Rifamycin SV Application to Subcutanous Tissue for Prevention of Post-Cesarean Surgical Site Infection

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ABSTRACT

Aim: *The aim of this study was to compare the effect of Rifamycin SV application to subcutaneous tissue for prevention of post-caesarean wound infection with a traditional method used for preoperative antisepsis of skin; povidone-iodine and also to calculate cost of the treatment.*

Method: *In this randomized prospective study, 1272 women were divided into two groups. Povidone-iodine was used for preoperative antisepsis and after closure of the skin in the first group. In the second group povidone-iodine was used in the same way but also subcutaneous tissue was irrigated with Rifamycin SV before closure of subcutaneous tissue.*

Result: *Surgical site infection (SSI) was developed in 12 of 600 patients in the first group. All of them were superficial incisional SSI. In 2 cases wound was opened up to fascia. The overall rate of wound infection with pus was 2%. Total cost of 12 patients with SSI was $5386. In the 2nd group, SSI wasn't develop in any of the 596 patients. Total cost of the rifamycin SV used for washing of subcutaneous tissue was $876.12.*

Conclusion: *Rifamycin SV application to subcutaneous tissue during cesarian effectively prevents SSI. It decreases both cost and morbidity caused by wound infection.*

Key words: *Cesarian section, surgical site infection, rifamycin, povidone-iodine*

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Sezaryen Sonrası Kesi Yeri Enfeksiyonunu Önlemek İçin Ciltaltı Rifamisin Sv Uygulanması.

Amaç: *Bu çalışmada sezeryan sonrası kesi yeri enfeksiyonunu önlemede Rifamisin SV ile geleneksel bir antisepsi yöntemi olan povidon iyotun cilt altı uygulamalarının etkinliklerinin ve tedavi maliyetlerinin kıyaslanması amaçlandı.*
Metod: *Bu randomize prospektif çalışmada 1272 kadın iki gruba ayrıldı. Birinci gruptaki hastalara preoperatif ve postoperatif kesi yerine povidon iyot uygulandı. İkinci gruptaki hastalara ise povidon iyot antisepsisine ek olarak cilt kapılmadan önce cilt altına Rifamisin SV uygulandı.*
Bulgular: *Birinci grupta 12/600 hastada kesi yeri enfeksiyonu saptandı. Bu enfeksiyonların tamamı yüzeyel enfeksiyondu. İki hastada cilt altı fasiaya kadar açıldı. Pürülan kesi yeri enfeksiyonu oranı %2 olarak tesbit edildi. 12 hastanın tedavi maliyeti 5386 dolar olarak hesaplandı. İkinci gruptaki 596 hastanın hiçbirinde kesi yeri enfeksiyonu gelişmedi. Cilt altı yıkamasında kullanılan Rifamisin SV nin toplam maliyeti ise 876.12 dolar olarak hesaplandı.*
Sonuç: *Sezeryan sırasında cilt altına Rifamisin SV uygulanması kesi yeri enfeksiyonunu önlemektedir. Bu uygulama hem tedavi maliyetini hemde kesi yeri enfeksiyonuna bağlı morbiditeyi azaltmaktadır.*
Anahtar kelimeler: *Sezaryen, kesi yeri enfeksiyonu, rifamisin, povidon iyot.*

INTRODUCTION

Wound infection complicating surgical procedures has been consideration of surgeons since the first operations were performed. Among surgical patients, surgical site infections (SSI) are the most common nosocomial infection, accounting for 38% of all such infections (1). SSIs are classified as being either incisional or organ/space. Incisional SSIs are further divided into those involving only skin and subcutaneous tissue (superficial incisional SSI) and those involving deeper soft tissues of the incision (deep incisional SSI). In superficial incisional SSI, infection occurs within 30 days after the operation and infection involves only skin or subcutaneous tissue of the incision and at least one of the following:

1. Purulent drainage, with or without laboratory confirmation, from the superficial incision.

2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.

3. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness or heat and superficial incision is deliberately opened by surgeon, unless incision is culture-negative.

4. Diagnosis of superficial incisional SSI by the surgeon or attending physician.

Deep incisional SSI is described as infection occurs within 30 days after the operation and infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision. Stitch abscess (minimal inflammation and discharge confined to the points of suture penetration) is not accepted as SSI (1).

Preoperative antisepsis of the skin is essential to prevent the occurrence of all types of infection. Preferred antiseptics for skin preparation of the patient are iodophors such as povidone-iodine, chlorhexidine preparation such as Hibitane and alcohol-containing products. Also effective are hexochlorophene (e.g., pHisoHex) for the surgical scrub and tincture of iodine for the operative site. Rifamycin SV is a semisynthetic macrocyclic antibiotic derived from natural rifamycin B. It has a large spectrum of bactericidal action on gram-positive and gram-negative microorganisms, so it is frequently preferred to treat infected surgical or traumatic cutaneous wounds in Turkey (2).

In this study, the effect of rifamycin SV application to subcutaneous tissue for prevention of post-caesarean wound infection was investigated.

MATERIALS AND METHODS

This is a randomized prospective study of post-cesarean wound infection among 1272 women, the effect of rifamycin application to subcutaneous tissue was investigated in a private hospital between 2004-2007. Two groups containing 636 patients who were admitted to two different polyclinics were selected based on simple random sampling. Physical examination, complete blood count, biochemistry, PT, aPTT and urinary analysis were done to all patients. Patients having coincident remote site infections or colonization, diabetes, cigarette smoking, systemic steroid use, obesity (>20% ideal body weight), excessive subcutaneous scar tissue due to previous operations, perioperative transfusion of blood products and altered immune response were excluded from the study (33 patients). Also cases in whom opera-

***Table 1**. Demographic variables of study and control groups.*

	Group 1	Group 2	p value
Age (year)	26,8±3,5	28,4±5,3	ns
Gravida	1,5±0,7	1,2±0,5	ns
Parity	0,8±0,5	0,7±0,4	ns
Weight (kg)	72.4±6,8	70±7,6	ns
Operation time (min)	25,7±2,5	26,4±2,5	ns

Group 1: Control group, Group 2: Study group, ns: not significant.

tion time lasted more than 2 hours or blood loss more than 1 litre or having premature rupture of membrane more than 6 hours were discharged from the study (26 patients). 17 patients were lost from follow up. An informed consent was taken from all patients for participation in research and a surgical consent for the cesarean delivery. Also, this research protocol approved by the Institutional Review Board.

1196 cases were left; 600 patients in the 1st and 596 patients in the 2nd group. Povidone-iodine 10% was used for preoperative antisepsis of skin and after closure of skin in the first group. In the second group povidone-iodine was used in the same way but also subcutaneous tissue was irrigated with rifamycin SV/ 250 mg, before closure of subcutaneous tissue.

All patients has been placed left lateral recumbent position on the operating table and a satisfactory level of anesthesia was obtained. Povidone-iodine was used for skin preparation, first with a 5 minute wash and than with four sponges on long sponge forceps. The area prepared includes the entire skin from the rib cage to the level of the mid-thigh, anterior, medial and lateral. Abdomen was opened by pfannenstiel incision. The rectus muscles were separated in the midline to expose the underlying peritoneum. Parietal peritoneum was opened by blunt dissection. The lower flap of peritoneum was elevated and the bladder was gently separated by blunt dissection from the underlying myometrium. The uterus was opened though the lower uterine segment by Kerr incision. After delivery of fetus and placenta, uterine cavity was inspected and was wiped out with a gauze pack to remove avulsed membranes, vernix, clots and other debris. The uterine incision was closed with 2 layers of running lock suture with 0 or #1 chromic suture. After hemostasis was obtained from uterine closure, visceral peritonisation was done. After cleaning of abdomen from clots and amniotic fluid, the abdominal incision was closed. Rectus fascia was closed by continuous locking suture of #1 vicryl. Subcutaneous tissue was approximated by 1-3 sutures of 2-0 chromic catgut. In the second group subcutaneous tissue was irrigated with 250 mg rifamycin before closure. Rifamycin was not diluted and applied directly to subcuatenous tissue and left in place. Skin was closed by subcuticular 3-0 propylen. Povidone-iodine was applied again after skin closure in both groups. Cautery was not used frequently during operation. Most of bleeding areas in subcutaneous tissue was spontaneously thrombosed before closure of the skin. So cautery was used only at the end of the operation for a few bleeding areas in subcutaneous tissue. All of the operations were done by same surgeons with the same method.

Single dose of 1 g ceftriaxone was given to all patients for prophylaxis in peroperative period after clamping of umblical cord. The incision was inspected each day during hospitalization period. Dressing was done only once on post-operative 2nd day. The sutures were removed on the 7th day after surgery. All patients were informed

***Table 2**. Difference between two groups in terms of surgical site infection and cost.*

	Percentage of SSI		Cost of treatment ($)	p value
	n	(%)		
Group 1	12/600	2	5386	<0.05
Group 2	0/596	0	876	<0.05

about wound infection and understood the importance of seeking immediate medical care if the incision becomes inflamed or tender, if there is bleeding and purulent discharge from the wound, or if fever develops. All patients examined in postoperatif 15th day again for wound infection. All cases called back in postoperative 40th day and asked about any signs of wound infection. Cases having wound infection culture was taken from infective site of incision. These patients were treated with oral antibiotic therapy according to culture antibiogram results. In 2 cases wound was opened up to fascia. They were hospitalized and were sutured again after treatment of infection and debridement.

Statistical analyses were performed using The Statistical Package for Social Sciences (SPSS, Chicago, IL, USA) (Ver.10.0).The results are expressed as mean ± Standart Deviation (SD) in the text. Normality of the age, parity,weight, laboratory and clinical findins distribution was confirmed using the Kolmogorov-Smirnov Z test. Homogeneity of Variances was tested by Levene statistic. Student's t test was used in comparison of data between groups. All tests were run at an overall 0.05 level of significance.

RESULTS

The groups were comparable at baseline with respect to age, parity, weight, clinical and laboratory findings. Mean age was 27.6±4.6, parity was 1.4±1.5, mean weight was 71.2±9.7 and mean operating time was 26,1± 2,5 minutes (Table 1).

Twelve of 600 patients in the first group were admitted to the hospital in postoperative 5th to 10th day for purulent discharge from the wound. All of them were superficial incisional SSI. Cultures were taken from the infection sites and they were showed 4 gram-negative bacilli (E. coli), 2 gram-positive organisms (enterococci), 1 group B streptococci and 1 anaerobe (Bacillus fragilis). These patients were treated by antibiotics according to culture antibiogram results. In 4 patients no microorganism was grown in culture. Ampiric antibiotic treatment was given them. In 2 cases wound was opened up to fascia. They were hospitalized and were sutured again after treatment of infection and enough debridement. The overall rate of wound infection with pus was 2%. SSI increased a patient's hospital stay by approximately 7 days in 2 cases in whom incision was opened up to fascia and cost an additional $1,103. The other 10 patients were treated by out-patient basis and each SSI resulted in $318 extra charges. Total cost of 12 patients with SSI was $5386.

In the second group, wound infection was developed in none of the patients. No problem was seen in the controls done in post operative 7th and 15th days. None of the patients had discharge from the incision during 40 day after surgery. Only in one patient a small haematoma was developed below muscular layer. The overall rate of wound infection with pus was 0 %. Cost of the rifamycin used for washing of subcutaneous tissue was $1.47 for a patient and $876.12 for 596 patients. When groups were compared, surgical site infection and cost were significantly lower in study group ($p<0.05$) (Table 2).

DISCUSSION

Even medical and surgical care are beyond reproach, infectious morbidity stil complicate the postoperative course. Despite advances in infection control practices, surgical site infections (SSI) remain a substantial cause of morbidity and mortality among hospitalized patients (1). SSI after cesarean section increases maternal morbidity and medical costs (3). The rates of SSI after cesarean section reported in the literature range from 0.3% to 17%, 0.3% in Turkey (4), 9.6% in Brasil (5) , 17% in Australia (6), depending on the surveillance methods used to identify infections, the patient population, and the use of antibiotic prophylaxis (7-12). Among hospitals reporting to the National Nosocomial Infections Surveillance (NNIS) System, the rate of SSI after cesarean section is 2.8% to 6.7% depending on the risk index category (13,14).

Microbial contamination of the surgical site is a necessary precursor of SSI. For most SSIs, the source of pathogens is the endogenous flora of the patient's skin, mucous membranes or hollow viscera (15). When mucous membranes or skin is incised, the exposed tissues are at risk for contamination with endogenous flora. Gram negative bacilli (e.g.,E. coli), gram-positive organisms (e.g., enterococci), and sometimes anaerobes (e.g.,Bacillus fragilis) are the typical SSI isolates (16). Exogenous sources of SSI pathogens include surgical personnel (especially members of the surgical team), the operating room environment (including air), and all

tools, instruments, and materials brought to the sterile field during an operation (1,17,18).

In certain kinds of operations, patient characteristics possibly associated with an increased risk of an SSI include coincident remote site infections or colonization, diabetes, cigarette smoking, systemic steroid use, obesity (>20% ideal body weight), extremes of age, poor nutritional status, perioperative transfusion of certain blood products, altered immune response, length of preoperative stay. Also duration of surgical scrub, skin antisepsis, preoperative shaving, preoperative skin prep, duration of operation, antimicrobial prophylaxis, operating room ventilation, inadequate sterilization of instruments, foreign material in the surgical site, surgical drains, surgical technique, poor hemostasis, failure to obliterate dead space and tissue trauma are important factors for prevention of SSI. Prevention of infections requires serious attention from personnel of surgical programs (1,19,20). In cesarean operation following factors also associated with increased risk of SSI: younger age, presence of hypertension or preeclampsia, chorioamnionitis, high preoperative severity of illness, nulliparity, premature rupture of membranes, emergency delivery, absence of antibiotic prophylaxis, use of staples for skin closure and twin delivery (11,21,22).

In a recent study done by Olsen et al in 2008, 81 (5.0%) cases out of 1,605 patients was found to have SSI with onset of infection within 30 days after low transverse cesarean section. 92.6% of patients had superficial incisional, 4.9% had deep incisional SSI, and 2.5% had organ space infection (23).

In another study done in 2007, total rate of SSI was found 8.9%, with an observation period of 30 days postoperatively, compared to 1.8% registered at hospital discharge. The total response rate was 100%. There was no significant difference in SSI rate in elective or emergency cesarean section, respectively. All SSI were superficial. Two 2 significant independent risk factors were found: operating time ≥38 min and body mass index (BMI) >30 (24).

Preoperative antisepsis of the skin is essential to prevent the occurrence of all types of infection. Several antiseptic agents are available for preoperative preparation of skin at the incision site. The iodophors (e.g., povidone-iodine), alcohol-containing products, and chlorhexidine gluconate are the most commonly used agents. No studies have adequately assessed the comparative effects of these preoperative skin antiseptics on SSI risk in well-controlled, operation-specific studies. Alcohol is readily available, inexpensive, and remains the most effective and rapid-acting skin antiseptic. Aqueous 70% to 92% alcohol solutions have germicidal activity against bacteria, fungi, and viruses, but spores can be resistant (25). One potential disadvantage of the use of alcohol in the operating room is its flammability. Both chlorhexidine gluconate and iodophors have broad spectra of antimicrobial activity (25,26). In some comparisons of the two antiseptics when used as preoperative hand scrubs, chlorhexidine gluconate achieved greater reductions in skin microflora than did povidone-iodine and also had greater residual activity after a single application (27). Further, chlorhexidine gluconate is not inactivated by blood or serum proteins. Iodophors may be inactivated by blood or serum proteins, but exert a bacteriostatic effect as long as they are present on the skin (28).

Before the skin preparation of a patient is initiated, the skin should be free of gross contamination (i.e., dirt,soil, or any other debris). The patient's skin is prepared by applying an antiseptic in concentric circles, beginning in the area of the proposed incision. The prepared area should be large enough to extend the incision or create new incisions or drain sites, if necessary (29). The application of the skin preparation may need to be modified, depending on the condition of the skin (e.g., burns) or location of the incision site (e.g., face).

There are reports of modifications to the procedure for preoperative skin preparation which include:

(1) removing or wiping off the skin preparation antiseptic agent after application,

(2) using an antiseptic-impregnated adhesive drape (30)

(3) merely painting the skin with an antiseptic in lieu of the skin preparation procedure

(4) using a "clean" versus a "sterile" surgical skin preparation kit (31)

(5) total body showering and incision site scrub with disinfectant agents (Patients showered with 4% chlorhexidine gluconate or povidone-iodine solution or medicated bar soap prior to the final scrub) (32).

(6) using a one-minute alcohol wash followed by application of an iodophor-impregnated adhesive film (33)

(7) Skin preparation with an antibacterial scrub and in-

traoperative pelvic irrigation with antibiotic solution (34)

(8) Skin preparation with 0.5 per cent chlorhexidine gluconate spray (29)

Rifamycin SV is a semisynthetic macrocyclic antibiotic derived from natural rifamycin B. It has a large spectrum of bactericidal action on gram-positive and gram-negative microorganisms, especially Staphylococcus aureus. Rifamycin was used for irrigation of open and closed wounds since 1963. First local use of it was in treatment of lung cavities in tuberculosis patients (35). Later studies done on animals showed that rate of healing increased with application of rifamycin (36). The rate of healing is considered to be significantly better than other forms of local antibiotics, so it is frequently preferred to treat infected surgical or traumatic cutaneous wounds in Turkey.

In 1990, a study was conducted in patients presenting with a hand injury requiring a surgical operation, in order to compare the efficacy of topical application of rifamycin SV with iodinated polyvidone dermal solution, in terms of the quality and rate of wound healing. Signs of infection was significantly less and rate of healing was faster in rifamycin group (37).

The adverse effects of rifamycin are few. Occasionally, it will produce a flu-like syndrome in individuals who take the drug intermittently. There have also been reports of interstitial nephritis, thrombocytopenia and hemolytic anemia. Side effects of rifamycin after local application are extremely rare but cases of allergic contact dermatitis have been described. Very rarely anaphylactic reactions after application of rifamycin SV to surgical wounds are seen (2,38).

In this study rifamycin SV was applicated to subcutaneous tissue in clean surgical incisions for prevention of post-operative wound infection. None of the patients developed SSI nor they had allergic contact dermatitis or anaphylactic reactions after application of rifamycin to surgical wounds.

In 1980, Cruse estimated that an SSI increased a patient's hospital stay by approximately 10 days and cost an additional $2,000 (39). A 1992 analysis showed that each SSI resulted in 7.3 additional postoperative hospital days, adding $3,152 in extra charges (40). Other studies corroborate that increased length of hospital stay and cost are associated with SSIs (41,42). Deep SSIs involving organs or spaces, as compared to SSIs confined to the incision are associated with even greater increases in hospital stays and costs (43,44).

In this study, 2 cases in whom incision was opened up to fascia in 1st group were hospitalised and others who had superficial infection were treated by out-patient basis. Cost of the treatment and morbidity were higher in the 1st group inspide of out-patient treatment. Irrigation of subcutaneous tissue with rifamycin was decreased morbidity and cost due to SSI.

As a result, rifamycin application to subcutaneous tissue during cesarean effectively prevents SSI in low risk population. It decreases both cost and morbidity caused by wound infection. So rifamycin can be applied to subcutaneous tissue for prophylaxis in surgical procedures. In this study a homogenous study population was used to scientifically isolate the effect of the intervention. So it is uncertain whether the intervention would reduce the rate of wound infection in a high risk population. New and larger population studies are needed to evaluate the efficiency of the intervention on patients having high risk factors for SSI.

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