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Prevention of Surgical Site Infections: A Systematic Review

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ABSTRACT

Introduction: The preoperative interventions used for prevention of SSIs have different effectiveness in the reduction of SSIs and subsequent surgical complications. This review aiming at evaluating the effectiveness of various methods of prevention for SSIs.

Methods: The systematic search was conducted in Medline and Embase databases. This search identified 990 relevant studies using filters of human studies and 10 years since publishing. After exclusion of irrelevant, duplicated, and reviews the remaining is 55 potentially relevant studies.

Results: The vast majority of studies were done in intra-abdominal procedures which were infection rate varied from 0% to 38.4%. The rate of SSIs was higher than 25% in two studies used cephalexine as prophylaxis, mohs micrographic surgery and assessed SSIs in perforated peptic ulcer. Intra-operative warming used in only one study which reported SSIs rate of 18%. In case of using a combination of oxygen and antibiotics the SSIs rate ranged from 7.9% to 38.4%. The lowest rate of SSIs was noted when antiseptic, and amoxicillin were used together 0% and it was only 0.009% when cefazolin was used.

Conclusions: The wide difference in infection rates among included studies may be patient-related and procedure-dependent.

INTRODUCTION

Surgical site infection (SSI) is an infection that follows an invasive surgical procedure. The incidence of SSIs varies depending on the definition of infection, the duration of postoperative monitoring, the institution and the type of performed surgical procedure. Surgical site injuries are serious complications in operations that occur in approximately 2% of surgical operations and constitute about 20% of health-related injuries [(1)].

Surgical site infections are associated with increased morbidity, mortality, and increased hospitalization, prolonged hospitalization on an average of 4 to 7 days and twice the risk of fatal outcome, twice increased probability for ICU treatment, and five times greater chance of post-discharge hospitalization [(2)]. Furthermore, due to the prolongation of the illness and the hospitalization, patients with SSIs suffer emotionally and physically, which results in prolonged absence from their usual activities, social life and family disruptions due to the deterioration in their status and the insecurity related to their health-related problems [(3)].

Although rates vary widely according to type of procedure. SSI can have a devastating impact on the patient's course of treatment and is associated with increased treatment intensity, prolonged length of stay, and higher costs [(4)]. The complete eradication of SSIs is not practically possible, most of them are potentially preventable with the help of efficient strategic prevention approaches.

The methods of prevention of SSIs mainly depend on preoperative antibiotic prophylaxis, other methods include administration of supplemental oxygen preoperatively and application of normothermia during surgery [(5)].

Skin sterilization is performed prior to surgery using antiseptics to reduce the risk of SSIs by removing the soil and transient organisms from the skin where a surgical incision will be made and thus actually reduces wound infection after surgery. Preparation of preoperative skin with 0.5% chlorhexidine in methylactic spirits resulted in a lower risk of SSIs compared with alcohol-based povidone iodine solution [(6)].

The preoperative interventions used for prevention of SSIs have different effectiveness in the reduction of SSIs and subsequent surgical complications. This review aiming at evaluating the effectiveness of various methods of prevention for SSIs.

METHODS

The systematic search was conducted in Medline and Embase using search strategy of surgical wound or SSIs or surgical site, and infection or sepsis or contamination or abscess and prophylaxis or antibiotic or antimicrobial or antiseptic or oxygen or normothermia. This search identified 990 relevant studies using filters of human studies and 10 years since publishing. After exclusion of irrelevant, duplicated, and reviews the remaining is 55 potentially relevant studies. The protocol of

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the review was approved by the technical and ethical committee in Jazan University.

RESULTS

The search resulted in 55 potentially relevant studies that reported prospective randomized controlled data on the use of antibiotic prophylaxis in surgical wound infection. Seventeen papers were excluded, one study was excluded for language reason and 16 studies were excluded due to inconsistent finding with defined outcomes of this review. Finally, 38 studies were included in this review.

Antibiotics were used as prophylaxis of SSIs either orally or intravenously in 22 studies, while 5 studies used antiseptics as prophylaxis. Oxygen was used for prevention of SSIs either alone or in combination by 10 studies, while only one study used hyperthermia. Overall sample size was ranged from 35 in a study of **Lohsiriwat *et al***.[7] to 1697 in **Phillips *et al*.[8]** study. Overall SSIs rate ranged between 0% found by **Lohsiriwat *et al*.[7]** to 38.4% reported by **Schietroma *et al*.[9]** study.

The vast majority of interventions which had done in these studies were intra-abdominal procedures (14 studies), hernia (4 studies), cesarean section (3 studies), wounds (3 studies) and vascular surgery (3 studies). Other surgical interventions included prostatectomy (2 studies), spinal surgery (2 studies), neck surgery (2 studies), breast surgery (1 study), skin lesions (1 study), open fixation (1 study), mohs micrographic surgery (1 study) and cardiac surgery (1 study) as demonstrated in table 1.

Antibiotics were used in all intra-abdominal procedures, hernia and prostatectomy either orally or intravenously. Two studies in cesarean section and one study in vascular surgery were using oxygen either alone or with antibiotic. Some studies used a combination of oxygen and antibiotic like gastric bypass and appendectomy. Oxygen alone was used in open fixation and cesarean section.

Rate of SSIs ranged from 0% in **Lohsiriwat *et al*.[7]** to 25% reported by **Cherian *et al*.[9]** when antibiotic alone was used, while it ranged from 12% in a study conducted by Stall *et al*. to 25 % in **Gardella *et al*.[10]** where studies used oxygen alone as prophylactic intervention. In case of using a combination of oxygen and antibiotics the SSIs rate ranged from 7.9% found by **Wadhwa *et al*.[11]** to 38.4% reported by **Schietroma *et al*.[8]** The lowest rate of SSIs was noted when antiseptic, and amoxicillin were used together 0% and when cefazolin was 0.009% [7].

According to the type of surgery, rate of SSIs ranged between 1.2% in a study of **Bahar *et al*.[12]** to 7% found by **Mazaki *et al*.[13]** in herniotomy, while it varied from 8.2% reported by **Duggal *et al*.[14]** to 25% found in a study of **Gardella *et al*.[10]** in cesarean delivery. In traumatic wounds, rate of SSIs ranged between 1.2% to 10.8% in studies of **Bracho *et al*.[15]** and Srinivas *et al*. respectively, while it was between 6% reported by **Almeida *et al*.[16]** to 23% in vascular surgery.

Two included studies were done in prostatectomy their SSIs rate ranged between 6.1% in a study conducted by **Oshima *et al*.[17]** and 18% reported by **Abreu *et al*.[18]** The included studies of spine surgery, reported very low SSIs rate ranged from 0% found by **Tofuku *et al*.[19]** to 0.7% [20].

Neck surgery also was done in two included studies with SSIs rate varied from 0.009% in a study of **Uruno *et al*.[21]** to 12.9% found by **Otake *et al*.[22]** Only one included study of **Cherian *et al*.[9]** reported SSIs in each of the following interventions, Mohs micrographic surgery reported infection rate of 25.8%, breast surgery reported infection rate of 15.2% [23], excision of skin lesions reported infection rate of 12.5% [24], open fixation with infection rate of 12% [25], and cardiac surgery with infection rate of 4.9% [26].

The vast majority of studies were done in intra-abdominal procedures which the infection rate varied from 0% reported by **Lohsiriwat *et al*.[7]** to 38.4% in a study of **Schietroma *et al*.[8]** The rate of SSIs was higher than 25% in two studies used cephalexine as prophylaxis, mohs micrographic surgery conducted by **Cherian *et al*.[9]** and study assessed SSIs in perforated peptic ulcer which was done by **Schietroma *et al*.[12]** Intra-operative warming used in only one study which reported SSIs rate of 18% [27].

Table (1): Summary of the findings

Study citation	Study design	Sample size	Age of patients (mean or range)	Type of surgery	Mean duration of surgery	Preoperative prophylaxis	Other new interventions	Outcomes
Vaze *et al.* [28]	A randomized prospective study	251	1-8 years old	Inguinal herniotomy and orchiopexy	Non-Reported	Prophylactic pre-operative antibiotics (intravenous antibiotic at the onset, then 3-4 days of oral antibiotic)	–	Infection Rate=2.9%
Duggal *et al.* [14]	A prospective, randomized trial	831	29 years old	Cesarean deliveries	Greater than 1 hour in 25%	Prophylactic antibiotics, mainly cefazolin, 2 g intravenously.	oxygen	Infection rate = 8.2%
Sadahiro *et al.* [29]	A prospective randomized trial	310	20-80 years old	Colon cancer surgeries	131-147 min	single intravenous dose of an antibiotic	-	Infection rate= 6.1%- 18%
Paocharoen *et al.* [30]	A prospective, randomized trial	500	18-60 years old	Various types of surgeries	1 hour 43 min - 1 hour 45 min	Two forms of antiseptics, povidone iodine and chlorhexidine	–	Infection rate= 2.15%- 3.55
Abreu *et al.* [18]	A randomized trial	70	Non-reported	Prostatectomy	Non-reported	Antiseptic, 0.5% povidone iodine or chlorhexidine	–	Infection rate =18%
Oshima *et al.* [17]	A randomized, nonblinded, single-center clinical trial.	200	Mean age 41 years	Restorative proctocolectomy	233-243 min	Oral antibiotics, (500 mg) and intravenous antimicrobial prophylaxis	–	Infection rate= 6.1%- 22.4%
Ishibashi *et al.* [31]	A prospective, randomized study	283	25-92 years old with mean age of 67	Elective surgery for colon cancer	122.5-140 min	Oral antibiotics, kanamycin and erythromycin divided into three doses after mechanical cleansing	–	Infection rate= 5.1%- 6.5%
Mazaki *et al.* [13]	A prospective, randomized study	200	Age range (57-77)	Open mesh-plug hernia repair.	66.3- 65.2 min	The antibiotic prophylaxis group received 100 mL sterile saline with 1.0 g cefazolin	Placebo, 100ml sterile saline	Infection rate= 7%- 16%

Phillips *et al.* [20]	A prospective, randomized study	1697	Mean age 61-62 years	Spine fusion surgery	Non-reported	Antiseptic, mupirocin group chlorhexidine wipes (2% Chlorhexidine Gluconate)	Povidone-iodine group	Infection rate= 0.7%-1.6%
Mehrabi *et al.* [32]	A prospective randomized control study	395	Mean age 50.6-53.6 years old	Mesh herniorrhaphy	Non-reported	Oral cefazol. 50 mL sterile saline with 1 g intravenous cefazolin	–	Infection rate= 1.27%-2.03%
Williams *et al.* [23]	A randomized controlled trial	150	Older than 18 years of age	Breast surgery	Non-reported	a single intravenous dose of 1 g of Augmentin	–	Infection rate= 15.2%,
Tofuku *et al.* [19]	A prospective cohort study	384	Range of 7 to 89 years old and mean age 55.1 years	Spinal instrumentation	215.4-228.1 min	1,000 KIE/mL of bovine aprotinin	300 U/mL of human thrombin and 5.88 mg/mL of CaCl2	Infection rate= 0% - 5.8%
Lin *et al.* [33]	A prospective randomized study	234	Mean age 65 years old	Coronary artery bypass graft	4.4 hours	Patients received 1 g cefazolin within 1hour prior to surgery	–	Infection rate= 8.1% - 10.8%
Smith *et al.* [24]	A prospective double-blinded placebo-controlled trial	52	Range (59 – 78)	Excision of skin lesions from the lower limb	Non-reported	Two g dose of cephalexin	–	Infection rate= 12.5%
Cherian *et al.* [9]	A prospective randomized Controlled stud	693	Mean age of 65 years old	Mohs micrographic surgery	Non-reported	Oral cephalexin 2,000 mg	–	Infection rate= 25.8%
Sharma *et al.* [34]	A prospective randomized Controlled trial	100	Mean age 36-39 years old	Elective laparoscopic cholecystectomy	64-71 min	Ceftriaxone sodium (1 g dissolved in 10 mL of 0.9% saline)	10 mL of saline	Infection rate= 2%-4%
Uruno *et al.* [21]	A prospective Randomized trial	1082	52 years	Thyroid and parathyroid surgery	74- 76 min	Two g of piperacillin or 1 g of cefazolin	-	Infection rate= 0.009%-0.28%
El-Mahallawy *et al.* [35]	A prospective Randomized trial	200	Mean of 42 years old	Cancer surgery	3.24 -3.74 hours	Intravenous penicillin G sodium (4,000,000 IU) and gentamicin 80 mg	Intravenous clindamycin 600 mg and amikacin 500 mg intravenous	Infection rate= 9.5%

Srinivas *et al.* [36]	A prospective randomized trial	351	Range (18–70 years old)	Clean-contaminated upper abdominal surgeries	159 min	Antiseptic chlorhexidine-alcohol (0.5 % CHG in 70 % isopropyl alcohol)	Antiseptic 5% PVI solution three times	Infection rate= 10.8%-17.9%
Otake *et al.* [22]	A prospective Randomized trial	62	Mean of 32 years old	Tonsillectomy	Non-reported	A sustained-release AZM preparation as a single 2 g oral dose	–	Infection rate= 12.9%-25.8%
Pochhamme *et al.* [37]	A randomized, double-blinded three-arm trial	291	Mean of 65 years old	Laparoscopic colorectal resections	182 min	Intravenous ceftriaxone 2 g with metronidazole 500 mg iv	–	Infection rate= 8.2%-13.5%
Wadhwa *et al.* [11]	A prospective Randomized trial	400	Mean of 44 years old	gastric bypass surgery	2.6- 2.7 hours	2 to 3 mg midazolam	10 L/min of oxygen	Infection rate= 7.9%_ 9.09%
Tijerina *et al.* [38]	A randomized, double-blind clinical trial	529	Range (5 -65 years old)	Appendectomy	Non-reported	Antibiotic application followed by either topical ionized solution (IS) or topical saline solution	Oxygenation was conducted at 3 l/min for 1 h pre-surgery and for 2 h post-surgery	Infection rate= 26.06%
Bracho-Blanchet *et al.* [15]	A controlled, blinded, randomized clinical trial	187	18 years or less	Clean or clean-contaminated surgery	109-150 min	Cefalotin or clindamycin and amikacin administered 2 h before surgery	The same medications IV in clean or clean-contaminated surgery but immediately before, during or after surgery and for 5 days postoperatively	Infection rate= 1.2%-10.8%
Kubota *et al.* [39]	A controlled, randomized clinical trial	44 children	Range (3-14 years old)	Appendectomy	Non-reported	Cefmetazole, 100 mg/kg/ day,		Infection rate = 0% - 20%
Williams *et al.* [40]	A randomized, controlled trial	179 women	Mean of 24 years old	Cesarean delivery	51 – 52 min	A single dose of antibiotics consisting of cefazolin 2 grams administered intravenously	Administration of FIO2 per assignment continued throughout the entire cesarean delivery	Infection rate= 13% -14.5%

Ruangsin *et al.* [41]	A randomized double-blind controlled trial	299	Mean of 54 years	Cholecystectomy	Non-reported	Cefazolin	isotonic sodium chloride	Infection rate= 1.67%-2.34%
Stall *et al.* [25]	A randomized controlled pilot trial	235 injuries	More than 18 years	Open fixation	Non-reported	Perioperative supplemental oxygen	Administration of 80% or 30% concentration of FIO2 during surgery and for 2 hours postoperatively	Infection rate= 12%
Turtiainen *et al.* [16]	A randomized controlled trial	274	Mean age of 72-73 years	Non-emergency lower limb arterial surgery	146- 152 min	Antibiotic prophylaxis was standardized to 3 g of cefuroxime being administered intravenously within 1 h before the incision	Venture masks were used to deliver 30% oxygen 5 l/min was used	Infection rate= 23%
Praveen and Rohaizak [42]	A prospective single blinded randomized clinical trial	202	Range (20-80 years old)	Inguinal hernioplasty	82 min	Either IV 240 mg gentamicin diluted into 10 mL saline, given during induction, or 160 mg gentamicin used as local antibiotic	-	Infection rate= 6.9%
Mingmalairak *et al.* [43]	A double blinded randomized controlled trial	100	Range (15-60 years-old)	Appendectomy	Non-reported	Prophylactic antibiotic, gentamicin 240 mg and metronidazole 500 mg,	-	Infection rate= 8%-10%
Lohsiriwat *et al.* [7]	A prospective opened non-comparative clinical trial	35	Mean of 37 (range, 18-72) years.	Elective intra-abdominal procedures	Non-reported	Prophylactic amoxycillin/clavulanate (Cavumox®) at a dose of 1.2 gram was given intravenously	-	Infection rate= 0%
Schietroma *et al.* [44]	A double blinded randomized controlled trial	239	Range (30-82 years old)	Perforated peptic ulcer	Non-reported	Intravenous fluid infusion, intravenous antibiotics in the hour prior to the start of surgery (cefotaxime every 8 h and tobramycin every 12 h: Dosage was adjusted for patient weight	Oxygen (FiO2 of either 30% or 80%	Infection rate= 38.4%

Schimmer *et al.* [26]	A randomized controlled trial	996	Mean of 67 years old	Cardiac surgery	243 min	cefuroxime	–	Infection rate= 4.9%-8.3%
Schietroma *et al.* [8]	A prospective, randomized, double blind, controlled, monocentric Trial	85	Range (71-86) years old	Acute Sigmoid Diverticulitis	195-200 min	Perioperative oxygen	80% FiO2 during and 6 hours	Infection rate= 24.7%
Whitney *et al.* [27]	A single-blinded randomized controlled trial	146	Mean age 48 years old	Open bariatric, colon, or gynecologic-oncologic related operations	Non-reported	Local warming	Intra-operative warming	Infection rate= 18%;
Gardella *et al.* **(10)**	A double blind randomized controlled trial	143	Range (16 – 47 years old)	Cesarean delivery	48 – 52 min	High-concentration supplemental perioperative Oxygen	80% oxygen	Infection rate=25%

DISCUSSION

Prophylactic administration of antibiotics can decrease post-operative morbidity, shorten hospitalization and reduce the overall costs attributable to infections [28], therefore it should be safe, cost-effective, and effective against common pathogens based on procedure type. But use of antibiotics is not free from antecedent ill adverse-effects. It increases the risk of allergic reactions, drug interactions, bacterial resistance and thrombophlebitis. Many included studies reported that there is no need of antibiotic prophylaxis in clean surgical cases [15,30,36].

Many of the included studies are carried out in developed countries and hence experience cannot be directly applied to scenario in developing countries where the operation theatre environment, post-operative wound care, patient literacy, nutrition, social hygiene, widely differ. Cefazolin was used in many included studies [13, 14, 33, 40, 41, 45], which used antibiotic alone or in combination because of its bactericidal activity against the pathogenic organisms in skin wound infection. Preoperative skin preparation is one of the important local factors concerning the development of surgical site infection. The lowest infection rate 0.0% was noted when antiseptic in combination with amoxicillin was used. The SSI rate was 0.009% in a study used cefazolin as a prophylactic of SSIs [45]. The development of surgical site infections is related to three factors, the degree of bacterial contamination during the operation, the duration of procedure, and underlying diseases of the patients such as immune deficiency, diabetes, and malnutrition.

Overuse of antibiotics results not only in the emergence of resistant organisms but also causes great economic burden on the health system [1]. Prolonged duration of surgery was reported in many studies [11, 17, 19, 26, 33, 35, 37]. Extended duration of surgery has been identified as an independent risk factor for SSI, and may serve as a marker for the complexity of the individual case, some aspect of surgical technique, prolonged exposure to microorganisms in the operating environment, and diminished efficacy of antimicrobial prophylaxis.

The type of bacteria usually involved in the infection is different according to surgical site, Staphylococcus and gram-negative bacteria are the main cause of SSI in vascular surgery, and because of that antibiotic shall be active against these germs [16].

CONCLUSION

The vast majority of studies were done in intra-abdominal procedures and studies used cephalexine as prophylaxis, mohs micrographic, intra-operative warming characterized by high rate on SSIs. In case of using a combination of oxygen and antibiotics the SSIs rate was widely variable. The lowest rate of SSIs was noted when antiseptic, and amoxicillin or cefazoline. The wide difference in infection rates among included studies may be patient-related and procedure-dependent.

CONFLICT OF INTERESTS

The authors stated no financial sponsoring was received and no conflicts of interests.

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