Topical Application of Antibiotic Prophylaxis in The Prevention of Surgical Site Infection after Elective Lower Segment Cesarean Section: A Randomized Controlled Study

Amr Abdelaziz El-Sayed[1], Magdy Mohammed Abdelgawad[1], Mina Botros[2], Hassan Helmy Mohamed[1]

[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, Egypt

[2]Department of Obstetrics and Gynecology, Farid Habib Hospital, Egypt

***Corresponding author:** Hassan Helmy Mohamed, **Mobile:** (+2) 01023308711, **E-mail:** drhassan.helmy@gmail.com

ABSTRACT

Background: Surgical site infections (SSIs) are a significant concern in surgical procedures, including elective lower segment cesarean sections (LSCS). The use of prophylactic antibiotics is a common practice aimed at reducing the incidence of SSIs. **Objective:** This study aimed to establish benefit from the use of topical antibiotics prophylaxis after skin closure to decrease rate of surgical site infection in women undergoing elective lower segment Caesarean section (LSCS) in comparison with ordinary dressing with povidone-iodine.

Subjects and methods: A randomized controlled trial was conducted on 122 subjects divided into 2 equal groups; group A (study) included patients who had topical fucidic acid immediately after subcuticular stitches followed by dry dressing and group B (control) included patients who had simple dressing with povidone-iodine. Postoperatively, maternal temperature was measured on 2 separate occasions 6 hours apart with exclusion of the first 12 hours following surgery. The wound was inspected 48 hours, 7 days and 30 days after Caesarean section for signs of superficial or deep incisional surgical site infection. Observation for endometritis and detection of urinary tract infection were also performed.

Results: Surgical site infection was significantly less frequent among study group than among control group 1 (1.6%) vs. 8 (13.1%). No significant differences were noted between study groups regarding age, body mass index (BMI), gestational age (GA), parity, previous Caesarean section (CS), rupture of membrane (ROM) and duration of CS.

Conclusion: The use of fucidin cream followed by dry dressing after closure of skin in elective Caesarean section do decrease the rate of SSIs.

Keywords: Cesarean section, Surgical site infection, Topical antibiotic prophylaxis.

INTRODUCTION

Approximately 16 million surgical procedures took place in United States in acute care hospitals in 2010 [(1)]. A new study on prevalence revealed that surgical site infections were the most common kind of healthcare-associated infection, accounting for 31% of all healthcare-associated infection (HAIs) among hospitalized patients [(2)]. According to the centers for disease control and prevention (CDC) and HAI prevalence survey, about 157,500 SSIs were linked to inpatient surgeries in 2011 [(3)]. Data from National Healthcare Safety Network (NHSN) from 2006-2008 (16,147 SSIs out of 849,659 operative procedures) indicated a total SSI rate of 1.9% [(4)].

Despite improvements in infection control measures such as better operating room ventilation, sterilization methods, barriers, surgical techniques, and access to antimicrobial prophylaxis, surgical site infections continue to cause significant morbidity, prolonged hospital stays, and fatalities. SSI has a mortality rate of 3%, with 75% of SSI-related deaths being directly linked to the infection [(5)].

Among other therapies, the pre-operative administration of antibiotic prophylaxis has been extensively researched and shown to be successful in avoiding SSI [(6)]. Topical antibiotics have been used to treat wounds that are infected. Certain disinfectants have been applied directly to help lower rates of surgical site infections. Although there are certain drawbacks, topical antibiotic application offers numerous benefits compared to systemic use. The general surgical cases do not have a well-documented record of the clinical advantages of using topical antibiotic prophylaxis. Different antibiotics like cephalosporins, aminoglycosides, glycopeptides, chloramphenicol, and bacitracin are commonly used for topical prophylaxis, their doses, administration methods, and pharmacological characteristics differ [(6)].

Local application offers advantages such as maintaining high concentrations directly at the infection site, overcoming potential efficacy issues with systemic antibiotics due to local physiological changes. Additional advantages include the restricted possibility of absorption into the body and toxicity, decreased amounts of antibiotic usage, and potentially lower chances of antibiotic resistance development due to minimal impact on, for instance, gut bacteria. Novel agents that are not accessible systemically can also be utilized. Although local antibiotics may cause issues like local hypersensitivity, contact dermatitis, and interference with wound healing, one significant drawback is the lack of standardized efficacy criteria approved by official oversight agencies to evaluate their effectiveness in this context [(7)]. As a result, the objective of this study was to evaluate the benefit from the use of topical antibiotics prophylaxis after skin closure to decrease rate of SSI in women undergoing elective LSCS.

SUBJECTS AND METHODS

Study area and subjects: The study was conducted during the time between August 2016 and February 2017 at Ain Shams Maternity Hospital. The targeted population was pregnant females underwent elective

Received: 02/06/2024
Accepted: 01/08/2024

LSCS. A structured case report form designed by the investigators was used in this rrandomized controlled trial to assess the benefit from the use of topical antibiotics prophylaxis after skin closure to decrease rate of SSI in women undergoing elective LSCS.

The study included 122 subjects divided into 2 equal groups: Group A included patients who had topical fusidic acid immediately after subcuticular stitches followed by dry dressing, and group B that included patients who had simple dressing with povidone- iodine.

Sample size was calculated at 80% power and with a significance level (alpha) of 0.05 using PASS 11 sample size calculator program based on a study finding carried out by Pradhan and Agrawal (2009) [(8)].

Inclusion criteria: Pregnant females with BMI between 20 and 30 Kg/m^2 underwent elective LSCS using Pfannenstiel incision with gestational age more than 38 weeks with single viable fetus.

Exclusion criteria: Women having rupture of membranes more than 6 hours, BMI more than $30kg/m^2$, diabetics or on long term steroids, known any local hypersensitivity to any chemical product, any previous history of septic wound, patients with preoperative systemic infection (e.g., chorioamnionitis) or those that needed systemic antibiotics for preoperative fever, those having midline incision and women with previous more than 2 Caesarean sections or extended duration more than one and half hour.

Randomization: Patients participating in the study was randomized by a computer–generated randomization plan:

Set #1(group A): 90, 99, 67, 23, 20, 88, 91, 9, 72, 36, 42, 86, 87, 98, 81, 84, 1, 21, 92, 50, 22, 71, 80, 39, 66, 8, 85, 51, 73, 44, 13, 46, 78, 17, 114, 27, 52, 70, 58, 119, 41, 5, 120, 19, 100, 29, 3, 25, 82, 57, 10, 106, 14, 24, 69, 7, 49, 56, 45, 93, 55

Set #2 (group B): 118, 7, 28, 61, 22, 81, 67, 73, 66, 63, 14, 111, 62, 119, 122, 74, 12, 76, 105, 54, 97, 109, 108, 33, 36, 98, 94, 106, 27, 55, 23, 107, 92, 20, 87, 86, 80, 45, 58, 1, 51, 101, 117, 26, 114, 31, 47, 41, 60, 95, 35, 53, 13, 8, 68, 24, 84, 29, 71, 40, 6

Allocation and concealment: The opaque envelopes were labelled with each of the 122 consecutive patient numbers, with the assignment code written on a separate paper inside, which was then sealed. During the Cesarean section, the individual in charge opened an envelope to disclose the task and then followed through.

METHODS

Every patient had undergone a thorough history evaluation that covered personal details (such as age and length of marriage), current health status (including any medical conditions, surgeries, and medications), and obstetric history (including number of children, stage of pregnancy, and pregnancy-related issues).

A thorough clinical examination was conducted, which included general assessment of vital signs such as temperature, as well as listening to the heart and lungs to check for any issues that may affect anesthesia. The abdomen was also examined, including checking the fundal level and any existing scars. Full laboratory investigations were also done as routine preoperative investigations as full blood count and random blood sugar.

Study tools: All Cesarean sections were carried out by a surgeon with a minimum of 2 years of experience in each group. Both groups were given Zinol, an intravenous antibiotic, specifically cefazolin 500 mg one hour prior to making the skin incision. Scrubbing the stomach was performed in the typical manner, and any scar from previous incision was eliminated in both groups.

Further detailed surgical technique was according to up-to-date recommendations for Caesarean section technique (e.g., skin incision was Pfannenstiel vs Joel Cohen, blunt entering the peritoneum preferred, closure of the uterus in two layers with no significance of closure of both visceral and parietal peritoneal membranes, closure of the rectus sheath by a ratio of 1 to 1 cm using vicryl 1, closure of the subcutaneous tissue if thickness was more than 2 to 3 centimetres with interrupted absorbable suture, finally closure of the skin by subcuticular suturing).

The skin was closed with non-absorbable polyproline suture 2.0 followed by application of Fucidin cream over the scar in group A followed by dry dressing and betadine dressing only in group B. Fucidin cream contains 2% fusidic acid as the active ingredient, along with butyl hydroxyanisole (E320), acetyl alcohol, glycerol, liquid paraffin, polysorbate 60, potassium sorbate, purified water, all-rac-α-tocopherol, hydrochloric acid, and white soft paraffin in a vial produced by RANBAXY-Crosland's. Zinol, a 500 mg vial of cefazolin (Pharco).

Wound dressing was removed after 24 hours postoperatively then cleaned with alcohol 70% antiseptic solution for 5 days for both groups. In cases with suspected SSI culture was taken from infected wounds by swab using aseptic technique and was sent to Ain Shams Maternity Hospital laboratory.

Safety considerations: The presence of liability of local skin reaction affecting wound healing process was avoided by applying test dose over the skin at the right arm and monitoring for presence of any signs of inflammation at the start of skin incision. Furthermore 1^{st} day post-operative 2^{nd} looks at the wound site before discharge of the patient was done to ensure absence of any local reaction.

Follow-Up: Postoperative maternal temperature was measured after 1^{st} 12 hours and again 2 times 6 hours apart, using sublingual route by mercury thermometer. The wound was inspected 48 hours later, 7 days and 30 days after Caesarean section.

Superficial incisional surgical site infection: Superficial incisional SSI meets specific criteria:

infection occurring within 30 days post-operatively involving only skin and subcutaneous tissue of the incision. Patients must exhibit purulent drainage, organisms in culture, deliberate opening of incision with positive culture, and show signs of pain, tenderness, swelling, erythema, or heat. A culture negative result didn't meet this requirement for diagnosing a superficial incisional SSI by the surgeon, attending physician, or another designated individual.

Diagnosing or treating cellulitis (redness, warmth and swelling) alone did not meet the criteria for superficial incisional SSI according to the NHSN definition. A draining incision with positive culture results was not diagnosed as cellulitis. An isolated stitch abscess is defined as minimal inflammation and discharge only at the suture entry points.

CDC definition of deep-seated wound infection has been excluded because duration of follow up was limited only to one month and according to the CDC the duration for deep seated infection is 30 days to 90 days.

Ethical approval: Ain Shams University Faculty of Medicine's Ethical Committee gave its approval for this study. At the top of the case report form for the electronic survey, it stated, "Completing this form indicates your consent to participate in this study". The study adhered to the Helsinki Declaration throughout its execution. Parents or guardians of patients were asked to provide consent after being informed about the potential advantages and drawbacks of the research study.

Statistical analysis

Data that were recorded were analyzed with SPSS version 23.0 (SPSS Inc., Chicago, Illinois, USA). The mean and standard deviation, along with the ranges, were used to present the quantitative data. Additionally, numerical and percentage values were used to represent qualitative variables. Fisher exact test and Student t test (t) were employed. $P \leq 0.05$ and $P \leq 0.01$ were used to determine whether the results were significant or very significant respectively.

RESULTS

There were no noticeable differences in demographic characteristics between the study and control groups as shown in table (1).

Table (1): Demographic data of both groups

Variables		Study (N=61)	Control (N=61)	^P
Age (years)	**Mean ± SD**	29.2±3.7	29.4±2.8	0.763
	Range	20.0–37.0	20.0–36.0	
BMI (kg/m^2)	**Mean ± SD**	27.3±1.4	27.1±1.4	0.506
	Range	24.4–29.9	24.3–29.9	
GA (weeks)	**Mean ± SD**	39.9±0.9	40.0±0.9	0.551
	Range	38.0–42.0	38.0–42.0	
Parity (n, %)	**Nulliparous**	10 (16.4%)	9 (14.8%)	#0.803
	Parous	51 (83.6%)	52 (85.2%)	

No significant difference was found between study and control groups regarding parity, previous CS, ROM and duration of CS as illustrated in tables (2).

Table (2): Previous CS, ROM and duration of CS in both groups

Variables		Study (N=61)	Control (N=61)	P
Previous CS (n, %)	**None**	53 (86.9%)	50 (82.0%)	#0.751
	One	6 (9.8%)	8 (13.1%)	
	Two	2 (3.3%)	3 (4.9%)	
ROM (hours)	**Mean ± SD**	2.2±1.8	2.3±1.8	^0.880
	Range	0.0–6.0	0.0–6.0	
	n, %	42 (68.9%)	45 (70.5%)	#0.844
Duration of CS (minutes)	**Mean ± SD**	43.2± 4.2	44.0± 4.8	^0.350
	Range	34.0– 57.0	35.0– 58.0	

^Independent t-test, #Fisher Exact test.

Surgical site infection was significantly less frequent among study group than among control group, as shown in table (3) and figure (1).

Table (3): Surgical site infection among the studied groups

Measures	Study (N=61)	Control (N=61)	P
(n, %)	1 (1.6%)	8 (13.1%)	0.032*
95% CI	0.0% – 4.8%	4.6% – 21.6%	
Efficacy of using topical fusidic acid in preventing infection			
Items	**Value**	**95% CI**	
Rate in study group	98.4%	92.9%– 99.9%	
Rate in control group	89.8%	88.2%– 94.9%	
Rate elevation	11.5%	0.6%–%14.6	
Relative Rate	1.13	1.01–1.17	
Number needed to prevent	8.7	6.9–176.8	

#Fisher Exact test, *Significant, **CI:** Confidence interval

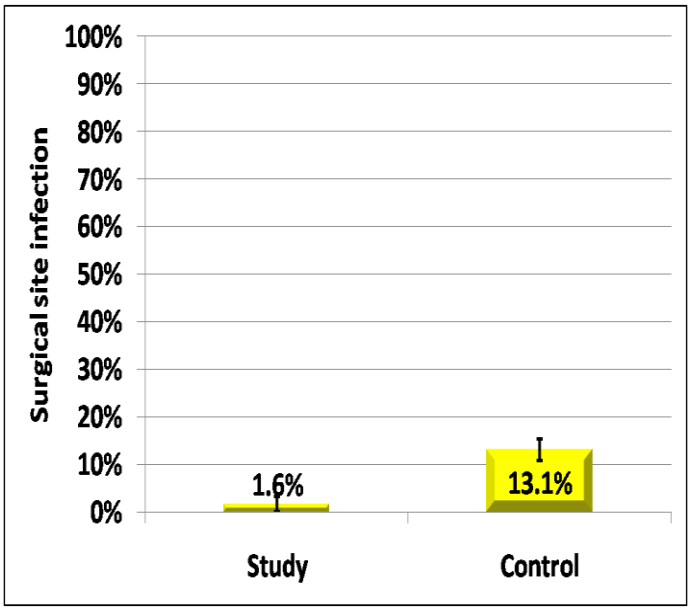

Figure (1): Surgical site infection among the studied groups.

No significant difference between cases with and cases without surgical site infection regarding age, BMI and GA among control group, as shown in table (4).

Table (4): Comparison between cases with and cases without surgical site infection regarding age, BMI and GA among control group

Variables		Infection (N=8)	No infection (N=53)	P
Age (years)	**Mean ± SD**	28.4±3.7	29.5±2.6	0.287
	Range	22.0–34.0	20.0–36.0	
BMI (kg/m^2)	**Mean ± SD**	26.6±1.0	27.2±1.4	0.256
	Range	25.6–28.4	24.3–29.9	
GA (weeks)	**Mean ± SD**	39.9±0.8	40.0±1.0	0.766
	Range	39.0–41.0	38.0–42.0	

^Independent t-test, #Fisher Exact test

There was no significant difference between cases with and cases without surgical site infection regarding parity, previous CS, ROM and duration of CS, as shown in table (5).

Table (5): Comparison between cases with and cases without surgical site infection regarding Parity, previous CS, ROM and duration of CS

Variables		Infection (N=8)	No infection (N=53)	P
Parity (n, %)	**Nulli-parous**	2 (25.0%)	7 (13.2%)	#0.381
	Parous	6 (75.0%)	46 (86.8%)	
Previous CS (n, %)	**None**	3 (37.3%)	9 (17%)	#0.290
	One	5 (62.5%)	38 (71.7%)	
	Two	0 (0%)	6 (11.3%)	
ROM (hours)	**Mean± SD**	2.8±1.8	2.2±1.7	^0.419
	Range	0.0–5.0	0.0–6.0	
	n, %	6 (75.0%)	37 (69.8%)	#1.000
Duration of CS (minutes)	**Mean± SD**	42.4±2.9	44.2±5.0	^0.311
	Range	38.0–47.0	35.0–58.0	

^Independent t-test, #Fisher Exact test.

DISCUSSION

In our study, no significant difference was found between study and control groups regarding parity, previous CS, ROM and duration of CS. Surgical site infection was significantly less frequent among study group than among control group. All other studies available conducted their research on abdominal, cardiothoracic, orthopaedic and ophthalmological sites. Strong evidence supports the use of systemic antibiotics to decrease rates of wound infection, and major guidelines advocate for their administration [(9)]. The approximate rate of SSI following abdominal surgery is around 15%. Previous research on the use of topical cephalosporin in gallbladder surgery suggested that topical antibiotics should not be used alone for prevention, particularly in high-risk patients for surgical site infections (SSI) [(10-11)].

A Japanese study in 1992 verified that antibiotic levels in the peritoneum helped protect against the bacteria that often cause SSI in these patients. The research followed two groups of patients in a prospective manner to monitor rates of SSI. One group got latamoxef, ceftizoxime, cefotiam or cefamandole applied locally during surgery, while a control group received the same prophylaxis intravenously. During the clinical follow-up, there were no notable distinctions between patients receiving topical antibiotics and those receiving intravenous prophylaxis. Nevertheless, the study's effectiveness was hampered by the small sample size of just 80 patients, making it insufficient to identify a notable discrepancy [(12)].

A study conducted in 2009 found that using gentamicin locally during inguinal hernia mesh repair was just as effective as administering it intravenously in

preventing surgical site infections [13]. Nevertheless, the patient count was low, with only 202 individuals, yet the collective SSI rate remained notably high at 6.9% within these two groups. A bigger study with randomization has raised doubts about the necessity of using antibiotics before uncomplicated inguinal hernia mesh surgeries [14].

A study done in the USA examined the use of gentamicin/collagen sponges above the fascia during postoperative closure in colorectal and cardiac surgery patients [15].

In our study, no significant difference between cases with and cases without surgical site infection regarding parity, previous CS, ROM and duration of CS. In a surprising turn of events, a study involving 602 colorectal patients found that the use of gentamicin/collagen sponges led to a higher incidence of surgical site infections (30% versus 20.9%, P = 0.01) compared to the control group. This was suggested to be because of the mechanical impact of the sponge and the insufficiency of a single dose of local gentamicin to stop Gram-positive cocci infections like S. aureus, in contrast to the effectiveness of high doses of gentamicin against Gram-negative bacilli infections. Additionally, these trials have challenged previous conclusions about the effectiveness of gentamicin sponges when used preventively, potentially due to the fact that they were conducted at a single location. An illustration is a single-center study, not blinded, with 221 patients having colorectal surgery that demonstrated a 70% decrease in surgical site infections (SSI) by using the sponge (18.4% versus 5.6%, P < 0.01) [16].

A new study investigated the application of topical fusidic acid, along with standard systemic antibiotics, after surgical closure in patients who had emergency C-sections. A drop in surgical site infection (SSI) rates was observed, decreasing from 17.1% to 2.8% (P = 0.046) with the application of topical antibiotics. Nonetheless, it was a limited study (just 70 participants overall) that had a significant initial incidence of SSI in the control group [8].

CONCLUSION

The use of fucidin cream followed by dry dressing after closure of skin in elective caesarean section decreased the rate of surgical site infections. We recommended routine use of fucidin cream for intraoperative dressing of wound of caesarean section after skin closure.

Acknowledgments: The authors express their gratitude to Ain Shams University.
Conflict of interest: None
Financial disclosures: None.

REFERENCES

1. **National Center for Health Statistics (2010):** National hospital discharge survey, 2010. Hyattsville, Maryland: Public Health Service. https://www.cdc.gov/nchs/nhds/index.htm
2. **Magill S, Hellinger W, Cohen J *et al.* (2012):** Prevalence of healthcare-associated infections in acute care hospitals in Jacksonville, Florida. Infection Control & Hospital Epidemiology, 33 (3): 283-291.
3. **Magill S, Edwards J, Bamberg W *et al.* (2014):** Multistate point-prevalence survey of health care–associated infections. New England Journal of Medicine, 370 (13): 1198-1208.
4. **Mu Y, Edwards J, Horan T *et al.* (2011):** Improving risk-adjusted measures of surgical site infection for the National Healthcare Safely Network. Infection Control & Hospital Epidemiology, 32 (10): 970-986.
5. **Awad S (2012):** Adherence to surgical care improvement project measures and post-operative surgical site infections. Surgical Infections, 13 (4): 234-237.
6. **McHugh S, Collins C, Corrigan M *et al.* (2011):** The role of topical antibiotics used as prophylaxis in surgical site infection prevention. Journal of Antimicrobial Chemotherapy, 66 (4): 693-701.
7. **Lipsky B, Hoey C (2009):** Topical antimicrobial therapy for treating chronic wounds. Clinical Infectious Diseases, 49 (10): 1541-1549.
8. **Pradhan G, Agrawal J (2009):** Comparative study of post-operative wound infection following emergency lower segment caesarean section with and without the topical use of fusidic acid. Nepal Medical College Journal, 11 (3): 189-191.
9. **Bowater R, Stirling S, Lilford R (2009):** Is antibiotic prophylaxis in surgery a generally effective intervention? testing a generic hypothesis over a set of meta-analyses. Annals of Surgery, 249 (4): 551-556.
10. **Freischlag J, McGrattan M, Busuttil R (1984):** Topical versus systemic cephalosporin administration in elective biliary operations. Surgery, 96 (4): 686-693.
11. **Pitt H, Postier R, Gadacz T *et al.* (1982):** The role of topical antibiotics in “high-risk” biliary surgery. Surgery, 91 (5): 518-524.
12. **Aoki Y, Tanimura H, Ohkohchi N (1992):** Topical Antibiotics in Cholecystectomy for Gallstone Diseases. Nihon Geka Hokan., 61 (5): 387-395.
13. **Praveen S, Rohaizak M (2009):** Local antibiotics are equivalent to intravenous antibiotics in the prevention of superficial wound infection in inguinal hernioplasty. Asian Journal of Surgery, 32 (1): 59-63.
14. **Aufenacker T, van Geldere D, Van Mesdag T *et al.* (2004):** The role of antibiotic prophylaxis in prevention of wound infection after Lichtenstein open mesh repair of primary inguinal hernia: a multicenter double-blind randomized controlled trial. Annals of Surgery, 240 (6): 955-961.
15. **Bennett-Guerrero E, Pappas T, Koltun W *et al.* (2010):** Gentamicin–collagen sponge for infection prophylaxis in colorectal surgery. New England Journal of Medicine, 363 (11): 1038-1049.
16. **Rutten H, Nijhuis P (1997):** Prevention of wound infection in elective colorectal surgery by local application of a gentamicin-containing collagen sponge. The European Journal of Surgery, 578: 31-35.