two groups of intervention and control in terms of incidence of fever and complications of infection in surgical site after cesarean section.[7] In the study performed by Hadavand and colleagues, which examined the effect of antibiotic prophylaxis (Intravenous cefazolin) on the rate of infection in low-risk women after cesarean section, like the current study there weren't any significant differences between the intervention and control groups in terms of incidence of infection after cesarean section.[8] A study by Rouzi and colleagues has studied the effect of antibiotic prophylaxis (single dose of intravenous cefazolin) in the prevention of infectious complications after cesarean section. The results showed significant differences between the intervention and control groups (placebo) in terms of fever and infectious complications.[9] A study by Magann and colleagues showed that the preparation ways of the skin and washing basin with antibiotic compounds in cesarean delivery (normal saline and antibiotics), significantly reduce the endometritis and infectious complications after cesarean.[10] Another study by Levin et al also

showed that washing with normal saline and antibiotics are effective in reducing infectious complications after cesarean section, compared to only washing with normal saline.[11] Mathelier and his colleagues also found that washing with saline and cefazolin compared to washing just with normal saline is an effective method to reduce infectious complications after cesarean section.[12] A study by Wu et al also indicates the positive effect of antibiotic prophylaxis (both in local washing way and in systematic use) on reduction of infectious complications after cesarean section.[13] In a study by Kayihura and colleagues, which examined the effect of a combination of single dose of gentamicin and metronidazole before cesarean section compared to the standard methods (prescribed antibiotics after surgery) for seven days after the surgery, there was no difference between the two methods. Because of costs decreasing, using the combination of a single dose of gentamicin and metronidazole before caesarean section to reduce the infectious complications after cesarean has been proposed by this study.[14] A separate study by Constantine et al.[15] and Owens et al.[16] also found that prescribing antibiotics before cesarean were effective.

In the current study, duration of hospitalization in the two groups was studied. In this study, the duration of hospitalization was 1-3 days. five patients had 1 day hospitalization; 1 case was from the intervention group and 4 cases were from the control group. Totally, 308 patients were hospitalized for two days, among which 155 cases were from the intervention group and 153 cases were from the control group. 47 patients were also hospitalized for 3 days, 24 women were from the intervention group and 23 women were from the control group. These results indicate that no statistically significant differences ($p = 0.4$) were observed between the intervention and control groups in terms of the duration of hospitalization. There were also two rehospitalization cases; one patient was from the intervention group and one from the control group that this represents the same patient rehospitalization rates in the two groups.

Among the studies which have investigated the effectiveness of antibiotics on duration of rehospitalization after cesarean section, Hadavand and colleagues found similar results to the results of current study. In their study, using intravenous cefazolin during clamping the umbilical cord, compared to non-use of cefazolin, had no effect on the duration of hospitalization.[8]

The study by Kayihura et al studied the effect of a single dose of combination of gentamicin and metronidazole before cesarean section compared to using the standard method

(antibiotics prescription after surgery) for seven days after the surgery. The results showed no significant difference in terms of the duration of hospitalization in both groups.[14] A study by Rouzi et al, which has evaluated the effect of antibiotic prophylaxis (single dose of intravenous cefazolin) on prevention of infectious complications after cesarean section, had different results compared to the current study's findings. The results of the study mentioned above indicate significant differences between the intervention and control groups (placebo) in terms of duration of hospitalization in which using antibiotics lead to reduce the duration of hospitalization.[9]

The current study shows there is no difference between the effects of subcutaneous washing of surgical site with saline solution mixed with gentamicin (intervention group) and washing with only normal saline (control group) on reducing post-operative wound infection, duration of hospitalization and rehospitalization. However the results of this study were in line with the results of internal investigations which had used prophylactic antibiotics for this aim. But its findings were inconsistent with international studies that focused on the effectiveness of using prophylactic antibiotics on infectious complications reduction, wound infection and duration of hospitalization. Given the foregoing cases, there is a need to study more about the mismatch between internal and external studies in terms of impact of the use of prophylactic antibiotics to reduce infectious complications and duration of hospitalization after a cesarean section. One of the possible causes can be antibiotic resistance in Iranian women which needs further review.

In addition to the cases mentioned above, other ways to reduce infection after cesarean section can be examined. These cases may include subcutaneous drainage, using supplemental oxygen, providing special training for clinical staff and patient, monitoring, special care and feedback.

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