The value of subcutaneous Fucidic acid instillation during elective cesarean delivery in prevention of surgical site infection

Keywords: Surgical site infection; elective cesarean delivery; fucidic acid

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Abstract

Background: Surgical site infections (SSI) in cesarean delivery (CD) can delay wound healing, impair cosmetic outcome and increase healthcare costs. Topical antibiotics are sometimes used to reduce microbial contaminant exposure following cesarean section.

Objective: The current study will investigate the role of subcutaneous Fusidic acid instillation for prophylaxis against surgical site infection in cesarean delivery.

Methods: This is a single blind randomized controlled trial that involved 200 females who underwent elective CD at the department of obstetrics and gynecology of Kasr Alainy medical school, Cairo university between February 2022 and August 2022

Results : Our study showed that with the use of subcutaneous fusidic acid before closing the skin in absorbable stitches, the infection rate was almost 6 times lower as compared to no fusidic acid before closing the skin.

Conclusion: Therefore, the use of subcutaneous fusidic acid instillation can be safely recommended for the prevention of wound infection (surgical site infection).

Key words: (Fucidic Acid – Surgical Site Infection – Subcutaneous Instillation – Elective Cesarean Delivery)

INTRODUCTION

Worldwide, the most common major operation is Cesarean delivery (CD) is. CD rates are continuously rising especially in developing countries. The rate of CD reaches more than 50% of deliveries in countries like Brazil and Egypt.(1)

Surgical site infections (SSI) is defined as any infection at the site of surgery that occurs up to 30 days of any operative intervention. It is classified to three main types: superficial and deep incisional (both have primary and secondary subcategories), and organ/space type (defined

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when the infection involve structures deeper than the muscle and the fascial spaces). [2]

SSI accounts for 25 % of hospital acquired infections despite the use of routine prophylactic antibiotics and the improvement in surgical techniques. SSI accounts for significant increase in morbidity, mortality and financial burdens. SSI occurs in 9% of women undergoing CD. Although most of these are superficial ,yet it is associated with prolonged hospital stay, increased hospital costs, maternal dissatisfaction .[3]

The main cause of postoperative wound infection is the bacterial contamination that may occur during or after the intervention [4].

Risk factors for SSI include preexisting morbidities as age, obesity, smoking, malnutrition, blood transfusion, lowered immunity, impaired glucose tolerance, immunosuppressive treatment, longer preoperative hospitalization [5], and factors related to pregnancy and delivery as history of prior CD, improper prenatal care, multifetal gestation, prolonged labor, chorioamnionitis, prolonged prelabor rupture of membranes, , emergency procedure, and obstetric services provided [6]

One of the major challenges that faces surgeons is wound infection. It represents a main complication for both surgery and trauma. Contamination with patient's own microorganisms during the procedure is the most common cause of wound infections. [7].

A global guideline for prevention of surgical site infection has been published by the world health organization. These included a list of 29 concrete recommendations on 23 topics based on 28 systematic reviews of the evidence that should be followed before, during, and after the operation. The guidelines were updated in 2018 to include an additional eight anesthesiology experts.[8]

Interventions advocated to reduce SSI include preoperative optimization of underlying morbidities as diabetes mellitus, the follow of aseptic surgical technique and the use of systemic prophylactic antibiotics [9].

Preoperative intravenous antibiotic prophylaxis has been thoroughly researched and has been demonstrated to be beneficial among the several therapies recommended to avoid SSI. [10].

To reduce post-operative surgical infections, particularly SSI, topical or local antimicrobial medicines are frequently used in surgical practise. Topical or local antibiotic distribution provides numerous potential benefits over systemic antibiotic therapy, as well as some drawbacks. [11].

High and persistent concentrations at the infection site, where local physiological changes may reduce systemic antibiotics' effectiveness, are some advantages of local administration. There are also fewer risks of systemic absorption and toxicity, lower doses of antibiotic usage, and perhaps a lower risk of the emergence of antibiotic resistance. [11].

An antibiotic known as fusidic acid is a member of the fusidanes family. Despite having a steroid-like structure, the molecule has no steroid-like properties. Fusidic acid's antibacterial activity is particularly targeted at the most prevalent skin pathogens, such as staphylococcus aureus, for which it is one of the most effective antibiotics. Treatment of minor to moderate skin and soft tissue infections with fusidic acid is successful. [12].

The study was carried on to assess the rate and type of wound infection after elective CD with and without the use of subcutaneous fucidic acid.

Material and methods

This is a single blind randomized controlled trial that involved 200 females who underwent elective CD at the department of obstetrics and gynecology of Kasr Alainy medical school, Cairo university between February 2022 and August 2022

An informed written consent was signed by all participating women after explanation of the

aim, procedure, risks and benefits of the trial. kasr Alainy ethical committee approved the study on 20/2/2022 with number MS-672-2021.

Inclusion criteria included women between 19 and 35 years of age, and 18 and 29.9 kg/m2 body mass index who were pregnant in their 3rd trimester and have history of prior CD and candidate for elective CD in the present pregnancy. Exclusion criteria were women with previous SSI after previous surgery, skin infections or skin diseases that may affect wound healing, or systemic diseases as diabetes or anemia (defined as hemoglobin < 10 mg/dL), those under steroid or immunosuppressive therapy within the last six months prior to surgery. Women also were excluded if they had a prolonged rupture of membranes, allergy to suture material and those who underwent midline incision.

All participants were evaluated through full history and examination then examined through obstetric transabdominal ultrasound to assess proper timing for the procedure. Preoperative laboratory investigations including complete blood count, kidney and liver functions, blood glucose assessment and coagulation status evaluation were done for all participants.

Participants were randomized in the morning of surgery using a computer generated system into two groups. Group F (Fucidic acid group) included 100 women who received 5 drops of subcutaneous fucidic acid 10mg (O fucidic , Orchidia, Egypt) instilled before closing the skin followed by dry dressing. and groups C (control group) included 100 women who received no fucidic acid instillation.

Allocation concealment was done through sequentially sealed opaque envelopes. The letter F was located in half of the envelopes, while the letter N was located in the other half. The corresponding letter that represents the assigned group was placed in each envelope in accordance with the randomization table, and all envelopes were then sealed and placed in a single box. The first envelope was opened when the first patient showed up, and the patient was assigned based on the note inside. Our study comprised pregnant women who had elective caesarean procedures.

CD was done under spinal anaesthesia and were carried out through surgeon with at least 5 years' experience in obstetric surgery and the same technique was used in all procedures.

All the procedures were done under complete aseptic measures. First by surgical hand scrub using standard 5 minutes surgical scrub using Iodophor, hair at operative site was clipped short with scissors if interfering with the operative procedure, then cleaning the operative site with povidone iodine scrub solution 7%, blotted with dry sterile towels and then painted by aqueous povidone iodine solution 10%.[13]

All of them were given preoperative antibiotics prophylaxis. Cefazolin (a first-generation cephalosporin) is classified as category- B that provides good and modest coverage for gram positive and negative organisms, respectively. Its recommended dose is 1-2 grams given through intravenous injection within 30 minutes of skin incision [14]

The dressing of all women was removed on the 3rd postoperative day and regularly followed up every week for four weeks for any wound infection. If infection was detected, swab and culture will be done to diagnose type of infection.

Any SSI within the thirty days following surgery was documented and classified following to Southampton Wound Grading system.

Southampton Wound Grading system includes 6 grades. Grade 0 indicates normal healing, Grade I indicates mild bruising or erythema (subdivided to a, b and c if some, considerable bruising and mild erythema respectively) , Grade II indicates erythema with signs of inflammation (subdivided to a, b, c and d if occurs at one point, around sutures, along wound and around wound respectively), Grade

III indicates clear or hemoserous discharge (subdivided to a, b, c and d if occurs at one point ≤2cm, along wound > 2cm, large volume and prolonged more than 3 days respectively), grade IV indicates presence of pus (subdivided to a and b if occurs at one point ≤ 2cm and along wound > 2cm, respectively) and grade V if it involves deep and/or severe infection or hematoma that requires aspiration regardless of the presence of tissue breakdown or not [15].

Primary outcomes

1. The role of fuidic acid as a prophylactic against SSI.
2. Assessment of infection rate and type of wound infection after elective CD with and without fucidic acid.

- Secondary outcome parameters

1. Overcome infection and better healing of wounds.
2. Enhance cosmetic outcome.
3. Decrease the incidence of SSI

Sample size calculation:

sample size calculation was done by comparing the incidence of surgical site infection (SSI) between women undergoing elective CD treated with subcutaneous fusidic acid installation and those treated with the standard care. Fisher Exact test was used in a prospective study to compare two proportions from separate samples; the 0.05 -error level was fixed, the power was set at 80%, and the intervention group ratio was set at 1. As previously published (16), the incidence of SSI among women treated with fusidic acid was 2.8% while it was 17.1% in control women. As a result, 68 individuals in each group should make up the minimum sample size. The PS Power and Sample Size Calculations software, version 3.0.11 for MS Windows, was used to calculate the sample size (William D. Dupont and Walton D., Vanderbilt University, Nashville, Tennessee, USA). • We recruited 100 women in each group.

statistical methods used in analysis

Mean and standard deviation (SD) were used to statistically describe numerical data that is normally distributed, whereas median and range or the IQR (interquartile range) were used to statistically describe data that is not normally distributed. Frequencies (number of cases) and percentages were used to describe qualitative (categorical) data. A Kolmogorov-Smirnov test was used to determine whether numerical data supports the normal assumption and to compare numerical variables between the research groups. When comparing regularly distributed data, the Student t test was used for independent samples, and when the data are not normally distributed, the Mann Whitney U test was used for independent samples. categorical data were compared using the Chi-square (2) test,. When the anticipated frequency is less than 5, an exact test was be employed instead. Statistical significance is defined as a probability value (p value) less than 0.05. Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows will be used for all statistical calculations.

Results

Figure 1 describes the consort flow chart of the study

RESULTS

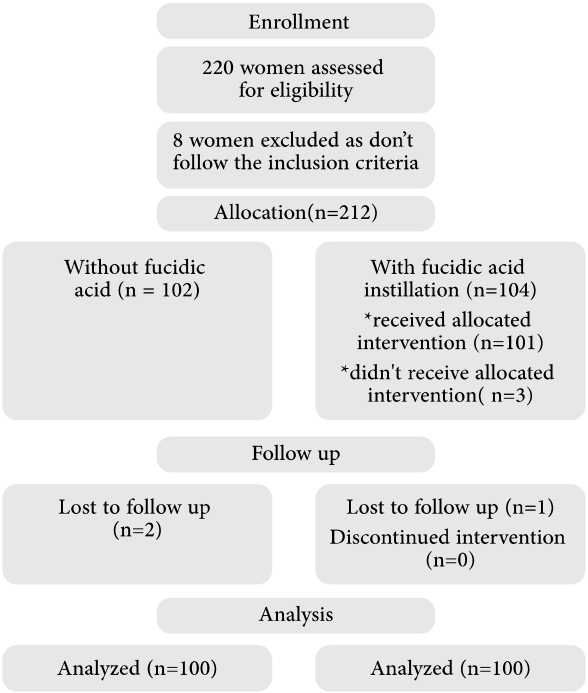

Fig (1): Consort Flow chart

Table 2 Demographic criteria of the study participants

	Group F	Group C	All	t-test	P value
Age (years)	29.8±4.59	29.79±4.31	29.8±4.44	0.016	0.987
Parity	2.53±1.37	2.54±1.37	2.53±1.37	-0.052	0.959
BMI (kg/m^2)	27.97±2.01	28.09±1.91	28.03±1.95	-0.433	0.665
GA (weeks)	38.02±0.98	38.05±0.93	38.03±0.96	-0.211	0.833

Table 3 SSI distribution among participants

		Group F	Group C	All	X^2	P value
SSI		4	17	21 (10.5)	8.992	0.003
1st week	0	78	63	141 (70.5)	16.662	0.046
	Ia	14	10	24 (12)		
	Ib	4	6	10 (5)		
	Ic	0	5	5 (2.5)		
	IIa	0	0	0		
	IIb	0	2	2 (1)		
	IIc	0	2	2 (1)		
	IId	1	2	3 (1.5)		
	IIIa	1	5	6 (3)		
	IIIb	0	1	1 (0.5)		
	IIIc	0	0	0		
	IIId	0	0	0		
	IVa	1	1	2 (1)		
	IVb	1	3	4 (2)		
	V	0	0	0		
2nd week	0	83	62	145 (72.5)	20.470	0.015
	Ia	9	12	21 (10.5)		
	Ib	4	4	8 (4)		
	Ic	0	5	5 (2.5)		
	IIa	0	0	0		
	IIb	0	3	3 (1.5)		
	IIc	0	0	0		
	IId	0	2	2 (1)		
	IIIa	1	1	2 (1)		
	IIIb	1	3	4(2)		
	IIIc	0	1	1 (0.5)		
	IIId	0	0	0		
	IVa	0	3	3 (1.5)		
	IVb	2	2	4 (2)		
	V	0	2	2 (1)		

3rd week	0	89	76	165 (82.5)	12.220	0.092
	Ia	**7**	10	17 (8.5)		
	Ib	0	0	0		
	Ic	0	0	0		
	IIa	0	2	2 (1)		
	IIb	0	1	1 (0.5)		
	IIc	0	1	1 (0.5)		
	IId	0	0	0		
	IIIa	1	0	1 (0.5)		
	IIIb	0	0	0		
	IIIc	0	0	0		
	IIId	0	0	0		
	IVa	0	3	3 (1.5)		
	IVb	1	5	6 (3)		
	V	2	2	4 (2)		
4th week	0	92	81	173 (86.5)	11.033	0.163
	Ia	5	5	10 (5)		
	Ib	0	0	0		
	Ic	0	0	0		
	IIa	0	2	2 (1)		
	IIb	0	2	2 (1)		
	IIc	0	1	1 (0.5)		
	IId	0	0	0		
	IIIa	0	1	1 (0.5)		
	IIIb	0	0	0		
	IIIc	0	0	0		
	IIId	0	0	0		
	IVa	0	4	4 (2)		
	IVb	1	2	3 (1.5)		
	V	2	2	4 (2)		

Table 2 show that there is statistically insignificant difference between women received fucidic acid and those who didn't receive fucidic acid regarding demographic and characteristics of the included cases.

Table 3 shows that there was statistically significant increase in the Southampton Wound Grading Scale in cases who did not receive fucidic acid at first week than who received fucidic acid with p value =0.046. Also the second week showed statistically significant increase in the Southampton grading scale in cases who did not receive fucidic acid than cases who received fucidic acid with p value = 0.015. However, there was no statistically significant difference in the Suthampton Wound Grading Scale between cases in third week with p value =0.092 and fourth week with p value =0.163.

DISCUSSION

This study confirmed that the administration of subcutaneous fusidic acid before closing the skin with absorbable sutures was associated with 6 times lower infection rate when compared to non fusidic acid administration.

Both Fucidic acid and mupirocin are recommended for treatment of acute skin pathology caused by staphylococci (17). However, their prolonged use (> 10 days) is associated with development of resistance [18].

Regarding surgical site infection after first week, there was statistically significant difference between the two groups regarding the incidence of surgical site infection favoring the fucidic acid group (4.0% in the C group vs. 2.0 % in the F group).

According to Southampton wound grading system, most cases of SSI in the C group were graded as (1A) followed by (1B). While all cases of SSI in F group were graded as (1A).

As for second week, there was significant statistical difference regarding the incidence of SSI between the two groups favoring the fucidic acid group (7.0% in the N group vs. 2.0% in the F group). Most of cases in the N group were graded as (1A) while in the F group were graded as (1A).

As for the third and fourth week, there was no statistically significant difference regarding the occurrence of SSI among the studied groups.

An antibiotic known as fusidic acid is a member of the fusidanes family. Although the molecule has a steroid-like structure, it lacks steroid-like action. Fucidic acid's antibacterial activity is particularly targeted at the most prevalent skin pathogens, such as staphylococcus aureus, for which it is one of the most effective antibiotics. Treatment of minor to moderate skin and soft tissue infections with fucidic acid is successful. [12].

The results of our study correspond to the study made by Pradhan and Agrawal, (16) which compared the rate of postoperative wound infection after emergency CD with and without the use of topical fucidic acid. They reported wound infection at the surgical site in 6/35 (17.1%) versus 1/35 (2.8%) in women with povidone iodine dressing versus women with fucidic acid respectively. They concluded that the use of fucidic acid is associated with 6 times reduction in wound infection rate.

Our results were against the results of the study made by Gupta et al., (19) which observe the efficacy of sodium fucidate and ethanol spray compared to conventional methods as savlon & spirit, povidone iodine and povidone iodine with metronidazole for skin preparation for the prevention of SSI. In clean contaminated wounds, the incidence of surgical site infection was 16.52%; the group treated with povidone iodine and metronidazole had the lowest SSI rate (13.04%). This finding can be explained by the fact that in clean contaminated surgeries, the source of infection is primarily endogenous from the genito-urinary or alimentary tract.

They reported the highest infection rate with the use of Savlon and spirit group (23.07%) compared to (16.28%) that was associated with fucidic acid spray use. However, this difference was not statistically significant (P = 0.295).

This is the first study in the literature to discuss the efficacy of Fucidic acid instillation in the subcutaneous space before closing the skin in cases of elective caesarean section. The two groups were similar regarding demographic data including age, parity, BMI. Another strength of our study is its proper randomization and allocation concealment.

The mail limitations of our study were the relatively small sample size, non - blinding of operator (although blinding of participants and outcome assessors was achieved) and the limited follow up duration.

We recommend many studies to be achieved on subcutaneous fucidic acid instillation before closing the skin as there are few studies in the literature about fucidic acid to investigate the role of fucidic acid in SSI prophylaxis and the adverse outcomes of it.

CONCLUSION

This study confirmed that the administration of subcutaneous fusidic acid before closing the skin in absorbable sutures was associated with 6 times reduced risk of infection when compared to non-use of fusidic acid before closing the skin.

Therefore, the subcutaneous instillation of fusidic acid is a safe method that could be used for for the prevention of SSI.

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