Original Article

Safety and efficacy of triclosan-coated polyglactin 910 suture in prevention of surgical site infection in postpartum women : A randomized controlled trial

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The objective of present study was to compare the safety and efficacy of two triclosan-coated polyglactin 910 sutures, MITSU AB and VICRYL Plus, in postpartum women. This was a prospective, multicenter, single-blinded, randomized controlled trial conducted at two clinical settings in India. Between February 2017 to July 2017, a total of 122 women were enrolled and randomly assigned (1:1) to either MITSU AB or VICRYL Plus (N=61 women in each arm) before surgical incision closure during episiotomy or caesarean section. All women were followed at 14 days, 30 days, and 6 months after the surgery. The safety endpoint was overall wound dehiscence recorded at each follow-up (FU). Efficacy endpoints were surgical site infection (SSI) rate at each FU and length of hospital stay. The suturing was performed at abdominal, uterine, vaginal and perennial areas and was significantly balanced in both arms. None of the women reported wound dehiscence nor reported SSI in both arms. The length of hospital stay did not differ significantly between MITSU AB and VICRYL Plus arms (3.25 ± 0.62 days *versus* 3.37 ± 1.57 days; p=0.58). There was no incidence of an adverse event or serious adverse event up to 6 months. The results of the study showed comparable safety and efficacy of the MITSU AB to VICRYL Plus suture in women requiring surgical closure during episiotomy or caesarean section. The study is registered at the clinical trial registry of India (CTRI/2017/01/007736).

[*J Indian Med Assoc* 2018; **116**: 12-4 & 35]

Key words **: Antimicrobial sutures, caesarean section, episiotomy, polyglactin 910, postpartum infection, surgical wound dehiscence, triclosan.**

Surgical site infections (SSIs) are persistent but preventable health care-associated infections. SSIs not only lead to substantial morbidity, mortality and extended hospital stay, but also increase health-care cost[1]. The epidemiology of postpartum SSI has not been well characterized in developing countries. The evidence of SSI incidences in postpartum women are scarce and of weaker quality. Several Indian hospital-based studies reported rate of SSI ranged from 3.5% to 12.6% after caesarean section[2-5]. Despite the high risk of contamination, the incidence of episiotomy infection seems to be relatively low and estimated between 0.3% and 5% depending on the setting[6].

The role of sutures in the development of SSI has been speculated by surgeons from many years[1]. Bacterial adherence and colonization were observed predominantly on suture knots and on braided sutures, and thereby increase the susceptibility of the surrounding tissue to the infections[7]. Hence, triclosan-coated sutures were developed to prevent microbial colonization on suture materials in operative wounds. After the launch of this sutures into the commercial market in 2002, its effectiveness was studied for several surgeries, including breast, abdominal, pediatric, gastrointestinal and cardiac surgeries[8]. Furthermore, triclosan-coated polyglactin 910 absorbable surgical suture is one of the non-parenteral antimicrobial prophylaxis approach recommended by the Centers for Disease Control and Prevention (CDC) in their recent guideline for the prevention of SSI[9].

MITSU AB, an absorbable polyglactin 910 surgical suture, coated with the broad-spectrum antimicrobial agent triclosan, is used for surgical incision closure in various surgeries. Although surgical incision closure with antimicrobial-coated sutures has been shown to reduce wound infections during many surgical procedures, none of the previous trials focused on caesarean section and episiotomy incisions in postpartum women. In the present study, we aim to evaluate the safety and efficacy of MITSU AB compared to VICRYL Plus in postpartum women.

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Material And Method

Study design and population :

This was a prospective, multicenter, single-blinded (patient-blinded), randomized controlled trial (RCT) comparing the safety and efficacy of two triclosan-coated polyglactin 910 sutures, namely MITSU AB and VICRYL Plus in the course of 6 months. The study protocol was approved by the local ethics committee. The study was conducted in compliance with the Declaration of Helsinki and written informed consent was obtained from all women before initiation of the study. The study was registered at the clinical trial registry of India (CTRI/2017/01/007736).

A total of 122 women (N=61 in each MITSU AB and VICRYL Plus arm) were enrolled between February 2017 to July 2017 at two centers in Gujarat, India. Patients aged ≥18 years who were undergoing surgical incision closure during an elective surgery and agreed not to participate in any other invasive study for a period of 6 months, and provided consent were included in the study. Patients with a known allergy of triclosan, history of HIV, on-going sepsis, on-going bacterial infection or already on antibiotic treatment (other than prophylaxis antibiotics given before and after surgery) were excluded. Patients with a history of prior SSI in past 1-month and those requiring other major emergency surgery were also considered ineligible for the study.

Study intervention and randomization :

Women were stratifically (block of 2) randomized in a 1:1 ratio to receive either MITSU AB™ Polyglactin 910 Suture (Meril Endo-Surgery Pvt Ltd) or Coated VICRYL® Plus Antibacterial Polyglactin 910 Suture (Ethicon USA, LLC) with PROC PLAN syntax using SAS® statistical software, version 9.3.

The MITSU AB suture is a braided synthetic absorbable sterile polyglactin 910 surgical suture used for the surgical incision closure except for ophthalmic, cardiovascular and neurological tissues. The suture is made up of a copolymer polyglactin 910 (90% glycolide and 10% L-lactide) which is then coated with a mixture of polyglactin 370 and calcium stearate; as well as the broad spectrum antimicrobial agent triclosan (≤472 µg/m). Polyglactin 910 and polyglactin 370 with calcium stearate exhibit non-antigenic and non-pyrogenic properties. During hydrolysis, the copolymer degrades to glycolic and lactic acids which are then absorbed and metabolized in the body. Its 75% of the original tensile strength is retained until the initial 14 days, and 50% of its original is retained until 21 days. Complete absorption of MITSU AB suture usually takes place between 56 to 70 days with subsequent growth of fibrous connective tissue.

Study endpoints and data collection :

Safety endpoint includes overall wound dehiscence as per investigator's discrimination evaluated at post-procedure and each follow-up (FU) visit. Wound dehiscence is defined as the rupture or splitting open of a formerly closed surgical incision site. According to the CDC, it can be classified as either superficial or deep10. Efficacy endpoints include the rate of SSI (evaluated by examining surgical site at baseline, post-procedure, and each FU visit) and length of hospital stay. The criteria of CDC's National Nosocomial Infections Surveillance system were followed for the identification of SSI and their classification[10]. Length of hospital stay is calculated by subtracting day of admission from the day of discharge. The FU visits were scheduled at 14 days (±2 days), 30 days (±7 days) and 6 months (±28 days) from the day of the surgery.

Demographics, vital signs, laboratory assessment, medical history, current medications were recorded during the study via electronic-CRF data capturing system. Details of surgical procedure, any procedural complication and adverse event (AE) or serious adverse event (SAE) were documented; sonography and tissue culture were performed (if required) during the study.

Statistics :

Continuous data were presented as mean ± SD, non-continuous as median (IQR) and categorical data as counts and percentages. The data were analyzed using SAS® statistical software, version 9.3. The continuous variables were compared using Student's t-test (normal distribution) or Mann-Whitney U-test. Categorical variables among both arms were analyzed using Fisher's exact test and chi-square test, as appropriate. Length of stay in hospital was presented as mean ± SD and evaluated using Student's t-test. The P value less than 0.05 were considered statistically significant.

An assumption of the 9.4% SSI rate difference between both sutures followed by one-sided 95% confidence interval with 85% power and a significance level of 5% to prove non-inferiority (non-inferiority margin 0.09) resulted in an estimated sample size of 55 women for both arms in the study. Considering 10% discontinuation rate, total 61 women were required to enroll in each arm. Hence, we recruited a total of 122 women in the present study.

Observations

The study enrolled 122 women, 61 in both arms (MITSU AB and VICRYL Plus). None of the women reported procedural complications. All the women completed post-procedure, 14 days, 30 days and 6 months FU. The study disposition is depicted in Fig 1.

Demographics and patient characteristics in both treatment arms are summarized in Table 1. The mean age reported was 29.58 ± 5.10 years and 27.89 ± 6.44 years for MITSU AB and VICRYL Plus arms, respectively. Overall, including both arms, there were 55.74% (68/122) overweight (BMI 26-30) women and 18.03% (22/122) obese

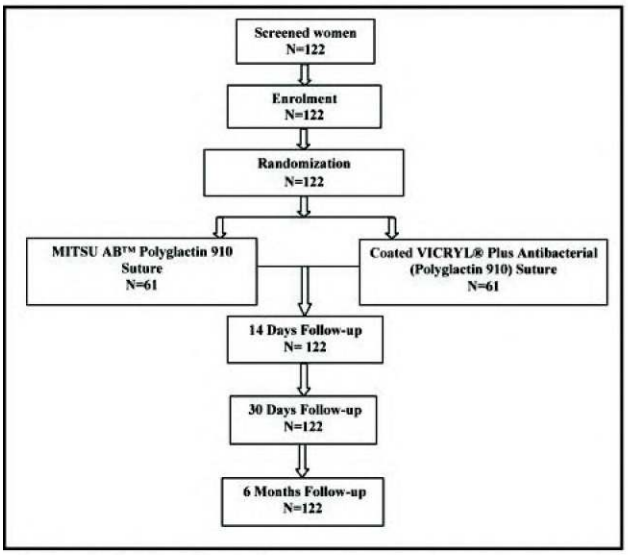

Fig 1 — Study disposition: patient enrollment, treatment allocation, and follow-up

Table 1 — *Baseline and pre-operative characteristics*

Demographics	MITSU AB N =61	VICRYL Plus N = 61	P value
Age, years, mean ± SD	29.58 ± 5.10	27.89 ± 6.44	0.11
BMI, kg/m², mean ± SD	27.44 ± 3.47	26.66 ± 3.07	0.19
BMI categories, n (%)			
BMI 19-25	13 (21.31%)	19 (31.15%)	0.45
BMI 26-29	37 (60.66%)	31 (50.82%)	
BMI ≥30	11 (18.03%)	11 (18.03%)	
Heart rate, bpm, mean ± SD	79.52 ± 5.26	78.33 ± 6.64	0.28
Systolic blood pressure, mmHg, Mean ± SD	116.23 ± 10.03	111.50 ± 6.50	0.002
Diastolic blood pressure, mmHg, Mean ± SD	75.90 ± 6.42	73.33 ± 6.81	0.03
Co-morbidities, n (%)			
Diabetes mellitus	2 (3.28%)	0	0.15
Hypertension	1 (1.64%)	3 (4.91%)	0.31
Others	1 (1.64%)	2 (3.28%)	0.56
Biochemistry			
Haemoglobin, g/dl, mean ± SD	11.76 ± 1.51	11.20 ± 2.71	0.16
WBC count, cell/mm³	11216	11467	0.68

BMI : body mass index, bpm: beats per minute,
SD: standard deviation, WBC : white blood cells

(BMI ≥ 30) women in the present study. The prevalence of diabetes mellitus (2 *versus* 0, p=0.15) and hypertension (1 *versus* 3, p=0.13) were reportedly low, in both MITSU AB and VICRYL Plus arms. No significant differences were found between the demographics, co-morbidities, and biochemistry of both arms, except for systolic blood pressure.

Suturing with either MITSU AB or VICRYL Plus intervention were performed at abdominal, uterine, vaginal and perennial areas during either lower (uterine) segment caesarean section (LSCS) or episiotomy surgeries. Majority of women underwent uterine suturing (62.30% *versus* 40.98%), followed by abdominal suturing (31.15% *versus* 47.54%) in both MITSU AB and VICRYL Plus arms. There was an insignificant difference (P=0.07) reported for all suturing sites between both arms. A significant difference (P=0.003) was reported between the numbers of stitches in both arms but, the incision lengths differ insignificantly (P=0.08). All the women received antibiotic prophylaxis before and after the surgery, which did not differ significantly between both arms. The preferred pre-operative antibiotics were a fixed-dose combination (FDC) of ampicillin and cloxacillin followed by ceftriaxone (a third generation ß-lactam antibiotics) and amikacin (aminoglycosides), intravenously. Post-operatively oral FDC of ampicillin and cloxacillin, and ceftriaxone were prescribed in the majority of women. The operational details are depicted in Table 2.

There was no case of wound dehiscence reported in both arms during 6-month FU. Moreover, none of the women presented with SSI in any arm. Length of hospital stay was 3.25 ± 0.62 days for MITSU AB arm and 3.37 ± 1.57 days for VICRYL Plus arm, which was insignificantly different (p=0.58). There wasn't any AE, or SAE reported in the study.

Discussion

The present study prospectively evaluated safety and efficacy of the two triclosan-coated polyglactin 910 sutures. The suturing was performed at abdominal, uterine, vaginal and perennial areas during the LSCS and episiotomy in 122 women. The study reported neither wound dehiscence nor SSI till 6-month FU. There is no significant difference between the lengths of hospital stay of both arms. Also, none of the women reported any AE/SAE. To the best of our knowledge, the present trial is the first one to report efficacy and safety of triclosan-coated sutures in a cohort of women requiring LSCS or episiotomy surgeries. We identified two such trials which are evaluating the efficacy of triclosan-coated suture in episiotomy (ClinicalTrials.gov: NCT02847936) and caesarean section (ClinicalTrials.gov: NCT03386240). Yet, they are currently in the recruitment phase.

The development of an antibacterial suture has been

Table 2 — *Operational characteristics*

Operational characteristics	MITSU AB N =61	VICRYL Plus N = 61	P value
Location of suturing, n (%)			
Abdomen	19 (31.15%)	29 (47.54%)	0.07
Uterus	38 (62.30%)	25 (40.98%)	
Vaginal	2 (3.28%)	6 (9.84%)	
Perennial	2 (3.28%)	1 (1.64%)	
Number of stitches, median (range)	1 (1 to 10)	1 (1 to 7)	0.003
Length of incision after suturing, median (range), cm	8 (3 to 9)	8 (3 to 9)	0.08
Length of hospital stay, days, mean ± SD	3.25 ± 0.62	3.37 ± 1.57	0.58

SD: standard deviation

under deliberation since the early 1980s. Triclosan is the broad-spectrum antimicrobial agent developed over 57 years ago and has been extensively used in disinfecting soaps, dentistry and lately in suture coating[1]. It has been evident from many studies that triclosan has no carcinogenic, genotoxic, pyrogenic, or teratogenic effects. Moreover, the use of triclosan in sutures causes extremely low systemic exposure[11]. In vitro studies showed that triclosan forms an inhibition zone around suture material and it is effective against the microbes most frequently responsible for SSI occurrence[12]. The reported primary causative pathogens for wound infection in episiotomy are Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Staphylococcus epidermidis and some strains of fungi[13]. Amongst the aerobic bacterial agents causing SSI in caesarean section patients, enteric gram-negative bacilli, group B streptococci, and enterococci are the most common[14]. The antimicrobial activity of triclosan for the said pathogens was proven in the numerous in-vitro studies[1,15].

With the increase in age, especially, in women older than 40 years, the risk of SSI increases[3]. However, the studied population was quite young in the present study, and did not vary statistically between both arms (P=0.11). Obesity is a risk factor for many obstetrical complications, including post-operative wound complication[16,17]. Yet, any SSI or wound dehiscence was not reported in 55.74% (68/122) overweight and 18.03% (22/122) obese women in the study.

Wound dehiscence did not appear in any woman till 6-month FU in both arms. A meta-analysis of thirteen randomized clinical trials involving 5256 participants reported similar risk of wound dehiscence between the coated and uncoated sutures based on the limited data of four RCTs (breast surgeries, abdominal surgeries, and cardiac surgeries), suggesting that triclosan might not interfere with wound healing[18]. A large high-level RCT is needed to examine and verify the effect of triclosan-coated sutures on wound complications.

A meta-analysis found that use of triclosan-coated sutures resulted in 30% reduction in the risk of SSI, especially in adult patients, abdominal procedures, and clean or clean-contaminated incisions[19]. An Indian study of 1173 patients in a rural hospital reported 1.23% (95% CI, 0.02-2.4) SSI rate in the obstetrics surgeries[3]. The present study does not report any incidence of SSI in both treatment arms till 6-month FU. Triclosan-coated sutures could significantly decrease both the risk of readmission and the length of hospital stay, and subsequently, reduce excess medical costs on medical systems[19]. Across 92 countries, the mean length of stay after childbirth reported was 1.3 to 6.6 days[20]. The average length of the stay was 3.25 ± 0.62 days (MITSU AB) and 3.37 ± 1.57 days (VICRYL Plus) in the present study which did not differ significantly (p=0.58).

The present study has several limitations. The diversity of the patient population was restricted to the female. Nevertheless, the efficacy of triclosan-coated sutures was not compared in the postpartum women previously. The study has a considerably higher number of caesarean section surgeries than the episiotomy, which demands further strong evidence for the efficacy of triclosan-coated sutures in episiotomy. Though the sample size was calculated not to be underpowered on the basis of the previous event rates, the findings of this study could be underpowered as a result of the unexpected absence of events. However, the difference in results from the anticipated SSI event rates in the study can be explained by the stringent infection control practices in the operation room, studied clean-contaminated incisions, and strong antibiotic prophylaxis.

In conclusion, the present study showed no incidence of wound complications and infections when the caesarean section and episiotomy incisions were sutured with triclosan-coated absorbable polyglactin 910 sutures. The safety and efficacy of the MITSU AB is comparable with that of the VICRYL Plus suture.

Acknowledgement

The study was funded by Meril Endo-Surgery Pvt Ltd., India. The authors express their sincere gratitude to Bhavi Patel (Clinical Research Department, Meril Life Sciences Pvt Ltd, India) for assistance with preparation of the manuscript.

Conflict of interest :

Dr. Ashok Thakkar is a full-time employee of Meril Life Sciences Pvt Ltd, India. The other authors have no potential conflict of interest to declare.

References

1 Mingmalairak C — Antimicrobial sutures: new strategy in surgical site infections. Science against Microbial Pathogens: Communicating Current Research and Technological Advances: Formatex Research Center. 2011: 313-23.
2 Kondakasseril NR, Hiran N, Andrews AM — Surgical site infection following lower segment caesarean section in a tertiary care hospital. *J Evolution Med Dent Sci* 2016; **2:** 4.
3 Pathak A, Mahadik K, Swami MB, Roy PK, Sharma M, Mahadik VK, *et al* — Incidence and risk factors for surgical site infections in obstetric and gynecological surgeries from a teaching hospital in rural India. *Antimicrob Resist Infect Control* 2017; **6:** 66.
4 Shrestha S, Shrestha R, Shrestha B, Dongol A — Incidence and risk factors of surgical site infection following cesarean section at Dhulikhel Hospital. *Kathmandu Univ Med J* 2014; **46:** 113-6.
5 Vijayan C, Mohandas S, Nath AG — Surgical Site Infection Following Cesarean Section in a Teaching Hospital. *Int J Sci Study* 2016; **3:** 97-101.
6 Bonet M, Ota E, Chibueze CE, Oladapo OT — Antibiotic prophylaxis for episiotomy repair following vaginal birth. *Cochrane Database Syst Rev* 2016.
7 Chang WK, Srinivasa S, Morton R, Hill AG — Triclosan-impregnated sutures to decrease surgical site infections: sys-

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tematic review and meta-analysis of randomized trials. *Annals of Surgery* 2012; **255:** 854-9.
8 Wu X, Kubilay N, Ren J, Allegranzi B, Bischoff P, Zayed B, *et al* — Antimicrobial-coated sutures to decrease surgical site infections: a systematic review and meta-analysis. *Eur J Clin Microbiol Infect Dis* 2017; **36:** 19-32.
9 Berrios-Torres SI, Umscheid CA, Bratzler DW — Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg* 2017; **152:** 784-91.
10 Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR — Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 1999; **20:** 250-78; quiz 79-80.
11 Barbolt TA — Chemistry and safety of triclosan, and its use as an antimicrobial coating on Coated VICRYL* Plus Antibacterial Suture (coated polyglactin 910 suture with triclosan). *Surg Infect* 2002; **3:** s45-s53.
12 Rothenburger S, Spangler D, Bhende S, Burkley D — In vitro antimicrobial evaluation of Coated VICRYL* Plus Antibacterial Suture (coated polyglactin 910 with triclosan) using zone of inhibition assays. *Surg Infect* 2002; **3:** S79-87.
13 Zhang H, Han S — Risk factors and preventive measures for postoperative infection in episiotomy of puerperal. *Biomed Res* 2017; 28(20).
14 Rongpharpi SR, Srivastava R, Kumar A, Gupta V, Chawla D, Pundhir S — Post Caesarean Surgical Site Infections. *Arch Clin Microbiol* **6:** 1-6.
15 Russell A — Whither triclosan? *J Antimicrob Chemother* 2004; **53:** 693-5.
16 Conner SN, Verticchio JC, Tuuli MG, Odibo AO, Macones GA, Cahill AG — Maternal obesity and risk of post-cesarean wound complications. *Am J Perinatol* 2014; **31:** 299.
17 Kabiru W, Raynor BD — Obstetric outcomes associated with increase in BMI category during pregnancy. *Am J Obstet Gynecol* 2004; **191:** 928-32.
18 Guo J, Pan L-H, Li Y-X, Yang X-D, Li L-Q, Zhang C-Y, *et al* — Efficacy of triclosan-coated sutures for reducing risk of surgical site infection in adults: a meta-analysis of randomized clinical trials. *J Surg Res* 2016; **201:** 105-17.
19 Wang Z, Jiang C, Cao Y, Ding Y — Systematic review and meta-analysis of triclosan-coated sutures for the prevention of surgical-site infection. *Br J Surg* 2013; **100:** 465-73.
20 Campbell OM, Cegolon L, Macleod D, Benova L — Length of stay after childbirth in 92 countries and associated factors in 30 low-and middle-income countries: compilation of reported data and a cross-sectional analysis from nationally representative surveys. *PLoS Med* 2016; **13:** e1001972.