ACORN AUSTRALIAN COLLEGE OF PERIOPERATIVE NURSES | JOURNAL OF PERIOPERATIVE NURSING

Volume 37 | Issue 2 Article 3

5-17-2024

Effectiveness of intra-operative gentamicin irrigation in reducing post-operative surgical site infections: A systematic review

Recommended Citation

Kumar, Kritika J. and Smith, Zaneta (2024) "Effectiveness of intra-operative gentamicin irrigation in reducing post-operative surgical site infections: A systematic review," *Journal of Perioperative Nursing*: Vol. 37 : Iss. 2 , Article 3.
Available at: https://doi.org/10.26550/2209-1092.1293

https://www.journal.acorn.org.au/jpn/vol37/iss2/3

Peer-reviewed article

Authors

Kritika J Kumar
MNSc, BN, DN, RN
Adelaide Nursing School, Faculty of Health and Medical Sciences, The University of Adelaide

Dr Zaneta Smith
PhD, MClin Prac with Distinction, MTerEd Mgmt, PGDip (Clin Prac-Periop), BN, RN, FACORN
Adelaide Nursing School, Faculty of Health and Medical Sciences, The University of Adelaide

Corresponding author

Kritika J Kumar
MNSc, BN, DN, RN
Adelaide Nursing School, Faculty of Health and Medical Sciences, The University of Adelaide

Effectiveness of intra-operative gentamicin irrigation in reducing post-operative surgical site infections: A systematic review

Abstract

Aim: To evaluate and synthesise the effectiveness of intra-operative gentamicin in reducing post-operative surgical site infections compared to other irrigating solutions or no irrigation.

Background: Surgical site infection has posed challenges to health care providers around the globe. It is influenced by many risk factors, only a few of which are under the control of the surgeon and operating team. Wound irrigation is considered an essential part of the intra-operative process. It aims to minimise the risk of surgical site infection by thorough lavage of the operative site.

Design: Systematic review of effectiveness.

Review methods: The databases CINAHL, Scopus, Embase, Medline, PubMed, OpenGrey, Google Scholar and ProQuest Dissertations & Theses Global were searched with parameters set between 1 January 2013 and 31 July 2023. The review followed the Joanna Briggs Institute (JBI) methodology for systematic reviews of effectiveness and the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA 2020) guidelines. Two independent reviewers conducted the selection process, critical appraisal and data extraction. The eligible studies were critically appraised using JBI critical appraisal tools for randomised controlled trials and cohort studies. Data synthesis was performed through subgroup analysis and narrative synthesis, since meta-analysis was not possible.

Results: The impact of intra-operative gentamicin irrigation on surgical site infections was analysed across eight studies. The subgroup analysis favoured the gentamicin saline group over the saline group in reducing post-operative surgical site infections (RR=0.27 [0.13;0.55], P < 0.001.)

Conclusion: This systematic review shows that intra-operative gentamicin irrigation lowers the incidence of surgical site infections when compared to normal saline irrigation. However, there were contradictory results when intra-operative gentamicin irrigation was compared to alternative interventions such as no irrigation, diluted povidone iodine and combination antibiotic irrigation.

Keywords: gentamicin, irrigation, lavage, surgical site infection, post-operative infection

Background

Substantial resources and professional efforts are dedicated to reducing post-operative infections due to their significant impact on short- and long-term surgical outcomes[1]. Some of these outcomes are increased pain, prolonged antibiotic use and increased risk of mortality and morbidity[1]. The incidence of post-operative infection is influenced by many factors, including the type of surgery performed, patients' susceptibility to infection, antibiotic prophylaxis and the method of surveillance used for infection detection[2]. Post-operative infection develops in the surgical incision site, leading to a surgical site infection (SSI) or a more remote infection, such as pneumonia or catheter-associated urinary infection[2].

Health care providers around the globe face constant challenges that are associated with SSI[3]. The frequency of SSI has imposed a burden on health care institutions and posed a potential threat to the health of patients[3]. The Centers for Disease Control and Prevention (CDC) defines SSI as 'an infection that occurs after surgery in the part of the body where the surgery took place'[4, p.1]. An SSI can be a superficial infection confined to skin or progress to more severe infections affecting tissues beneath the skin, organs and implanted material[4]. SSI may have a negative effect on a patient's physical and mental health[3,5], and can lead to additional surgical procedures, increased pain, higher financial burden, risk of nosocomial infections and prolonged hospital stays[3,5,6].

There are various risk factors which influence the occurrence of SSI; however, only a few are within the control of the surgeon and surgical team. Numerous studies suggest that factors influencing the development of SSI include the host defence, the amount of microbes present at the incision site, and the virulence of those microbes[5,7]. The occurrence of SSI among patients who undergo inpatient surgical procedures is reported as being between 'two and four per cent'[8, p.1]. *Staphylococcus aureus,* coagulase-negative *Staphylococcus* and *Escherichia coli* are the most prevalent microorganisms associated with SSI[9, p.814].

The financial burden of post-operative SSI significantly impacts health institutions and patients[10]. From an Australian perspective, it has been estimated that the average incidence rate of SSI across all types of surgery is 3.3 per cent resulting in total direct expenses of around A$323.5 million[11]. From a patient perspective, SSI causes stress and anxiety from lengthy hospital stays and delayed wound healing, thereby lowering their quality of life. In addition, many patients face financial struggles as a consequence of unexpected medical expenses and lost income[11].

To eliminate bacterial contamination and lower the incidence of SSI, intra-operative wound irrigation is undertaken as a complementary approach to the intravenous (IV) antibiotic regime[12]. Using the antibiotic and directly on the operative sites reduces systematic exposure[13]. The concentration of the antibiotics is high and prolonged when applied to the targeted operative site, and the antimicrobial agents are used where they are most required[14]. Conversely, physiological changes may prevent the optimal efficacy of systematic antibiotics[14].

Wound irrigation is referred to as lavage, washout or wound washes and is an essential part of the intra-operative process[3]. Irrigation with normal saline (NS) is a generally established practice in the operating room[3]. Wound irrigation is performed by pouring the solution over the surface of the surgical wound to dilute and remove blood, tissue debris, metabolic waste, exudates and other body fluids and debris[6]. There are various solutions available for surgical irrigation, such as antibiotics, surfactants and antiseptics; and these vary in delivery availability, mechanisms, solution composition and the type of base solution[3,15].

The surgical intra-operative irrigation of interest for this systematic review is gentamicin irrigation. Gentamicin is a potent antibiotic from the aminoglycoside class used to treat gram-negative infections[16]. Its mode of action is to disrupt the structural integrity of the bacterial cell membrane, by targeting the bacterial ribosomes, which eventually leads to the inhibition of protein synthesis in the bacteria[16]. High doses and prolonged administration of aminoglycosides may cause toxicity in the kidneys and ears[14]; however, a single dose diluted in NS has not been associated with these toxicities[14]. Gentamicin irrigation is frequently used in orthopaedic procedures such total joint arthroplasty and open fracture[17]. It also has broad-spectrum capabilities and is cost effective[17].

Studies conducted over the last decade revealed conflicting evidence regarding the use of gentamicin in intra-operative wound irrigation. While some studies[16,18–20] indicate that gentamicin effectively reduces SSI, others have contrasting findings, especially when compared to other irrigating solutions[21–24]. Emile et al.[21] demonstrated that intra-operative wound irrigation with gentamicin–saline or NS decreased the risk of SSI in open appendectomy

procedures compared to no irrigation. Similarly, a meta-analysis by Fu et al.[25] revealed that irrigation using various antibiotics (such as clindamycin, gentamicin, lincomycin, rifampicin and others), alone or in combination, or aqueous PI solution significantly reduced the risk of SSI when compared to NS irrigation or no irrigation[25]. Meanwhile, Inojie et al.[22] compared the effectiveness of gentamicin and diluted povidone-iodine (PI) in intra-operative wound irrigation for preventing SSI in open spine surgery and found that, while both solutions effectively reduced SSI, diluted PI had a more significant effect than gentamicin[22].

A recent systematic review by Mo et al.[26] found that antibiotic wound irrigation during surgery resulted in a statistically significant decrease in the incidence of SSI; however, there was a moderate to high heterogeneity among the included studies[26]. In contrast, a systematic review by de Jonge et al.[6] found that intra-operative antibiotic wound irrigation did not significantly reduce the incidence of SSI.

Only a limited number of guidelines for preventing SSIs focus on intra-operative wound irrigation; and even among these, conflicting recommendations have been made[27]. Regulatory bodies such as the World Health Organization (WHO), the National Institute for Health and Care Excellence (NICE) and CDC have not been able to standardise perioperative procedures for intra-operative wound irrigation practices aimed at preventing SSI[27]. This is due to the heterogeneous nature of the available research evidence[27]. In Australia, very few investigations or studies have explored the benefits of antibiotic intra-operative irrigation.

The WHO[28], CDC[29] and NICE[30] published evidence-based guidelines for preventing SSI, in 2016, 2017 and 2019 respectively, that included the use of antibiotics for intra-operative wound irrigation. Since then, several studies have been carried out correlating gentamicin irrigation with SSI and numerous systematic reviews and meta-analyses have explored the effectiveness of various types of intra-operative wound irrigation to minimise SSI[6,15,25,26,31,32]. However, a systematic review focussing explicitly on gentamicin irrigation has not previously been carried out. Hence, this systematic review will explore current evidence of the potential efficacy, benefits, risks and limitations of using gentamicin for intra-operative wound irrigation to reduce SSI.

Aim

The aim of this review is to offer a thorough overview of the current knowledge about the effectiveness of gentamicin when used for intra-operative irrigation to reduce the incidence of SSI. This systematic review seeks to gather the existing evidence, evaluate the quality of

Table 1. Summary of PICO selection criteria

	Inclusion criteria details
Population	Patients undergoing surgery regardless of: • age • gender • type of surgery (all surgical specialities including emergency, elective, open and laparoscopic surgeries) • country of residence.
Intervention	Use of intra-operative gentamicin irrigation regardless of the dosage diluted in normal saline and the amount used for the washout.
Comparators	Intra-operative gentamicin irrigation was compared with: • standard irrigation (normal saline 0.9%) • no irrigation • other antibiotics • combination of gentamicin and other antibiotics.
Outcomes	Primary outcome: the incidence of post-operative SSI in surgical patients. Secondary outcomes: duration of hospital stay, factors that affected wound healing and post-operative complications (as a result of the surgery or SSI).

Table 2: Review concepts and search terms

Key concept	Search terms
gentamicin irrigation	gentamicin, therapeutic irrigation, lavage, wash, washout
post-operative infections	surgical site infection, surgical wound infection, post-operative wound infection

the relevant studies and synthesise findings. The review focuses on the following question: Is intra-operative gentamicin irrigation effective in reducing post-operative surgical site infections in comparison to other irrigating solutions or no irrigation?

Method

The review was conducted in accordance with the Joanna Briggs Institute (JBI) systematic reviews of effectiveness methodology[33] and followed the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines[34].

Study selection

The inclusion criteria were established based on population, intervention, comparator and outcomes (PICO) framework for study selection (see Table 1). Case studies, reviews and meta-analyses were excluded. As well as aligning with the PICO criteria, the selected studies had human subjects and were published in English between 1 January 2013 and 31 July 2023.

Search strategy

The search strategy was based on three steps to locate relevant published and unpublished studies (see Figure 1). The first step was conducted between 2018 and 2023 using identified keywords in a preliminary search on five databases – Cumulated Index to Nursing and Allied Health Literature (CINAHL), Scopus, Embase, Medline and PubMed. Keywords and search terms (see Table 2) were used to identify and assess the volume of results that met the review's inclusion criteria. In the preliminary search, only a few articles were identified; therefore, the time frame for article retrieval was expanded to ten years.

The second step involved consulting an experienced librarian to assist in formulating the logic grid according to the database requirements to conduct an extensive search for the potential articles. The Boolean terms 'AND' and 'OR' were used to retrieve relevant articles. The elaborated search results are attached as supplemental material. The databases were also searched with the following restrictions, wherever applicable: human subjects, English language, publication date between 1 January 2013 and 31 July 2023.

The third step was manually searching for articles through Google Scholar, Open Grey and ProQuest Dissertations & Theses. Additionally, the reference lists of the retrieved articles were checked for relevant and related studies.

A total of 52 studies were identified from the search of databases, grey literature and registers. These were uploaded into the Endnote 20.6/2022 (Clarivate Analytics) citation manager, and all duplicate entries were removed. The Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information (JBI-SUMARI) was used to manage the review of articles[35]. Eighteen studies were imported into JBI SUMARI and these were screened for abstract, title and full text by the two reviewers, KK and ZS, independently.

Studies were excluded if they failed to meet the inclusion criteria. The reasons for exclusion after the screening phase were ineligible outcome, ineligible population, ineligible intervention and unavailability of full text. Whenever a conflict emerged, it was resolved through discussion between the two reviewers. Since these conflicts were managed by the two reviewers, a third reviewer was not required.

Methodological quality appraisal

The included studies were four cohort studies[14,16,18,23] and four RCTs[19–22]. The two reviewers used the standardised JBI critical appraisal checklist for cohort studies and randomised control trials (RCTs)[36] to assess the methodological quality of the eligible studies (see supplemental material).

Of the four cohort studies, three received an overall percentage score of 73 per cent (8/11)[16,18,23], the fourth[14] had an overall percentage score of 55 per cent (6/11). All the studies ensured that the recruited groups were similar (question 1), measured outcomes reliably (question 7) and used appropriate statistical analysis (question 11). There were notable gaps in strategies to deal with confounding factors (question 5), reasons for loss of follow-up (question 9) and strategies to address incomplete follow-up (question 10). This indicated that improvement is needed to address potential sources of biases.

Of the four RCTs, one received an overall percentage score of

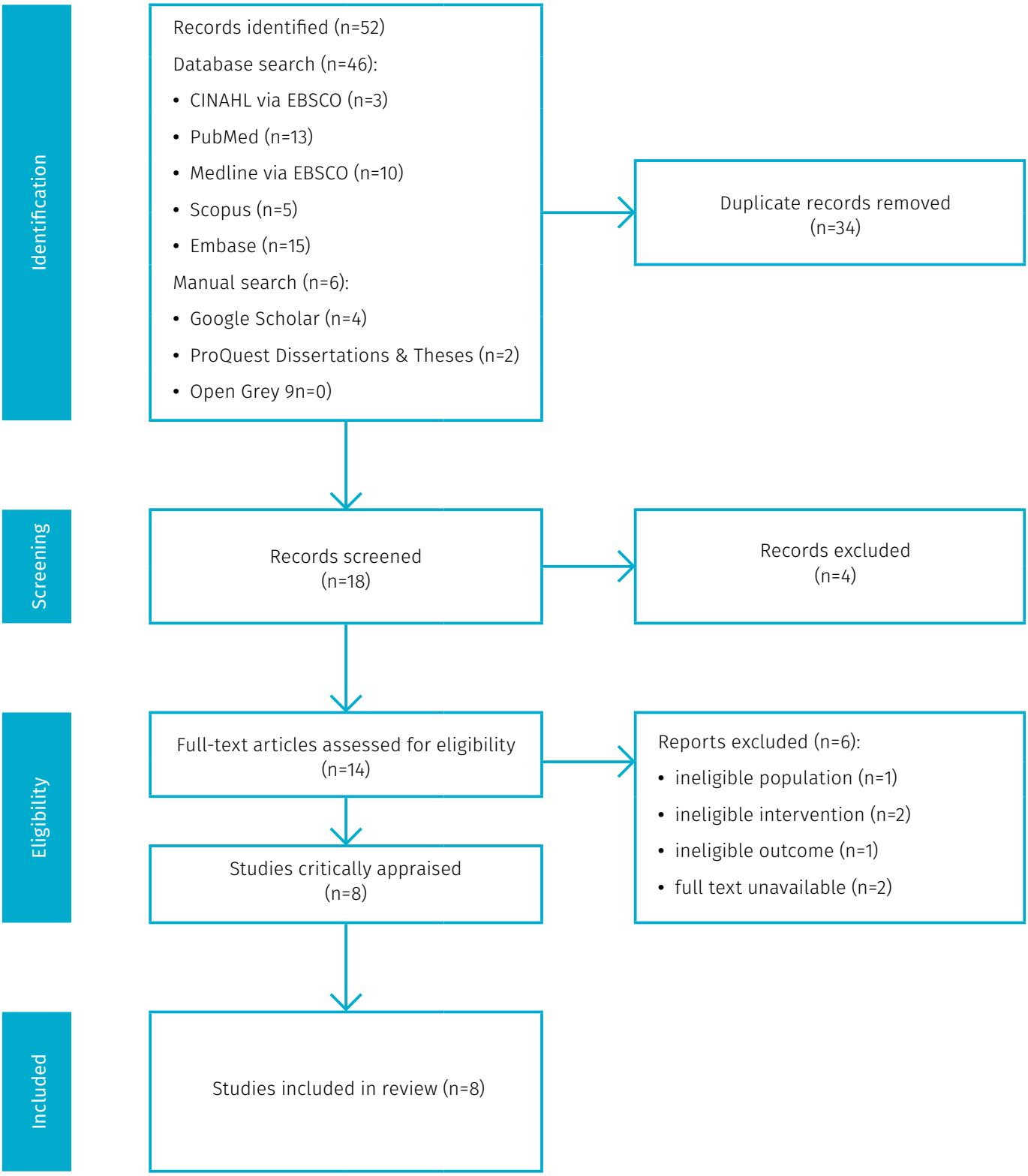

Figure 1: PRISMA flow diagram of paper selection process

100 per cent (13/13)[22], one received an overall percentage of 92 per cent (12/13)[21] and two received 69 per cent (9/13)[19,20]. All the studies used true randomisation to assign participants to treatment groups (question 1), had treatment groups similar at baseline (question 3), treated groups in an identical way apart from the intervention (question 7), analysed participants in treatment groups (question 9), measured outcomes in the same way for all treatment groups (question 10), measured outcomes in a reliable way (question 11), used appropriate statistical analysis (question 12) and used an appropriate trail design (question 13). Three studies[20–21] had concealed allocation to groups (question 2), while the concealment methods were not clearly reported in the fourth study[19]. There were notable gaps concerned with blinding – of participants (question 4), of those delivering treatment (question 5) and those assessing outcomes (question 6); in only one study[22] were all three roles blinded to treatment assignment.

Data extraction

Reviewer KK used the JBI data extraction tool for systematic data extraction for RCTs and cohort studies, and reviewer ZS verified the data extracted. The extracted data included details such as articles' authors, year, country, settings/context, participant characteristics, risk factors of SSI, groups (intervention and control), outcomes and description of the main results. Extraction of unnecessary data was avoided as it would have been time-consuming. Disagreements did not occur during the data extraction process; therefore, a third reviewer was not required.

Synthesis

Subgroup analysis was performed as meta-analysis was not possible due to the heterogeneity in study types and outcome measures. The studies were pooled for subgroup analysis based on the characteristics of the studies using JBI SUMARI[35] whenever possible. Effect measures were expressed as relative risk (for dichotomous data), and confidence intervals (95%) were calculated for the analysis. Statistical analyses were performed using fixed effects and the Mantel-Haenszel statistical method. The heterogeneity of the studies was assessed statistically by standard Chi-square and I^2 tests. Additionally, the findings were presented in the narrative form, wherever statistical pooling was not possible.

Results

Characteristics of included studies

Sample size and setting

The total number of participants from the eight included studies was 3622. The study samples of individual studies ranged from 80 to 1464 participants. The geographical locations of the included studies were Africa[22], China[16], Czech Republic[14], Egypt[20,21], Iran[18,19] and the United States of America (USA)[23]. Six studies[16, 18-22] identified the setting as a tertiary hospital, the remaining two studies[14,23] did not specify the setting.

Participant characteristics

Only four studies[16,20–22] established the criteria for age range, while the remaining studies[14,18,19,23] provided the mean age range. Seven studies[14,16,18,19,21–23] involved participants of both genders; one study[20] had an intake of only female participants as the surgery performed was elective caesarean section. Some studies reported the presence of comorbidities such as diabetes mellitus[16, 21–23], obesity[18,19,20,22,23], and chronic obstructive pulmonary disease[23].

Surgical speciality

The surgical specialties of the selected studies varied, with three being gastroenterology[14,21,23], two neurosurgery[16,22], two orthopaedic[18,19] and one obstetric[20].

Comparator and intervention group

All of the included studies compared gentamicin irrigation with one or two comparators. Six studies[14,16,18–20,22] had two study groups – one group received gentamicin irrigation while the other received a comparator – no irrigation[14], saline irrigation[16,18–20] or PI solution[22]. Two studies[21,23] had three groups – the first group received gentamicin irrigation and the second group received no irrigation. In one study the third group received NS irrigation[21], in the other study the third group received a combination of gentamycin (240mg) and clindamycin (600mg)[23].

Concentrations and dosages of gentamicin

All the studies used NS as a diluent although the concentration and dosage of gentamicin used for intra-operative irrigation varied between the studies. Four studies[16,18,19,22] used a gentamicin concentration of 80 mg/L, although three studies[16,18,19] used a volume of three litres while one[22] used one litre. The concentrations used in the remaining four studies were 1 mg/kg of gentamicin in 200 ml of NS[20], 160 mg of gentamicin in 400 ml of NS[21], 80mg of gentamicin in 10mls of NS[14] and 240mg gentamicin mixed with 500ml of NS[23].

Technique for intra-operative irrigation

Four studies[14,16,21,22] specified the technique used for intra-operative wound irrigation. Emile et al.[21] irrigated each wound layer separately, during open appendectomy, before the layer was closed. In the study by Bayer et al.[14] irrigation was directly into the 'submucosal tunnel'[14, p.301] during peroral endoscopic myotomy (POEM) procedure. In the study by Inojie et al.[22], the surgeons filled the wound cavity up to the level of the skin without solution spillage around the operative site. Subsequently, they drained the irrigating solution within the predetermined duration.[22] Surgeons in the study by Wang et al.[16] used one of two techniques, depending on type of surgery – a 50 mL syringe was used for irrigation during open procedures, such as craniotomies and burr holes, and continuous wound irrigation was used for endoscopic procedures.

Outcome measures

Seven of the studies[16,18–23] investigated surgical site infection as the primary outcome; the eighth study[14] investigated infectious adverse events including SSI. Six studies[14,18–21, 23] reported on secondary outcomes related to the length of the stay (LOS) in the hospital, and two studies[21,22] focused on wound dehiscence.

Surgical site infection

Gentamicin versus normal saline

Three RCTs[18,20,21] and two cohort[16,19] studies, with a total of 2527 participants, compared gentamicin to NS irrigation. Across the five studies there were 1775 participants who received gentamicin irrigation and 752 who received NS irrigation. Four of the five studies[16,18–20], reported that irrigating with gentamicin decreased the incidence of SSI compared to irrigating with NS.

Wang et al.[16] conducted a cohort study with 444 participants, above the age of 18, who underwent neurosurgery. Of these, 265 patients received intra-operative irrigation with gentamicin 240 mg IV diluted in three litres of NS (the gentamicin–saline group) while 179 patients received intra operative irrigation with three litres of NS with no additives (the NS group). It was found that the SSI rate in the neurosurgeries was lower in the gentamicin–saline group (1.1%) when compared to the NS group (8.3%) with a P value of 0.001.

The retrospective cohort study by Yazdi et al.[19] investigated the effects of using gentamicin in intra-operative irrigation to prevent post-operative joint infections. This study had 1464 participants, comprising 1287 patients in the gentamicin–saline group and 177 patients in the NS group who underwent arthroscopic anterior cruciate ligament (ACL) reconstruction surgery. The gentamicin–saline group had 240mg IV gentamicin diluted in three litres of NS (80 mg/L) as intra-operative wound irrigation. In comparison, the NS group had three litres of NS without additives for irrigation. This study showed a lower incidence of septic arthritis in the gentamicin–saline group (0.23%) compared to the NS irrigation group (2.2%) with a statistical significance of $P < 0.05$.[19]

An RCT by Maaty et al.[20] compared the SSI rate between gentamicin–saline and saline irrigation of the subcutaneous tissue in obese patients having elective caesarean section (CS). There were 132 participants in this study, 66 in the gentamicin–saline study group and 66 in the saline control group. The participants in both groups ranged in age from 20 to 35 years, with body mass indexes of 30–40kg/m^2. The study group had 1mg/kg IV gentamicin diluted in 200ml of saline (0.9%) as the irrigation solution, while the control group had 200ml of saline (0.9%) as the irrigation solution. The SSI rates in the gentamicin–saline group were lower (3%) than in the saline irrigation group (4.5%). However, the difference was not statistically significant as indicated by the P value of 0.999. The relative risk (95% CI) that represented the effective size was 0.67 (0.12–3.86).

The prospective RCT by Yazdi et al.[18], had a total of 351 participants who underwent arthroscopic ACL reconstruction surgery. There were 174 patients in the gentamicin–saline group, and 177 patients in the NS group. The gentamicin–saline group received intra-operative irrigation with 240 mg IV gentamicin diluted in three litres of NS (0.9% sodium chloride). The NS group received three litres of NS (0.9% sodium chloride) without any additives. Yazdi et al.[18] found a lower risk of septic arthritis in the gentamicin–saline group (0.57%) compared to the NS group (2.2%); however, this was not statistically significant ($P = 0.4$)[18].

Emile et al.[21] conducted a prospective RCT study that examined the effect of 'layer-by-layer' wound irrigation on incisional SSI in open appendectomy. In the study, 69 patients received irrigation with 160mg IV gentamicin diluted in NS (0.9%) and 67 patients received irrigation with NS (0.9%). In contrast to the other four studies[16,18–20], Emile et al.[21] reported that the rate of SSI was greater (4.3%) in the group receiving gentamicin–saline irrigation than it was in the NS irrigation group (2.9%).

Gentamicin versus diluted povidone iodine

One study[22] compared gentamicin with diluted PI. Inojie et al.[22] conducted a prospective comparative RCT study with 80 participants who underwent non-instrumented open spine surgery (that is, spinal procedures that did not involve the use of implants and prostheses[22]). Participants were randomly assigned to two equal groups – the gentamicin group (n = 40) received wound irrigation with 80 mg IV gentamicin diluted in a litre of NS and the PI group (n = 40) received wound irrigation with a litre of dilute PI (3.5%). The overall SSI rate was higher in the gentamicin group (17.5 %) compared to the PI group (2.5%). The incidence of SSI varied significantly between the groups (P = 0.025), which is statistically significant. The SSI was further categorised into deep SSI and superficial SSI. The incidence of SSI was higher in the gentamicin group than the PI group for both deep SSI (5% compared to 2.5%, P = 0.556) and superficial SSI (12.5% compared to 0%, P = 0.025)[22].

Gentamicin alone versus gentamicin with antibiotics

Fatula et al.[23] conducted a retrospective cohort study of participants who underwent open ventral hernia repair (OVHR) with mesh. In the study, 263 patients received irrigation with 240 mg of gentamicin in 500 ml of NS (the gentamicin–saline group) and 299 patient received irrigation with 240 mg gentamicin and 600mg clindamycin diluted in 500 mL of NS (the G+C group). The incidence of SSI was significantly lower (P < 0.001) in the G+C group (5.35%) than the gentamicin–saline group (15.21%)[23].

Gentamicin irrigation versus no irrigation

One RCT[21] and two cohort studies[14,23] compared wound irrigation with gentamicin to no irrigation, with a total of 785 participants, 392 who received irrigation with gentamicin and 393 who received no irrigation. Emile et al.[21] conducted a prospective RCT study of open appendectomy patients in which 69 patients received irrigation with 160mg IV gentamicin diluted in 400ml NS (0.9%) and 69 patients received no irrigation. The gentamicin–saline group had significantly lower SSI rates than the no-irrigation group (respectively, 4.3 % and 17.4%)[21]. The retrospective cohort study by Fatula et al.[23] involved patients who had OVHR with mesh – 263 patients received irrigation with gentamicin and 260 patients received no irrigation. The SSI rate in the no-irrigation group was slightly higher than in the gentamicin group (respectively, 16.54% and 15.21%)[23].

In a retrospective cohort study of 124 patients who underwent a POEM procedure, by Bayer et al.[14], 60 patients received 80mg of IV gentamicin diluted in 10 ml of NS as intra-operative submucosal lavage and 64 patients did not. In contrast to Emile et al.[21] and Fatula et al.[23], Bayer et al.[14] found that the incidence of infectious adverse events was higher in patients who received gentamicin lavage than in patients who did not (2% compared to 0%); however, the results were not statistically significant (P = 0.48).

Length of hospital stay

The length of hospital stay (LOS) is a challenging outcome to measure due to the presence of confounding factors in the studies. Six studies reported LOS as a secondary outcome. In the study by Bayer et al.[14], the group that received gentamicin irrigation had a longer LOS than the group with no irrigation (respectively, 2.6 +/- 1.4 and 1.9 +/- 0.8, P < 0.01). Emile et al.[21] reported the average LOS for the three study groups – no irrigation 1.14 (SD 0.3), gentamicin–saline irrigation 1.1 (SD 0.26) and NS irrigation 1.05 (SD 0.24), with a P value of 0.18. The average LOS in the study by Fatula et al.[23] was three days for the group that received no irrigation, four days for the group that received gentamicin–saline irrigation and four days for the group that received irrigation with a combination of gentamicin and clindamycin (P < 0.001).

Maaty et al.[20] reported a shorter average LOS in the gentamicin group (1.3 +/- 0.5) than the saline group (1.4+/-0.7); however, the difference was insignificant (P = 0.302). The LOS for the NS group in the earlier study by Yazdi et al.[18] was from 8 to 14 days; however, the LOS of one patient in the gentamicin–saline group who developed deep infection post-operatively was not specified. In their later study, Yazdi et al.[19] found that the LOS for the NS group ranged from 8 to 14 days, while the LOS for the gentamicin–saline group was 13 to 30 days.

Wound dehiscence

Two studies[21,22] included wound dehiscence as one of the secondary outcomes. The study by Emile et al.[21] reported that the no irrigation group had a higher wound dehiscence rate than both the gentamicin–saline group and the NS group (respectively (2.8% (n=2), 0% and 0%, P = 0.22). On the other hand, Inojie et al.[22] reported that wound dehiscence was higher in the gentamicin–saline group (n=6) than in the diluted PI group (n=1).

Study	Gentamicin-saline		Normal saline		Weight	M-H,	Relative Risk
	Events	Total	Events	Total			Fixed, 95% CI
Emile et al.[21]	3	69	2	67	6.01%	1.46	[0.25, 8.44]
Maaty et al.[20]	2	66	3	66	8.88%	0.67	[0.12, 3.86]
Wang et al.[16]	2	179	22	265	52.53%	0.13	[0.03, 0.57]
Yazdi et al.[18]	1	174	4	177	11.74%	0.25	[0.03, 2.25]
Yazdi et al.[19]	3	1287	4	177	20.83%	0.10	[0.02, 0.46]
Total (95% CI)		**1775**		**752**	100.00%	0.27	[0.13, 0.55]

Heterogeneity: x^2=7.06, df=4 (P=0.133) 1^2=43
Test for overall effect: Z=-3.63 (P<0.001)

Favours [Gentamicin-saline] Favours [Normal saline]

Figure 2: Forest plot of gentamicin–saline irrigation versus normal saline irrigation

Subgroup analysis

The subgroup analysis of two cohort studies[16,19] and three RCTs[18,20,21] (including a total of 2527 participants) favoured the gentamicin–saline group over the saline group in reducing post-operative SSI (see Figure 2). The relative risk (RR) of 0.27 (95% confidence interval between 0.13 to 0.55) and Z value of -3.93 (P < 0.001) indicated that there is a statistically significant difference. Therefore, the null hypothesis is rejected, suggesting that there is a lower rate of post-operative SSI with gentamicin–saline irrigation than with normal saline irrigation. The analysis also revealed moderate heterogeneity (x^2 = 7.06, df = 4 (P = 0.133), I^2=43) implying some variability across the studies.

Discussion

The primary purpose of this systematic review was to determine whether intra-operative gentamicin irrigation effectively reduced the incidence of SSI. The review comprised eight papers (four cohort studies[14,16,18,23] and four RCTs[19–22]) comparing the efficacy of gentamicin irrigation with other comparators. Several studies in the review provided consistency by controlling the variables to some degree, such as the same surgeon, or surgeons with similar experience[16,18,21]; pre-operative preparation[18] and surgical techniques[18,21]. Participants in seven of the eight selected studies were administered the same pre-operative and post-operative antibiotics[14,16,18–22]. However, this review found conflicting results in relation to the effect of intra-operative gentamicin wound irrigation on SSI incidence.

Overall, intra-operative gentamicin irrigation reduced the incidence of SSI when compared to NS irrigation. This is consistent with the findings of Ruiz-Tovar et al.[37] who reported a substantial decrease in contamination when lavage was performed with gentamicin solution compared to when lavage was performed with normal saline. Similarly, a study by Ma et al.[38] investigated the effect of intra-operative gentamicin irrigation (in surgical solution) on the incidence of endophthalmitis following cataract surgery. They found a lower incidence of endophthalmitis in patients who received intra-operative gentamicin irrigation than patients who did not receive this (respectively 0.2% (n=5 of 21 469) and 0.8% (n=8 of 16 395), P = 0.016)[38].

The results of the reviewed studies varied when gentamicin–saline irrigation was compared with diluted PI irrigation, no irrigation, and irrigation with a combination of antibiotics. These findings align with a study by van Herwijnen et al.[24] into intra-operative irrigation in adolescent idiopathic scoliosis surgery. van Herwijnen et al.[24] reported that wound irrigation with diluted PI dramatically reduced the SSI rate by around 20 per cent when compared to gentamicin irrigation. Meanwhile, a univariable analysis by Hemmingsen et al.[39] revealed that intra-operative gentamicin wound irrigation significantly reduced deep infections compared to no irrigation. However, intra-operative gentamicin wound irrigation was not statistically significant in the multivariable analysis compared to other factors influencing the risk of infection[39]. Moreover, a

recent scoping review of 17 articles suggested that vancomycin, gentamicin and streptomycin were the most efficacious antibiotics for using in intra-operative antibiotic irrigation to decrease SSI rates[12]. In contrast, a meta-analysis by de Jonge et al.[6] discouraged the use of antibiotic agents for intra-operative irrigation as no benefits in reducing SSI were found.

As well as discussing the potential benefits of gentamicin use, it is essential to address potential adverse effects, namely toxicity and resistance. Two studies[14,18] in this review mentioned that participants in their study did not have renal failure, which is one of the potential effects of gentamicin toxicity. However, no studies discussed gentamicin resistance in study participants. There is potential for gentamicin resistance to occur due to inadequate drug–microbe interaction periods and systemic absorption of antibiotics at subtherapeutic levels[5]. A World Health Organisation (WHO) expert panel also concluded that the possibility of antibiotic resistance may be linked to using antibiotics for wound irrigation[40]. Moreover, a study by Lee et al.[41] showed systematic absorption of gentamicin in surgical patients undergoing joint replacement surgeries with intra-operative gentamicin irrigation. They further concluded that this could lead to toxicity if used repeatedly or in large amounts[41].

Several factors have contributed to variability in the findings of the studies in this review. The efficacy of intra-operative gentamicin irrigation in reducing SSI may vary depending on the operative site and the nature and complexity of the surgical procedure.[16,19,21] This review included studies with different surgical procedures because of limited publications about intra-operative gentamicin irrigation in a specific speciality or procedure. Moreover, across the studies, the patient population was heterogeneous with varying demographics, comorbidities and overall health status. This diversity may have affected how participants responded to intra-operative gentamicin irrigation. Furthermore, the dosage and concentrations of gentamicin and the volume of the NS as diluent also varied across the studies. The duration of exposure to gentamicin also differed depending on the surgical context, and this may have affected the effect of the gentamicin on SSI. Lastly, the findings of included studies would have been influenced by the approach to methodology, data reporting and analysis that was used.

The WHO's Global guidelines for preventing surgical site infection[28] advocate against antibiotic use for intra-operative wound irrigation prior to closure to prevent SSI. The reason for this is the low quality of evidence supporting this practice in the published literature[28]. Similarly, CDC guidelines[29] do not recommend intra-operative antibiotic irrigation due to low-quality evidence of its harm or benefit in SSI prevention. However, CDC guidelines do recommend using diluted PI for intra-operative wound irrigation[29]. The NICE guidelines[30] also advise against wound irrigation or intracavity lavage to prevent SSI; however, they have suggested using antibiotics on the wounds before the closure for research purposes only[30]. The Australian Commission on Safety and Quality in Health Care (ACSQHC) also states 'avoid routine use of wound irrigation or intracavity antibiotic lavage'[42, p. 179] as there is a lack of evidence suggesting that these practices lowers SSI risk.

Recommendations for future research

This systematic review highlights the need for more primary studies exploring the effect of intra-operative gentamicin wound irrigation on SSI rates to strengthen existing findings. Future studies must include well-designed RCTs with a large sample and consider various surgical specialisations. Investigating the intra-operative use of gentamicin irrigation in neurosurgery, orthopaedic surgery, gastrointestinal surgery and other surgical specialisations may yield important information about the efficacy of the practice in different surgical contexts. This may produce more accurate results, address confounding variables and biases and contribute to more in-depth insights into the effects of intra-operative gentamicin irrigation on SSI and patient outcomes.

Strengths and limitations

A comprehensive search strategy captured articles and publications pertinent to the review topic. The PRISMA guideline was used to show that this review was conducted and reported in a structured and consistent manner, increasing its transparency and credibility. The included studies were characterised in detail, which assisted in comprehending the significance and relevance of the results. Conversely, this review was limited by flaws in the included studies. The sample size for most studies was small, diminishing their external and internal validity and potentially predisposing the studies to failure to discover a true effect[43]. It is important to note that studies were not excluded based on the quality, and differences in the methodological quality of the included studies may have

caused potential biases. Hence, it is necessary to recognise that some studies had drawbacks due to how they managed confounding factors, dealt with insufficient follow-up and handled blinding techniques. Additionally, none of the studies compared different irrigation volumes nor evaluated the possible toxic effect of gentamicin on the surgical patient.

Implications for practice

While some of the findings of this review point to the benefits of intra-operative wound irrigation, they also indicate ambiguous or conflicting evidence. This is consistent with the position regulatory bodies, such as the WHO, CDC and NICE, have taken in not recommending that antibiotics be used for intra-operative wound irrigation because of lack of conclusive evidence. The ambiguity in the results could contribute to the lack of standardisation of intra-operative antibiotic wound irrigation. The findings of the study may also enlighten and provide valuable insight to perioperative personnel who still use intra-operative gentamicin irrigation during surgical procedures.

Conclusion

The outcome of this systematic review indicates that intra-operative gentamicin irrigation lowers the incidence of SSI when compared to NS irrigation. However, there were contradictory results when intra-operative gentamicin irrigation was compared to other alternative interventions such as irrigation with diluted PI, irrigation with a combination of antibiotics and no irrigation. The variations in surgical specialities, patient demographics, gentamicin dose, volume of dilution and surgical technique affect the efficacy of gentamicin irrigation in reducing SSI. The moderate heterogeneity across the studies indicates the need to standardise the intra-operative gentamicin irrigation protocols. Furthermore, future research should investigate potential issues associated with intra-operative gentamicin irrigation, including toxicity and resistance, to better understand its effects on patients and SSI prevention.

Acknowledgment

This review contributes towards the completion of the Master of nursing science program. It would not have been possible without the invaluable support of the Australia Awards in sponsoring the authors' study in Master of Nursing Science at the University of Adelaide.

Declaration of conflicting interests

The authors have declared no conflict of interest while compiling this systematic review of research.

References

1. O'Brien WJ, Gupta K, Itani KMF. Association of postoperative infection with risk of long-term infection and mortality [Internet]. JAMA surgery. 2020[cited 2023 Aug 20];155(1):1–8. DOI: 10.1001/jamasurg.2019.4539
2. Sarani B. Infection in the post-operative patient [Internet]. New York: Haymarket Media, Inc; 2019 [cited 2023 Aug 20]. Available from: www.cancertherapyadvisor.com/home/decision-support-in-medicine/critical-care-medicine/infection-in-the-post-operative-patient/
3. Barnes S, Spencer M, Graham D, Johnson HB. Surgical wound irrigation: A call for evidence-based standardization of practice [Internet]. Am J Infect Control. 2014[cited 2023 Aug 20];42(5):525–9.
4. Surgical Site Infection (SSI) [Internet]. Atlanta: The Centers for Disease Control and Prevention (CDC); 2010 [updated November 24, 2010; cited 2024 Jan 26]. Available from: www.cdc.gov/hai/ssi/ssi.html
5. Edmiston CE, Leaper D, Spencer M, Truitt K, Fauerbach LL, Graham D et al. Considering a new domain for antimicrobial stewardship: Topical antibiotics in the open surgical wound [Internet]. Am J Infect Control. 2017[cited 2024 Jan 26];45(11):1259–66. DOI: 10.1016/j.ajic.2017.04.012
6. de Jonge SW, Boldingh QJJ, Solomkin JS, Allegranzi B, Egger M, Dellinger EP et al. Systematic review and meta-analysis of randomized controlled trials evaluating prophylactic intra-operative wound irrigation for the prevention of surgical site infections [Internet]. Surg Infect (Larchmt). 2017[cited 2024 Jan 26];18(4):508–519. DOI: 10.1089/sur.2016.272
7. Fry DE. Topical antimicrobials and the open surgical wound [Internet]. Surg Infect (Larchmt). 2016[cited 2024 Jan 26];17(5):520–4.
8. Agency for Healthcare Research and Quality (AHRQ). Surgical site infections [Internet]. Rockville: AHRQ; 2019 [cited 2023 Aug 20]. Available from: www.psnet.ahrq.gov/primer/surgical-site-infections
9. Patel NV, Patel VA, Bhatt PD. Prospective study of surgical site infections: A cross-sectional study. International Journal of Academic Medicine and Pharmacy. 2023;5(1): 813–5.
10. Ban KA, Minei JP, Laronga C, Harbrecht BG, Jensen EH, Fry DE et al. American college of surgeons and surgical infection society: Surgical site infection guidelines, 2016 update. J Am Coll Surg. 2017[cited 2024 Jan 26];224(1):59–74. DOI: 10.1016/j.jamcollsurg.2016
11. Royle R, Gillespie BM, Chaboyer W, Byrnes J, Nghiem S. The burden of surgical site infections in Australia: A cost-of-illness study [Internet]. J Infect Public Health. 2023[cited 2024 Jan 26];16(5):792–8. DOI: 10.1016/j.jiph.2023.03.018
12. Duquette E, Bhatti P, Sur S, Felbaum DR, Dowlati E. History and use of antibiotic irrigation for preventing surgical site infection in neurosurgery: A scoping review [Internet]. World Neurosurg. 2022[cited 2024 Jan 26];160:76–83. DOI: 10.1016/j.wneu.2022.01.098
13. Steadman W, Chapman PR, Schuetz M, Schmutz B, Trampuz A, Tetsworth K. Local antibiotic delivery options in prosthetic joint infection [Internet]. Antibiotics (Basel). 2023[cited 2024 Jan 26];12(4):752. DOI: 10.3390/antibiotics12040752

14. Bayer J, Vackova Z, Svecova H, Stirand P, Spicak J, Martinek J. Gentamicin submucosal lavage during peroral endoscopic myotomy (POEM): A retrospective analysis [Internet]. Surg Endoscop. 2018[cited 2024 Jan 26];32(1):300–6. DOI: 10.1007/s00464-017-5677-8

15. Norman G, Atkinson RA, Smith TA, Rowlands C, Rithalia AD, Crosbie EJ et al. Intracavity lavage and wound irrigation for prevention of surgical site infection [Internet]. Cochrane Database Syst Rev.. 2017[cited 2024 Jan 26];2017(10): CD012234. DOI: 10.1002/14651858.CD012234.pub2

16. Wang J, Yang Y, Lv W, Xu S, Mei S, Shi F et al. Gentamycin irrigation significantly reduces 28-day surgical site infection after emergency neurosurgery. [Internet] Br J Neurosurg. 2024[cited 2024 Jan 26];38(2):481–5. DOI: 10.1080/02688697.2021.1902472

17. Bansal D, Khatri K, Dahuja A, Lakhani A, Malhotra N. Comparison between vancomycin and gentamicin for intraoperative presoaking of hamstring graft in primary anterior cruciate ligament reconstruction [Internet]. Curēus. 2022[cited 2024 Jan 26];14(2):e22550. DOI: 10.7759/cureus.22550

18. Yazdi H, Moradi A, Herbort M. The effect of gentamicin in irrigating solutions on articular infection prophylaxis during arthroscopic ACL reconstruction [Internet]. Arch Orthop Trauma Surg. 2014[cited 2024 Jan 26];134(2):257–61. DOI: 10.1007/s00402-013-1910-7

19. Yazdi H, Gomrokchi AY, Nazarian A, Lechtig A, Hanna P, Ghorbanhoseini M. The effect of gentamycin in the irrigating solution to prevent joint infection after anterior cruciate ligament (ACL) reconstruction. Arch Bone Jt Surg. 2019;7(1):67–74.

20. Maaty AM, Yehia AA, Abdelaleem MM, El-Fattah MA. Subcutaneous antibiotic irrigation to prevent wound infection in obese patients undergoing cesarean section [Internet]. Women Health Care and Issues. 2021[cited 2024 Jan 26];4(3):1–5. DOI: 10.31579/2642-9756/060

21. Emile SH, Elfallal AH, Abdel-Razik MA, El-Said M, Elshobaky A. A randomized controlled trial on irrigation of open appendectomy wound with gentamicin-saline solution versus saline solution for prevention of surgical site infection {internet]. Int J Surg. 2020[cited 2024 Jan 26];81:140–6. DOI: 10.1016/j.ijsu.2020.07.057

22. Inojie MO, Okwunodulu O, Ndubuisi CA, Campbell FC, Ohaegbulam SC. Prevention of surgical site infection following open spine surgery: The efficacy of intraoperative wound irrigation with normal saline containing gentamicin versus dilute povidone-iodine [Internet]. World Neurosurg. 2023[cited 2024 Jan 26];173(1):e1–e10. DOI: 10.1016/j.wneu.2022.12.134

23. Fatula LK, Nelson A, Abbad H, Ewing JA, Hancock BH, Cobb WS et al. Antibiotic irrigation of the surgical site decreases incidence of surgical site infection after open ventral hernia repair. The Am Surg. 2018;84(7):1146–51.

24. van Herwijnen B, Evans NR, Dare CJ, Davies EM. An intraoperative irrigation regimen to reduce the surgical site infection rate following adolescent idiopathic scoliosis surgery [Internet]. Ann R Coll Surg Engl. [cited 2024 Jan 26]DOI: 10.1308/rcsann.2016.0132

25. Fu C, Meng L, Ma M, Li N, Zhang J. Effect of wound irrigation on the prevention of surgical site infections: A meta-analysis [Internet]. Int Wound J. 2022[cited 2024 Jan 26];19(7):1878–86. DOI: 10.1111/iwj.13794

26. Mo YW, Choi JH, Lee WJ. Prophylactic intraoperative wound irrigation with antibiotic solution for the prevention of surgical incisional wound infections: Systematic literature review and meta-analysis [Internet]. J Plast Reconstr Aesthet Surg. 2023[cited 2024 Jan 26];76:121–32. DOI: 10.1016/j.bjps.2022.10.014

27. Lindahl SB. Intraoperative irrigation: Fluid administration and management amidst conflicting evidence [Internet]. AORN J. 2020[cited 2024 Jan 26];111(5):495–507. DOI: 10.1002/aorn.13010

28. World Health Organization (WHO). Global guidelines for the prevention of surgical site infection [Internet]. Geneva: WHO; 2018 [cited 2023 Aug 13]. Available from: www.who.int/publications/i/item/global-guidelines-for-the-preventionof-surgical-site-infection-2nd-ed

29. Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR et al. Centers for Disease Control and prevention guideline for the prevention of surgical site infection, 2017 [Internet]. JAMA Surg. 2017[cited 2023 Aug 13];152(8):784–91. DOI: 10.1001/jamasurg.2017.0904

30. National Institute for Health and Care Excellence (NICE). Surgical site infections: Prevention and treatment [Internet]. London: NICE; 2020 [cited 2023 Aug 13]. Available from: www.nice.org.uk/guidance/ng125/resources/surgical-site-infections-prevention-and-treatment-pdf-66141660564421

31. Mueller TC, Loos M, Haller B, Mihaljevic AL, Nitsche U, Wilhelm D et al. Intra-operative wound irrigation to reduce surgical site infections after abdominal surgery: A systematic review and meta-analysis [Internet]. Langenbecks Arch Surg. 2015[cited 2024 Jan 26];400(2):167–81. DOI: 10.1007/s00423-015-1279-x

32. Thom H, Norman G, Welton NJ, Crosbie EJ, Blazeby J, Dumville JC. Intra-cavity lavage and wound irrigation for prevention of surgical site infection: Systematic review and network meta-analysis [Internet]. Surg Infect. 2021[cited 2024 Jan 26];22(2):144–67. DOI: 10.1089/sur.2019.318

33. Tufanaru C MZ, Aromataris E, Campbell J, Hopp L. Chapter 3: Systematic reviews of effectiveness. In: Aromataris E, Munn Z (Editors). JBI manual for evidence synthesis [Internet]. Adelaide: JBI; 2020 [cited 2023 August 1]. Available from: https://synthesismanual.jbi.global

34. Page M, McKenzie, JE, Bossuyt PM, Boutron, I, Hoffmann TC, Mulrow, CD et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews [Internet]. BMJ. 2021[cited 2023 Sep 10];Mar 29:372:n71. DOI: 10.1136/bmj.n71

35. Munn Z, Aromataris E, Tufanaru C, Stern C, Porritt K, Farrow J et al. The development of software to support multiple systematic review types: The JBI system for the unified management, assessment and review of information (JBI SUMARI) [Internet]. Int J Evid Based Healthc. 2018 [cited 2023 Sep 1];17(1):36–43. DOI: 10.1097/XEB.0000000000000152

36. Joanna Briggs Institute. Critical appraisal tools, JBI Global [Internet]. Adelaide: JBI Global; n.d. [cited 2023 Sep 2]. Available from: www.jbi.global/critical-appraisal-tools

37. Ruiz-Tovar J, Cansado P, Perez-Soler M, Gomez MA, Llavero C, Calero P et al. Effect of gentamicin lavage of the axillary surgical bed after lymph node dissection on drainage discharge volume [Internet]. Breast. 2013[cited 2023 Sep 1];22(5):874–8. DOI: 10.1016/j.breast.2013.03.008

38. Ma W, Hou G, Wang J, Liu T, Tian F. Evaluation of the effect of gentamicin in surgical perfusion solution on cataract postoperative endophthalmitis [Internet]. BMC Ophthalmol. 2022[cited 2023 Sep 1];22(1):410. DOI: 10.1186/s12886-022-02633-2

39. Hemmingsen MN, Bennedsen AK, Kullab RB, Weltz TK, Larsen A, Ørholt M et al. Antibiotic implant irrigation and deep infection: A retrospective study of 1508 patients undergoing breast reconstruction with implants [Internet]. Plast Reconstruct Surg. 2023[cited 2023 Sep 1]. DOI: 10.1097/PRS.0000000000010869

40. Allegranzi BD, Zayed BMD, Bischoff PMD, Kubilay NZMD, de Jonge SMD, de Vries FMD et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: An evidence-based global perspective [Internet]. Lancet Infect Dis. 2016[cited 2023 Sep 1];16(12):e288–e303. DOI: 10.1016/S1473-3099(16)30402-9
41. Lee KH, Ng ABY, Tan TB, Mossinac K, To BCS. Systemic absorption of gentamicin irrigation in joint replacement surgery: A cause of concern. Malays Orthop J. 2008;2(2):11–6.
42. National Health and Medical Research Council (NHMRC). Australian guidelines for the prevention and control of infection in healthcare [Internet]. Canberra: NHMRC; 2019 [cited 2023 August 13]. Available from: www.nhmrc.gov.au/sites/default/files/documents/infection-control-guidelines-feb2020.pdf.
43. Faber J, Fonseca LM. How sample size influences research outcomes. Dental press journal of orthodontics. 2014;19(4):27-9.

Effectiveness of intra-operative gentamicin irrigation in reducing post-operative surgical site infections: A systematic review

Supplement 1: Critical appraisal of included studies

Table 1: Critical appraisal of cohort studies using Joanna Briggs Institute cohort study checklist

Study	Q1: Were the two groups similar and recruited from the same population?	Q2: Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Q3: Was the exposure measured in a valid and reliable way?	Q4: Were confounding factors identified?	Q5: Were strategies to deal with confounding factors stated?	Q6: Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Q7: Were the outcomes measured in a valid and reliable way?	Q8: Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Q9: Was follow-up complete, and if not, were the reasons to loss to follow-up described and explored?	Q10: Were strategies to address incomplete follow-up utilised?	Q11: Was appropriate statistical analysis used?	Score
Bayer et al.[1]	Y	U	U	U	U	Y	Y	Y	Y	N/A	Y	6/11
Fatula et al.[2]	Y	Y	Y	Y	Y	Y	Y	U	U	U	Y	8/11
Wang et al.[3]	Y	Y	Y	Y	U	U	Y	Y	Y	U	Y	8/11
Yazdi et al.[4]	Y	Y	Y	Y	U	Y	Y	Y	N	N	Y	8/11
Percentage	100	75	75	75	25	75	100	75	50	0.0	100	

Y = yes, N = no, U = unclear, N/A = not applicable

Table 2: Critical appraisal of randomised controlled trials using Joanna Briggs Institute appraisal tool for randomised controlled trials

Study	Q1: Was true randomisation used for assignment of participants to treatment groups?	Q2: Was allocation to treatment groups concealed?	Q3: Were treatment groups similar at baseline?	Q4: Were participants blind to treatment assignment?	Q5: Were those delivering treatment blind to treatment assignment?	Q6: Were outcome assessors blind to treatment assignment?	Q7: Were treatment groups treated identically other than the intervention of interest?	Q8: Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?	Q9: Were participants analysed in the groups to which they were randomised?	Q10: Were outcomes measured in the same way for treatment groups?	Q11: Were outcomes measured in a reliable way?	Q12: Was appropriate statistical analysis used?	Q13: Was the trial design appropriate, and any deviations from the standard RCT design (individual randomisation, parallel groups) accounted for in the conduct and analysis of the trial?	Score
Emile et al.[5]	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	12/13
Inojie et al.[6]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	13/13
Maaty et al.[7]	Y	Y	Y	U	N	U	Y	U	Y	Y	Y	Y	Y	9/13
Yazdi et al.[8]	Y	U	Y	U	U	U	Y	Y	Y	Y	Y	Y	Y	9/13
Percentage	100	75	100	50	25	50	100	75	100	100	100	100	100	

Y = yes, N = no, U = unclear, N/A = not applicable

References (Supplement 1)

1. Bayer J, Vackova Z, Svecova H, Stirand P, Spicak J, Martinek J. Gentamicin submucosal lavage during peroral endoscopic myotomy (POEM): A retrospective analysis [Internet]. Surg Endoscop. 2018[cited 2024 Jan 26];32(1):300–6. DOI: 10.1007/s00464-017-5677-8
2. Fatula LK, Nelson A, Abbad H, Ewing JA, Hancock BH, Cobb WS et al. Antibiotic irrigation of the surgical site decreases incidence of surgical site infection after open ventral hernia repair. The Am Surg. 2018;84(7):1146–51.
3. Wang J, Yang Y, Lv W, Xu S, Mei S, Shi F et al. Gentamycin irrigation significantly reduces 28-day surgical site infection after emergency neurosurgery. [Internet] Br J Neurosurg. 2024[cited 2024 Jan 26];38(2):481–5. DOI: 10.1080/02688697.2021.1902472
4. Yazdi H, Gomrokchi AY, Nazarian A, Lechtig A, Hanna P, Ghorbanhoseini M. The effect of gentamycin in the irrigating solution to prevent joint infection after anterior cruciate ligament (ACL) reconstruction. Arch Bone Jt Surg. 2019;7(1):67–74.
5. Emile SH, Elfallal AH, Abdel-Razik MA, El-Said M, Elshobaky A. A randomized controlled trial on irrigation of open appendectomy wound with gentamicin- saline solution versus saline solution for prevention of surgical site infection {internet]. Int J Surg. 2020[cited 2024 Jan 26];81:140–6. DOI: 10.1016/j.ijsu.2020.07.057
6. Inojie MO, Okwunodulu O, Ndubuisi CA, Campbell FC, Ohaegbulam SC. Prevention of surgical site infection following open spine surgery: The efficacy of intraoperative wound irrigation with normal saline containing gentamicin versus dilute povidone-iodine [Internet]. World Neurosurg. 2023[cited 2024 Jan 26];173(1):e1–e10. DOI: 10.1016/j.wneu.2022.12.134
7. Maaty AM, Yehia AA, Abdelaleem MM, El-Fattah MA. Subcutaneous antibiotic irrigation to prevent wound infection in obese patients undergoing cesarean section [Internet]. Women Health Care and Issues. 2021[cited 2024 Jan 26];4(3):1–5. DOI: 10.31579/2642-9756/060
8. Yazdi H, Moradi A, Herbort M. The effect of gentamicin in irrigating solutions on articular infection prophylaxis during arthroscopic ACL reconstruction [Internet]. Arch Orthop Trauma Surg. 2014[cited 2024 Jan 26];134(2):257–61. DOI: 10.1007/s00402-013-1910-7

Effectiveness of intra-operative gentamicin irrigation in reducing post-operative surgical site infections: A systematic review

Supplement 2: Characteristics of selected studies

Authors (year) Country	Procedure	Study design Setting/context	Participant numbers and characteristics	Risk factors	Groups (sample size)	Outcomes measured	Description of main results
Bayer et al.[1] (2018) Czech Republic	peroral endoscopic myotomy (POEM)	cohort study IKEM Centre	124 patients with dysphagia: • 68.5% had achalasia • 89.6% had regurgitation • 87.9 % occasional chest pain • Mean age: 46.4 years	Leak during the procedure	Group 1 (n=60): gentamicin lavage (80mg gentamicin in 10 mL NS) Group 2 (n=64): no lavage	• infectious adverse events • length of hospital stay (LOS)	Group 1 had more infectious adverse events than Group 2 (n=1 (2%) compared to n=0 (0%), P=0.48) but this was not statistically significant. Group 1 had longer LOS than Group 2 (2.6 (+/- 1.4) compared to 1.9 (+/-0.8), P<0.01).
Emile et al.[2] (2020) Egypt	open appendectomy	RCT General surgery department, Mansoura University Hospital	205 patients with acute appendicitis Age: 16–65 years	Age Diabetes mellitus (DM)	Group 1 (n=69): irrigation with 160 mg gentamicin in 400 ml 0.9% NS Group 2 (n=67): irrigation with 0.9% NS Group 3 (n=69): no irrigation	• SSI incidence • LOS (in days) • wound dehiscence	Groups 1 and 2 had significantly lower rates of incisional SSI than Group 3 (G1: n=3 (4.3%), G2: n=2 (2.9%), G3: n=12 (17.4%), P=0.005). Groups 1 and 2 had similar SSI rates (n=3 (4.3%) and n=2 (2.9%)). There was no significant difference in average LOS between the groups (G1: 1.1(SD 0.26), G2: 1.05(SD 0.24), G3 1.14 (SD 0.3), P=0.18). There was no significant difference in wound dehiscence between the groups (G1: n=0 (0%), G2: n=0 (0%), G3: n=2 (2.8%), P=0.22)
Fatula et al.[3] (2018) United States of America	open ventral hernia repair (OVHR)	cohort study Data from databases of: • Greenville Health System Hernia Center database (2008–2013) • Americas Hernia Society Quality Collaborative (AHSQC) (2013–2017)	822 patients who had OVHR with Mesh Age: • Group 1: 56.5 +/- 12.4 years • Group 2: 56.7 +/- 13.8 years • Group 3: 57.9 +/- 14.0 years	Age Body Mass Index (BMI) >25 DM Smokers	Group 1 (n=260): no antibiotic Irrigation Group 2 (n=263): irrigation with 240 mg gentamicin in 500 mL NS Group 3 (n=299): irrigation with 240 mg gentamicin and 600mg clindamycin in 500 mL NS	• SSI incidence • LOS (in days)	Group 3 had significantly lower SSI incidence than groups 1 and 2 (G1: n=43 (16.54%), G2: n=40 (15,21%), G3: n=16 (5.35%), P>0.001). There was no significant difference in average LOS between the groups (G1: 3 days, G2: 4 days, G3: 4 days, P<0.001).
Inojie et al.[4] (2023) Nigeria	neurosurgical spine surgery	RCT Memfys Hospital for Neurosurgery	80 patients who had non-instrumented surgery (Class 1 wounds) Age: 18 years and older	Age BMI >25 DM	Group 1 (n=40): irrigation with 80 mg of IV gentamicin in 1L NS Group 2 (n=40): irrigation with 1L 3.5% diluted PI	• SSI incidence • wound dehiscence	The overall SSI rate was significantly higher in Group 1 than Group 2 (n=7 (17.5%) compared to n=1 (2.5%), P=0.025). SSI was additionally divided into two categories: deep SSI and superficial SSI. The SSI rate was higher in Group 1 than Group 2 for both deep SSI (n= 2 (5%) and n=1 (2.5%)) and superficial SSI (n=5 (12.5%) and n=0 (0%)). Wound dehiscence was higher in Group 1 (n=6) than in Group 2 (n=1).

Authors (year) Country	Procedure	Study design Setting/context	Participant numbers and characteristics	Risk factors	Groups (sample size)	Outcomes measured	Description of main results
Maaty et al.[5] (2021) Egypt	elective caesarean section (C/S) – primary or repeated	RCT Ain Shams University Maternity Hospital	132 patients Age: 20–35 years BMI: 30-40 kg/m2 Single viable foetus, term pregnancy Hb level: >10 gm%	Obesity	Group 1 (n=66): irrigation with 200ml 0.9% saline Group 2 (n=66): irrigation with 1mg/kg gentamicin in 200ml 0.9% saline	• SSI incidence • LOS	Group 1 had higher SSI incidence than Group 2 but the difference was not statistically significant (n=3 (4.5%) compared to n=2 (3.0%), P=0.999). LOS was shorter in Group 2 than Group 1 but the difference was not statistically significant (1.3 +/- 0.5) compared to 1.4+/-0.7, P=0.302).
Wang et al.[6] (2021) China	Emergency neurosurgeries such as: • craniotomy • neuro-endoscopic procedures • Burr holes.	cohort study Emergency Centre operating theatre at Shenzhen People's Hospital	444 patients Age: >18 years Not allergic to gentamicin Not pregnant	Age DM	Group 1 (n=265): irrigation with 3L NS Group 2 (n=179): irrigation with 80mg/L gentamicin (240 mg gentamicin in 3L NS)	• SSI incidence	Group 1 had higher SSI incidence than Group 2 (n= 22 (8.3%) compared to n=2 (1.1%), P=0.001). The use of gentamicin irrigation reduced SSI incidence in Group 2 by 86.7% compared to the incidence in Group 1.
Yazdi et al.[7] (2019) Iran	arthroscopic anterior cruciate ligament (ACL) reconstruction – primary procedure	cohort study Orthopaedic department of Firoozgar Hospital	1464 patients requiring a simultaneous partial meniscectomy No pre-existing infections Mean age: • Group 1: 27.20 years • Group 2: 25.75 years	Age BMI >25	Group 1 (n=177): irrigation with 3L NS Group 2 (n=1287): irrigation with 80mg/L gentamicin (240 mg gentamicin in 3L NS)	• post-operative deep infections • post-operative septic arthritis (SA) • LOS	Group 1 had higher post-operative infection rates than Group 2 n=4 (2.2%) compared to n=3 (0.23%), P<0.05). LOS in Group 1 ranged from 8 to 14 days, and in Group 2 from 13 to 30 days.
Yazdi et al.[8] (2014) Iran	arthroscopic ACL reconstruction – primary procedure	RCT Firoozgar Hospital	351 patients requiring a simultaneous partial meniscectomy No skin lesions or pre-existing infection Mean age: • Group 1: 27.2 years • Group 2: 25.9 years	Age BMI >25	Group 1 (n=177): irrigation with 0.9% NS Group 2 (n=174): irrigation with 80mg/L gentamicin (240 mg gentamicin in 3L NS) Age and gender distributions were similar in the two groups.	• post-operative septic arthritis (SA) • LOS	Post-operative SA was higher in Group 1 than in Group 2 but the difference was not statistically significant (n=4 (2.2%) compared to n=1 (0.57%), P=0.4). The LOS in group 1 ranged from 8 to 14 days. The LOS of one patient who developed post-operative deep infection in group 2 was not specified.

References (Supplement 2)

1. Bayer J, Vackova Z, Svecova H, Stirand P, Spicak J, Martinek J. Gentamicin submucosal lavage during peroral endoscopic myotomy (POEM): A retrospective analysis [Internet]. Surg Endoscop. 2018[cited 2024 Jan 26];32(1):300–6. DOI: 10.1007/s00464-017-5677-8
2. Emile SH, Elfallal AH, Abdel-Razik MA, El-Said M, Elshobaky A. A randomized controlled trial on irrigation of open appendectomy wound with gentamicin- saline solution versus saline solution for prevention of surgical site infection {internet]. Int J Surg. 2020[cited 2024 Jan 26];81:140–6. DOI: 10.1016/j.ijsu.2020.07.057
3. Fatula LK, Nelson A, Abbad H, Ewing JA, Hancock BH, Cobb WS et al. Antibiotic irrigation of the surgical site decreases incidence of surgical site infection after open ventral hernia repair. The Am Surg. 2018;84(7):1146–51.
4. Inojie MO, Okwunodulu O, Ndubuisi CA, Campbell FC, Ohaegbulam SC. Prevention of surgical site infection following open spine surgery: The efficacy of intraoperative wound irrigation with normal saline containing gentamicin versus dilute povidone-iodine [Internet]. World Neurosurg. 2023[cited 2024 Jan 26];173(1):e1–e10. DOI: 10.1016/j.wneu.2022.12.134
5. Maaty AM, Yehia AA, Abdelaleem MM, El-Fattah MA. Subcutaneous antibiotic irrigation to prevent wound infection in obese patients undergoing cesarean section [Internet]. Women Health Care and Issues. 2021[cited 2024 Jan 26];4(3):1–5. DOI: 10.31579/2642-9756/060
6. Wang J, Yang Y, Lv W, Xu S, Mei S, Shi F et al. Gentamycin irrigation significantly reduces 28-day surgical site infection after emergency neurosurgery. [Internet] Br J Neurosurg. 2024[cited 2024 Jan 26];38(2):481–5. DOI: 10.1080/02688697.2021.1902472
7. Yazdi H, Gomrokchi AY, Nazarian A, Lechtig A, Hanna P, Ghorbanhoseini M. The effect of gentamycin in the irrigating solution to prevent joint infection after anterior cruciate ligament (ACL) reconstruction. Arch Bone Jt Surg. 2019;7(1):67–74.
8. Yazdi H, Moradi A, Herbort M. The effect of gentamicin in irrigating solutions on articular infection prophylaxis during arthroscopic ACL reconstruction [Internet]. Arch Orthop Trauma Surg. 2014[cited 2024 Jan 26];134(2):257–61. DOI: 10.1007/s00402-013-1910-7

Effectiveness of intra-operative gentamicin irrigation in reducing post-operative surgical site infections: A systematic review

Supplement 3: Database logic grids

Table 1: CINHAL

Gentamicin irrigation	Post-operative infections
(MH "Therapeutic Irrigation+" AND MH "Gentamicins+") OR TI ((Lavage* OR wash* OR wash out OR irrigat*) AND (Gentamicin* OR gentamycin*)) OR AB ((Lavage* OR wash* OR wash out OR irrigat*) AND (Gentamicin* OR gentamycin*))	MH "Surgical Wound Infection+" OR TI ("Surgical site infection*" OR "post-operative infection*" OR "postoperative infection*" OR "postoperative wound infection*" OR "post-operative wound infection*") OR AB ("Surgical site infection*" OR "post-operative infection*" OR "postoperative infection*" OR "postoperative wound infection*" OR "post-operative wound infection*")

Table 2: Scopus

Gentamicin irrigation	Surgical site infections
((Lavage* OR wash* OR wash out OR irrigat*) AND (Gentamicin* OR gentamycin*))	"Surgical site infection*" OR "post-operative infection*" OR "postoperative infection*" OR "postoperative wound infection*" OR "post-operative wound infection*"

Table 3: PubMed

Gentamicin irrigation	Surgical site infections
((Lavage*[tiab] OR wash*[tiab] OR wash out[tiab] OR irrigat*[tiab]) AND (Gentamicin*[tiab] OR gentamycin*[tiab])) OR ("Therapeutic Irrigation"[mh:noexp] AND "Gentamicins"[mh])	"Surgical Wound Infection"[mh] OR Surgical site infection*[tiab] OR post-operative infection*[tiab] OR postoperative infection*[tiab] OR postoperative wound infection*[tiab] OR post-operative wound infection*[tiab]

Table 4: Embase

Gentamicin irrigation	Surgical site infections
((Lavage* OR wash* OR wash out OR irrigat*) AND (Gentamicin* OR gentamycin*)).ti,ab OR ((lavage.sh OR stomach lavage.sh OR peritoneum lavage.sh) AND Gentamicin.sh)	Surgical infection.sh OR (Surgical site infection* OR post-operative infection* OR postoperative infection* OR postoperative wound infection* OR post-operative wound infection*).ti,ab

Table 5: Medline

Gentamicin irrigation	Surgical site infections
((Lavage*[tiab] OR wash*[tiab] OR wash out[tiab] OR irrigat*[tiab]) AND (Gentamicin*[tiab] OR gentamycin*[tiab])) OR ("Therapeutic Irrigation"[mh:noexp] AND "Gentamicins"[mh])	"Surgical Wound Infection"[mh] OR Surgical site infection*[tiab] OR post-operative infection*[tiab] OR postoperative infection*[tiab] OR postoperative wound infection*[tiab] OR post-operative wound infection*[tiab]