Meta-analysis

Use of antibacterial sutures for skin closure in controlling surgical site infections: a systematic review of published randomized, controlled trials

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Objective: The objective of this article is to systematically analyse the randomized, controlled trials that compare the use of antibacterial sutures (ABS) for skin closure in controlling surgical site infections.

Methods: Randomized, controlled trials on surgical patients comparing the use of ABS for skin closure in controlling the surgical site infections were analysed systematically using RevMan® and combined outcomes were expressed as odds ratios (OR) and standardized mean differences (SMD).

Results: Seven randomized, controlled trials evaluating 1631 patients were retrieved from electronic databases. There were 760 patients in the ABS group and 871 patients in the simple suture group. There was moderate heterogeneity among trials (Tau² = 0.12; chi² = 8.40, df = 6 [P < 0.01]; I² = 29%). Therefore in the random-effects model, the use of ABS for skin closure in surgical patients was associated with a reduced risk of developing surgical site infections (OR, 0.16; 95% CI, 0.37, 0.99; z = 2.02; P < 0.04) and postoperative complications (OR, 0.56; 95% CI, 0.32, 0.98; z = 2.04; P = 0.04). The durations of operation and lengths of hospital stay were similar following the use of ABS and SS for skin closure in patients undergoing various surgical procedures.

Conclusion: Use of ABS for skin closure in surgical patients is effective in reducing the risk of surgical site infection and postoperative complications. ABS is comparable with SS in terms of length of hospital stay and duration of operation.

Keywords: wound closure; surgical site infection; antibacterial sutures; operative complications.

INTRODUCTION

Surgical site infection (SSI) is an immense burden on healthcare resources even in the modern era of immaculate sterilization approaches and highly effective antibiotics. An estimated 234 million various surgical procedures, involving skin incisions requiring various types of wound closure techniques, are performed in the world, with the majority resulting in a wound healing by primary intention [1]. Skin wounds are at risk of SSI and therefore may lead to increased morbidity, delayed recovery and prolonged hospital stay [2]. The prevalence of SSI in the developed world is variable but reported figures are estimated at around 5% [3–4]. The development of SSI is a multifactorial phenomenon, which requires a multimodal approach to prevent and treat it in a timely manner to avoid financial, psychological and health-related quality of life
consequences. Various predisposing aetiopathological factors for SSI include immunosuppression, nutritional deficiencies, hypoproteinemia, congestive cardiac failure, hepatic failure, renal failure, use of steroids, chemotherapy agents, steroids and diabetes mellitus [5–8]. In additions to these factors, wound contamination, contaminated instruments, surgical technique and sutures used to close skin have also been reported to be responsible for SSI and cosmetic outcomes [9–11]. The prevention of the SSI by various invasive and non-invasive interventions is the most common measure surgeons and other healthcare professional advocate to tackle the problem of SSI. This includes use of prophylactic antibiotics [12–13] and various other multimodal approaches already reported in the medical literature [14–15].

Triclosan [5-chloro-2-(2,4-dichlorophenoxy)phenol] is a broad-spectrum bactericidal agent that has been used for more than 40 years in various products, such as toothpaste and soaps. Higher concentrations of triclosan work as a bactericide by attacking different structures in the bacterial cytoplasm and cell membrane [16]. At lower concentrations, triclosan acts as bacteriostatic agent, binding to enoyl-acyl reductase (ENR), a product of the Fab I gene and thus inhibiting fatty acid synthesis [17–18]. Use of triclosan-coated sutures should theoretically result in the reduction of SSI. Several studies have shown a reduction in the number of bacteria in vitro and also of wound infections in animals [19–21]. The objective of this article is to systematically analyse the randomized, controlled trials comparing the use of triclosan-coated antibacterial sutures (ABS) versus simple sutures (SS) for skin closure in controlling the SSIs. We aimed to include only those trials in which the SSI was investigated as a primary outcome regardless the surgical specialty. The SSI was the primary outcome of this study, whereas postoperative complications, duration of the operation and length of the hospital stay (if reported) were analysed as secondary outcome measures.

METHODS
Identification of trials
Randomised, controlled trials (irrespective of language, country of origin, hospital of origin, blinding, sample size or publication status) comparing ABS against SS were included in this review. The Cochrane Colorectal Cancer Group (CCCG) Controlled Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, Medline, Embase and Science Citation Index Expanded were searched for articles published up to October 2012, using the medical subject heading (MeSH) terms “skin closure” and “wound closure” in combination with free text search terms, such as “suture closure”, “sub-cuticular closure”, “absorbable suture”, “non-absorbable suture”, “antibiotic-coated suture”, “triclosan-coated sutures” and “primary wound closure”. A filter for identifying randomized, controlled trials recommended by the Cochrane Collaboration was used to filter out non-randomized studies in Medline and Embase [22]. The references from the included trials were searched to identify additional trials.

Data extraction
Two authors independently identified the trials for inclusion and exclusion and extracted the data. The accuracy of the extracted data was further confirmed by a third author. There were no discrepancies in the selection of the trials or in data extraction between the reviewers, except in the case of recording the severity of pain according to the measurement scales and timing of the recorded data. All reviewers agreed that blinding was impossible to achieve in the case of the operating surgeon. However, there was disagreement with regard to whether the trials should be classified as having a high or low risk of bias, based on four parameters, namely randomization technique, power calculations, blinding and intention-to-treat analysis. It was agreed that the lack of an adequate randomisation technique and an intention-to-treat analysis would result in the trials being classified as having a high risk of bias. In case of any unclear or missing information, the reviewers planned to obtain those by contacting the authors of the individual trials.

Statistical analysis
The software package RevMan® 5.1.2 [23], provided by the Cochrane Collaboration, was used for the statistical analysis to achieve a combined outcome. The odds ratio (OR) with a 95% confidence interval (CI) was calculated for binary data and the standardised mean difference (SMD) with a 95% CI was calculated for continuous data variables. The random-effects model was used to calculate the combined outcomes of both binary and continuous variables [24, 25]. Heterogeneity was explored using the chi-squared test, with significance set at \( P < 0.05 \) and was quantified using I-squared [26], with a maximum value of 30% identifying low heterogeneity [26]. The Mantel-Haenszel method was used for the calculation of RR under the random-effect models [27]. In a sensitivity analysis, 0.5 was added to each cell frequency for trials in which no event occurred in either the treatment or control group, according to the method recommended by Deeks et al. [28]. If the standard deviation was not available, it was calculated according to the guidelines of the Cochrane Collaboration [22]. This process involved assumptions that both groups had the same variance—which may not have been true—and variance was either estimated from the range or from the \( P \)-value. The estimate of the difference between both techniques was pooled, depending upon the effect weights in results.
determined by each trial estimate variance. A forest plot was used for the graphical display of the results. The square around the estimate stood for the accuracy of the estimation (sample size) and the horizontal line represented the 95% CI. The methodological quality of the included trials was initially assessed using the published guidelines of Jadad et al. and Chalmers et al. [29–30]. Based on the quality of the included randomized, controlled trials, the strength and summary of the evidence was further evaluated by GradePro® [31], a tool provided by the Cochrane Collaboration.

RESULTS

The PRISMA flow chart to explain the literature search strategy and trial selection is given in Figure 1. Seven randomized, controlled trials recruiting 1631 patients were retrieved from commonly used standard medical electronic databases [32–38]. There were 760 patients in the ABS group and 871 patients in the SS group. The characteristics of the included trials are given in Table 1. The salient features and treatment protocols adopted in the included randomized, controlled trials are given in Table 2. The short summary of data, selected primary and secondary outcome measures used to achieve a summated statistical effect are given in Table 3.

Methodological quality of included studies

According to Jadad et al. and Chalmers et al. [29, 30], the quality of the majority of included trials was moderate due to the inadequate randomization technique, adequate allocation concealment, power calculations, blinding and intention-to-treat analysis [Table 4]. Based on the quality of included randomized, controlled trials, the strength and summary of evidence analysed on GradePro® [31] is given in Figure 2.

Primary outcomes measures

Surgical site infection. Seven randomized, controlled trials contributed to the combined calculation of this variable [32–38]. There was minimal heterogeneity (Tau² = 0.12, chi² = 8.40, df = 6, [P = 0.21]; I² = 29%) among trials.
random-effects model (OR, 0.61; 95% CI, 0.37, 0.99; z = 2.02; P < 0.04; Figure 3), the risk of developing SSI following the use of ABS for skin wound closure was statistically lower compared to SS.

Secondary outcomes measures

Postoperative complications. All postoperative conditions (excluding SSI) leading to either delayed discharge of the patients or requiring medical or surgical intervention to treat—such as urinary tract infection, lower respiratory tract infection, cardiac or respiratory events and general anaesthesia-related complications—were jointly analysed as ‘postoperative complications’. Four randomized, controlled trials contributed to the combined calculation of this variable [32, 33, 36, 38]. There was minimal heterogeneity (Tau² = 2.45, chi² = 2.0, df = 2, [P = 0.29]; I² = 18%) among trials. In the random-effects model (OR, 0.56; 95% CI, 0.32, 0.98; z = 2.04; P < 0.04; Figure 4), the risk of developing postoperative complications was statistically lower in the ABS group.

Duration of operation. Two randomized, controlled trials contributed to the combined calculation of this variable [32, 36]. There was significant heterogeneity (Tau² = 0.06; chi² = 2.80, df = 1, [P < 0.09]; I² = 64%) among trials. Therefore, in the random-effects model (SMD, -1.85; 95% CI, -5.51, 1.79; z = 1.0; P = 0.32; Figure 5), the duration of operation for both approaches was similar.

Length of hospital stay. Two randomized, controlled trials contributed to the combined calculation of this variable [32, 36]. There was significant heterogeneity (Tau² = 6.90; chi² = 138.51, df = 1, [P < 0.00001]; I² = 90%) among trials. Therefore, in the random-effects model (SMD, -1.85; 95% CI, -5.51, 1.79; z = 1.0; P = 0.32; Figure 6), the duration of hospital stay for both approaches was similar.

DISCUSSION

This systematic review demonstrates that the use of ABS for skin closure in surgical patients is an effective measure in reducing the risk of postoperative surgical site infections and postoperative complications. ABS is comparable with SS in terms of length of hospital stay and duration of operation. Therefore, it may be used more judiciously to counteract the economic, cosmetic and morbidity-related issues arising from SSI.

There are several limitations to the present review. Randomized, controlled trials with fewer patients in this review may not have been sufficient to recognise small differences in outcomes. Quality of included trials was not good, due to inadequate randomization technique, allocation concealment, power calculations, blinding and intention-to-treat analysis [Table 4]. Variables like health-related quality of life measurement and cosmetic score should have been considered due to long-term psychological and social consequences of SSI.

| Trial          | Type of trial | Country | Surgical procedure                        | Comparison groups                                      | Follow-up duration |
|----------------|---------------|---------|------------------------------------------|--------------------------------------------------------|-------------------|
| Chatchai [32]  | RCT           | Thailand| Appendectomy                             | Triclosan-coated polyglactin 910 vs Traditional coated polyglactin 910 | 1 year            |
| Ford [33]      | RCT           | USA     | All general surgical procedures          | Triclosan-coated polyglactin 910 vs Traditional coated polyglactin 910 | 80 ± 5 days       |
| Galal [34]     | RCT           | Egypt   | Across all surgical specialties          | Triclosan-coated polyglactin 910 vs Conventional polyglactin 910 | 12 months         |
| Isik [35]      | RCT           | Turkey  | Cardiothoracic                           | Triclosan-coated polyglactin 910 vs Traditional coated polyglactin 910 | 30 days           |
| Rašić [36]     | RCT           | Croatia | Open elective colorectal operations      | Triclosan-coated polyglactin 910 vs Conventional polyglactin 910 | Not recorded      |
| Williams [37]  | RCT           | UK      | Breast surgery (Cancer)                  | Triclosan-coated polyglactin 910 vs Conventional polyglactin 910 | 6 weeks           |
| Zhang [38]     | RCT           | China   | Modified radical mastectomy              | Triclosan-coated polyglactin 910 vs Chinese silk suture | 90 days ± 7       |
Table 2. Treatment protocol adopted in included trials

| Trial            | AMS                                                                 | Control                                                                 |
|------------------|----------------------------------------------------------------------|------------------------------------------------------------------------|
| Chatchai [32]    | • Patients with appendicitis                                         | • Patients with appendicitis                                           |
|                  | • Triclosan-coated polyglactin 910 suture                          | • Polyglactin 910 suture                                               |
|                  | • Prophylactic antibiotics given iv 30–60 mins prior to operation   | • Prophylactic antibiotics given IV 30–60 mins prior to operation       |
|                  | • Study suture selected to close the abdominal sheath                | • Study suture selected to close the abdominal sheath                   |
|                  | • Appendectomy done with standard technique                         | • Appendectomy done with standard technique                             |
| Ford [33]        | • Paediatric patients undergoing various general surgical procedures | • Paediatric patients undergoing various general surgical procedures    |
|                  | • Triclosan-coated polyglactin 910 suture                          | • Traditional coated polyglactin 910 suture                            |
| Galal [34]       | • Patients selected from all surgical specialties                    | • Patients selected from all surgical specialties                        |
|                  | • Triclosan-coated polyglactin 910 suture                          | • Conventional polyglactin 910 suture                                  |
| Isik [35]        | • Patients undergoing cardiac surgery                                | • Patients undergoing cardiac surgery                                   |
|                  | • Wound closure with antibacterial polyglactin 910 suture           | • Wound closure with traditional polyglactin 910 suture                 |
| Rasic [36]       | • Patients undergoing elective surgery for colorectal cancer        | • Patients undergoing elective surgery for colorectal cancer            |
|                  | • Pre-op investigation included complete colonoscopy, CXR, CT and   | • Pre-op investigation included complete colonoscopy, CXR, CT and       |
|                  |   relevant serum tests                                              |   relevant serum tests                                                  |
|                  | • Ops performed through a midline incision: skin incised with a     | • Ops performed through a midline incision: skin incised with a         |
|                  |   scalpel; all other layers were transected with diathermy          |   scalpel; all other layers were transected with diathermy              |
|                  | • Prophylactic abx given during induction of anaesthesia             | • Prophylactic abx given during induction of anaesthesia                 |
|                  | • Wound closure was performed with a continuous single-layer mass   | • Wound closure was performed with a continuous                        |
|                  |   technique (peritoneum, muscles and fascia)                         |   single-layer mass technique (peritoneum, muscles and fascia)           |
|                  | • Triclosan-coated polyglactin 910 suture                          | • Polyglactin 910 suture                                               |
|                  | • Skin closed with polyamide                                        | • Skin closed with polyamide                                            |
| Williams [37]    | • Breast cancer surgery                                             | • Breast cancer surgery                                                |
|                  | • Subcutaneous triclosan-coated polyglactin 910 and                  | • Subcutaneous standard coated polyglactin 910 and                      |
|                  |   poliglecaprone 25                                                 |   poliglecaprone 25                                                    |
|                  | • Wounds dressed with Steri-Strips and Tegaderm or Cosmopore        | • Wounds dressed with Steri-Strips and Tegaderm or Cosmopore            |
| Zhang [38]       | • Patients undergoing modified radical mastectomy                    | • Patients undergoing modified radical mastectomy                         |
|                  | • Intradermal closure                                               | • Simple interrupted closure                                            |
|                  | • Triclosan-coated polyglactin 910 suture                          | • Chinese silk suture                                                  |

Evaluating cost-effectiveness should also be considered before recommending the routine use of ABS for skin closure in surgical patients. This analysis involved the trials run in various surgical specialties, which may be a source of bias. There was insufficient information regarding the use of various confounding interventions in both arms of included randomized, controlled trials, such as use of prophylactic antibiotics, timing and duration of antibiotics and, more importantly, the use of wound protectors. These confounding interventions can directly influence the incidence of SSI and may be a source of bias in the summated conclusion of this article, since a majority of the variables showed significant heterogeneity among included trials and trials are very diverse in terms of inclusion criteria, exclusion criteria, clinical and methodological patterns. The majority of the variables showed significant heterogeneity among included trials because they are very diverse in terms of inclusion criteria, exclusion criteria and in clinical as well as methodological patterns. While there are statistically significant findings using the random-effects model, with a lower rate of SSI associated with the use of ABS, the clinical significance and cost–benefit significance remains unknown. Causes of reduced SSI in ABS are apparent due to the presence of antibiotics at wound sites preventing microbial colonization. However, it is difficult to explain the similar length of stay in both groups despite the
reduced incidence of SSI in the ABS group. There may be many reasons behind this outcome. In the majority of cases, diagnosis of SSI is made in the community and therefore it would not influence the length of stay. Variable follow-up, the diverse group of patients analysed summatively in this review and statistically significant heterogeneity among trials in case of length stay may all be responsible for this difference. The development of SSI is multifactorial, making it extremely difficult to account for the different confounding factors and reducing bias even in a well-designed, randomized, controlled trial. This task becomes significantly more challenging when a systematic review of highly heterogeneous studies—like our meta-analysis—is undertaken. The aetiopathogenesis of SSI can be influenced by i) patient-dependent factors such as immunosuppression, hypoalbuminemia, use of steroids, diabetes mellitus, renal failure, hepatic failure, and congestive cardiac failure, ii) surgeon-related factors including proper sterility, hand washing, surgical technique and iii) type of operation, such as clean, clean contaminated, contaminated and dirty. These factors are difficult to randomize and a study such as this, that reviews various surgical techniques, specialties and patient population, may be of little help.

| Variables | Chatchai 2009 [32] | Ford 2005 [33] | Galal 2011 [34] | Isik 2011 [35] | Rašić 2011 [36] | Williams 2011 [37] | Zhang 2011 [38] |
|-----------|--------------------|----------------|----------------|----------------|----------------|-------------------|----------------|
| Patients (n) |                    |                |                |                |                |                   |                |
| ABS       | 50                 | 98             | 230            | 170            | 91             | 74                | 47             |
| SS        | 50                 | 49             | 220            | 340            | 93             | 73                | 46             |
| Operation time (minutes) |            |                |                |                |                |                   |                |
| ABS       | 41 ± 21.6          | Not reported   | Not reported   | Not reported   | 95.5 ± 17.3    | Not reported     | Not reported    |
| SS        | 45 ± 21.6          | Not reported   | Not reported   | Not reported   | 91.3 ± 18.6    | Not reported     | Not reported    |
| SSI (n)   |                    |                |                |                |                |                   |                |
| ABS       | 5                  | 0              | 17             | 9              | 4              | 11                | 2              |
| SS        | 4                  | 3              | 33             | 22             | 12             | 9                 | 5              |
| Length of stay (days) |            |                |                |                |                |                   |                |
| ABS       | 3.7 ± 0            | Not reported   | Not reported   | Not reported   | 13.2 ± 1.3     | Not reported     | Not reported    |
| SS        | 3.7 ± 0            | Not reported   | Not reported   | Not reported   | 21.4 ± 2.8     | Not reported     | Not reported    |
| Complications (n) |            |                |                |                |                |                   |                |
| ABS       | 0                  | 17             | Not reported   | Not reported   | 1              |                   | 15             |
| SS        | 0                  | 10             | Not reported   | Not reported   | 7              |                   | 21             |

Table 4. Quality assessment of included trials

| Trial        | Randomization technique                  | Power calculations | Blinding                | Intention-to-treat analysis | Concealment |
|--------------|------------------------------------------|--------------------|-------------------------|-----------------------------|-------------|
| Chatchai     | Random table                             | Yes                | Yes                     | Not documented              | Yes         |
| Ford         | Computer generated                       | No                 | No                      | Not documented              | No          |
| Galal        | Computer generated, sealed pack for suture | No                 | Yes                     | Not documented              | Yes         |
| Isik         | Sequential? technique                    | Yes                | Unable to determine     | Not documented              | Unable to determine |
| Rašić        | Computer generated, blind envelope system for suture | No                 | Yes                     | Not documented              | Yes         |
| Williams     | Computer generated, sequential envelope system for suture | Yes                | Yes                     | Not documented              | Yes         |
| Zhang        | Computer generated                       | No                 | Yes                     | Yes                         | Yes         |
Although our conclusion is based on the summated outcome of seven randomized, controlled trials, it should be considered cautiously because the quality of the majority of included trials was poor. There is still a lack of stronger evidence to support the routine use of ABS but it can be considered an alternative and may initially be applied in selected groups of patients. A major, multicentre, randomized, controlled trial of high quality according to CONSORT guidelines is mandatory to validate these findings.
**Conflict of interest:** none declared.

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