European Journal of Obstetrics & Gynecology and Reproductive Biology 244 (2020) 45–50

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Povidone-iodine vs chlorhexidine alcohol for skin preparation in malignant and premalignant gynaecologic diseases: A randomized controlled study

Sener Gezer*, Hayriye M. Yalvaç, Kübra Güngör, İzzet Yücesoy

Kocaeli University School of Medicine, Kocaeli, Turkey

ARTICLE INFO

Article history:
Received 11 June 2019
Received in revised form 17 October 2019
Accepted 18 October 2019

Keywords:
Chlorhexidine
Iodine
Gynaecologic cancer surgery
Surgical site infection

ABSTRACT

Objectives: To compare povidone-iodine with chlorhexidine alcohol solutions for the prevention of surgical site infection (SSI) in malignant and premalignant gynaecologic diseases, and to evaluate the effects of temperature on SSI at 25 °C and 37 °C.

Study design: This was a randomized controlled trial of a cohort of 220 patients undergoing surgery for malignant or premalignant conditions. Preoperative skin preparations were performed with 10% povidone-iodine at 25 °C (PI), 10% povidone-iodine at 37 °C (warm PI), 4% chlorhexidine gluconate with alcohol at 25 °C (CH) and 4% chlorhexidine gluconate with alcohol at 37 °C (warm CH) for each group. All women included in the study received 1 g intravenous cefazolin antibioprophylaxis 30 min before skin incision. The primary outcome was SSI within 30 days of surgery, and secondary outcomes were identification of the causative organism and clinical factors that may be associated with SSI.

Results: SSIs were detected in 24 (10.9%) patients. Except for two organ/space-specific SSIs, all were superficial SSIs. The frequency of SSI was significantly lower in the warm PI group than in the PI group ($p = 0.032$). There were no significant differences in the frequency of SSI between the groups in other binary comparisons. In addition, there was no significant difference between both povidone-iodine groups compared with both chlorhexidine alcohol groups in terms of the development of SSI (10.9% vs 11%, $p = 1.00$). SSI caused by micro-organisms was found in 18 patients, and *Enterococcus faecalis* was the most common reproducing organism in wound culture. Patients with SSI were significantly older (58.9 ± 11.4 vs 52.8 ± 12.3 years) and more likely to be readmitted to hospital [15 (62.5%) vs 9 (37.5%)] than patients without SSI.

Conclusions: SSI rates can be reduced by warming povidone-iodine, but this effect could not be demonstrated with chlorhexidine solutions. When both groups of povidone-iodine were compared with both groups of chlorhexidine alcohol, no significant difference was found in the prevention of SSI in malignant and premalignant gynaecologic operations.

© 2019 Elsevier B.V. All rights reserved.

Introduction

Surgical site infections (SSIs) are the most common infections found among hospitalized patients after surgical treatment [1], and lead to increased hospital stay, hospitalization costs, and overall morbidity and mortality [2]. Despite various prevention strategies, SSIs are associated with longer hospital and intensive care unit stays, increased readmission to hospital after discharge, and a two-fold increase in mortality [3–6]. Among all gynaecologic procedures, SSI is the leading cause of postoperative morbidity in the 30 days following surgery [7].

After all hysterectomy procedures, the overall rate of SSI was reported as 4.2% [8]. The SSI rate has been estimated to be between 6% and 15% after gynaecologic cancer surgery [9–11]; however, a few studies have reported rates of up to 34% [12]. The reasons for high SSI rates include advanced age of patients, accompanying systemic diseases, and complicated and prolonged surgery. In a similar study, the SSI rate was reported to be 10.8% after epithelial ovarian cancer. In this study, the occurrence of superficial or organ/space SSI was found to be independently associated with worse overall survival (OS), but not with disease-free survival (DFS). The time interval from surgery to adjuvant chemotherapy was significantly shorter in women without SSI than in women with SSI

* Corresponding author.
E-mail addresses: dr.senergezer@gmail.com, dr.gezer@mynet.com (S. Gezer).

https://doi.org/10.1016/j.ejogrb.2019.10.035
0301-2115/© 2019 Elsevier B.V. All rights reserved.

(median 31 vs 44 days) [13]. Late onset of chemotherapy after primary surgery worsens DFS and OS in patients with epithelial ovarian cancer [14,15].

The use of antiseptic agents for preoperative skin preparation is important to reduce the risk of postoperative SSI. The two most frequently used antiseptic agents for this purpose are povidone-iodine and chlorhexidine gluconate. Although chlorhexidine gluconate is generally similar to povidone-iodine regarding antimicrobial activity, it is considered to be superior in terms of long-term activity [16], as it is not inactivated by blood and serum proteins [17]. Povidone-iodine has been found to be as effective at 32 °C as at 25 °C [18], and can also be stored at 32 °C without any loss of available iodine for up to 6 months [19].

Providing normothermia during surgery may reduce the development of SSI [20]. In this study, different skin preparation groups (10% povidone-iodine and 4% chlorhexidine gluconate with alcohol) were divided into cold (25 °C) and warm (37 °C) groups, and the effects of temperature on the development of SSI were evaluated in gynaecologic malignant and premalignant diseases.

Materials and methods

Following approval by the institutional review board and ethics committee (Protocol No. KIA 2017/283), women were included in this prospective randomized clinical study at Kocaeli University Hospital between June 2017 and January 2019. Written informed consent was obtained from all women enrolled in this study.

Women who underwent surgery for malignant or premalignant conditions of the uterus, cervix or ovary, or peritoneal carcinomatosis were allocated at random to one of four groups: 10% povidone-iodine at 25 °C (PI), 10% povidone-iodine at 37 °C (warm PI), 4% chlorhexidine gluconate with alcohol at 25 °C (CH) and 4% chlorhexidine gluconate with alcohol at 37 °C (warm CH). A blocked random assignment was used for the allocation sequence. Randomization allocation was performed using opaque, sequentially numbered envelopes. A numbered envelope was opened when a patient entered the operating room, and the participants were blinded to their group assignment.

Skin preparations were performed using Poviderm 1000 mL solution (Necm Chemistry, İstanbul, Turkey) in the povidone-iodine groups, and Habitanol 1000 mL solution (Kimpa Drugs, İstanbul, Turkey) in the chlorhexidine groups. Povidone-iodine and chlorhexidine gluconate were heated to 37 °C using a gel warmer (KGW-1 Keewell Medical Technology, Foshen, China) in the warm groups. It was not possible to blind the surgeons because the two antiseptic agents have different colours. A gynaecologic oncology fellow or upper-level gynaecology resident was involved in all cases. All women included in the study received 1 g intravenous cefazolin antibioprophylaxis 30 min before skin incision. All procedures were performed via laparotomy. In vertical incisions, the fascia was closed using a #1 loop polydioxanone suture, closure of Camper's fascia was performed using a 3-0 plain catgut suture if thicker than 2 cm, and skin closure was performed with staples. In Pfannenstiel incisions, the fascia was closed using #1 polyglactin, Camper's fascia was closed with 3-0 plain catgut suture if thicker than 2 cm, and the skin was closed with #2-0 Prolene.

Women were included in the study if they underwent surgery for malignant or premalignant conditions of the uterus, cervix or ovary, or peritoneal carcinomatosis. Patients were excluded if they were unable to give informed consent; had a known allergy to the disinfectants; were currently using antimicrobials, immunosuppressant drugs or insulin for uncontrolled diabetes; or had an open wound. The subject selection process is shown in Fig. 1.

The primary outcome of this study was SSI within 30 days of surgery, as defined by the Centers for Disease Control and Prevention [21]. Secondary outcomes were identification of the causative organism, and investigation of clinical factors such as body mass index (BMI), operation time, days of hospitalization, etc. that may be associated with SSI. All patients were followed up for SSI until discharge from hospital and at the outpatient visits. SSI surveillance data forms were used for the collection of primary and secondary outcome data. SSI rates and distribution of identified micro-organisms for each group were measured.

The sample size calculation was based on a study by Uppal et al. [22]. It was calculated that, with a power of 0.80 and an alpha level of 0.05, 197 participants would be needed to detect a statistically significant difference. The fact that the study would be performed with four groups was taken into consideration when calculating the power. In order to compensate for possible dropouts, 220 women were included in the study.

Data were analysed using SPSS Version 20.0 (IBM Corp., Armonk, NY, USA). The normality of distribution was evaluated

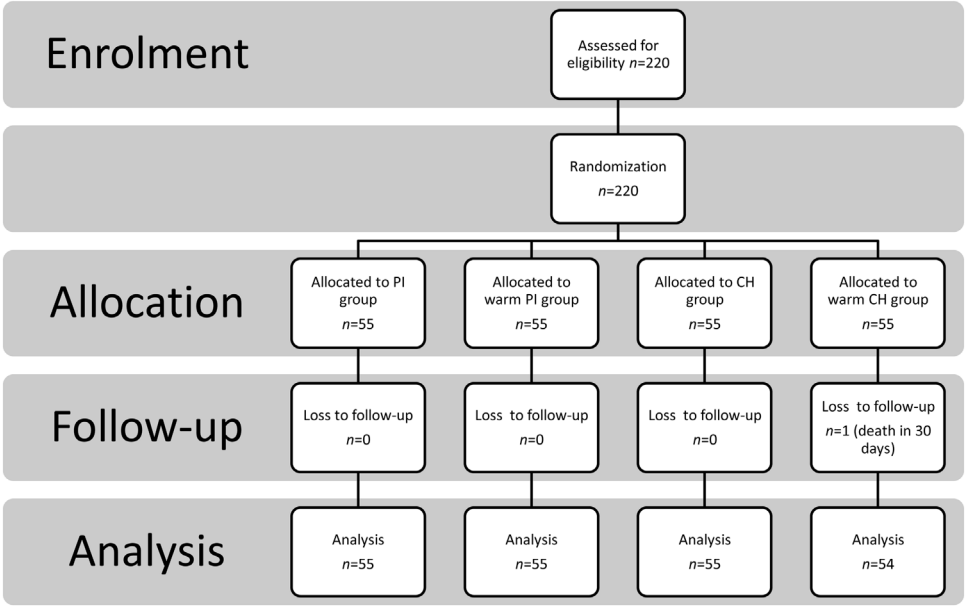


Fig. 1. Consort diagram for the trial.

using the Kolmogorov–Smirnov test. Numerical variables with a normal distribution are presented as mean [± standard deviation (SD)], numerical variables that were not normally distributed are presented as median (25th percentile–75th percentile), and categorical variables are presented as frequency. The independent samples *t*-test, one-way analysis of variance and Tukey's post-hoc test were used for comparison of normally distributed variables between the groups. The Mann–Whitney *U*-test, Kruskal–Wallis test and Dunn's post-hoc test were used for comparison of non-normally distributed variables. Finally, Fisher's exact test, Monte Carlo Chi-squared test and Yates's correction were used for categorical data. $p<0.05$ was considered to indicate statistical significance.

Results

In total, 220 patients were included in the study, but one patient from the warm CH group was excluded from the analysis due to death by heart attack within 30 days of surgery. Apart from this patient, there was no loss to follow-up, and this may have been due to outpatient visits performed once per week during the post-operative period. There were no significant differences between the groups with regards to demographic and clinical characteristics (Table 1).

Infraumbilical vertical incisions were performed more often than supraumbilical incisions or Pfannenstiel incisions. No significant differences were found between the groups for any other categorical variables (Table 2).

SSIs were detected in 24 (10.9%) patients as the primary outcome. SSI distributions were as follows: 10 patients (18.2%) from PI group, two patients (2.6%) from warm PI group, seven patients (12.7%) from CH group, and five patients (9.3%) from warm CH group. Except for two organ/space-specific SSIs (one patient from the PI group and the other from the CH group), all were superficial SSIs. The frequency of SSI was significantly lower in the warm PI group than in the PI group ($p = 0.032$). There were no significant differences in the frequency of SSI between the groups in other binary comparisons (Table 3). In addition, there was no significant difference between both povidone-iodine groups compared with both chlorhexidine alcohol groups in terms of the development of SSI (10.9% vs 11%, $p = 1.00$). Among the 24 patients with SSI, causative organisms were found in 18 patients (Table 4). *Enterococcus faecalis* was the most common reproducing organism in wound cultures (3/18). *Acinetobacter baumannii* was only detected in one patient in blood culture.

When the relationship between SSI and other factors was examined, the age of patients was significantly higher among those with SSI (58.9 ± 11.4 years) than in those without SSI (52.8 ± 12.3 years) ($p = 0.016$). Also, the rate of hospital readmission was significantly higher in patients with SSI (15 (62.5%) vs 9 (37.5%)] ($p = 0.001$). Other variables such as BMI, surgical time, packed red cell transfusions, incision type and intestinal surgery were not associated with the development of SSI.

Discussion

Reducing the SSI rate improves the quality of patient care and reduces the cost of healthcare services. Many studies have compared povidone-iodine with chlorhexidine solutions for the prevention of SSI, but they involve patients undergoing different types of surgery. In a meta-analysis of 19 randomized controlled trials, the authors found a reduction in bacterial skin colonization [risk ratio (RR) 0.45, 95% confidence interval (CI) 0.36–0.55] and incidence of SSI (RR 0.70, 95% CI 0.52–0.92) with chlorhexidine [23]. Similar results showing a decrease in SSI with chlorhexidine were obtained in two reviews [24,25]. Only one study found lower SSI rates using 0.5% chlorhexidine methylated spirits in a Cochrane meta-analysis, which was evaluated in 13 randomized controlled studies [26]. A limitation of this meta-analysis is that it only evaluated studies with clean surgery. In a review of six studies with 2484 patients who underwent clean and clean-contaminated surgery, a significantly lower overall rate of SSI was found with chlorhexidine than povidone-iodine (6.8% vs 11.0%) [27]. Chlorhexidine was superior for the prevention of SSI, with a pooled RR of 0.62 (95% CI 0.48–0.81). In contrast, one prospective study reported increased SSI rates with chlorhexidine alcohol [28].

In a retrospective study of patients undergoing abdominal hysterectomy, the authors calculated 44% lower odds for SSI [adjusted odds ratio (OR) 0.56, 95% CI 0.37–0.85, $p = 0.01$] with chlorhexidine alcohol compared with povidone-iodine [22]. The superiority of chlorhexidine to povidone-iodine has also been shown among patients undergoing elective gynaecologic laparotomies [29].

Patients with gynaecologic malignancies are more likely to develop SSI due to their older age, increased BMI and accompanying comorbidities. The SSI rates found in the present study were similar to those from other studies in the field of gynaecologic oncology [9–11,13]. On the other hand, SSI may have a negative effect on survival by delaying the initiation of adjuvant therapy in these patients. Efforts to lower SSI rates will also improve survival

Table 1
Demographic and clinical characteristics of patients by group.

	Group				*p*
	PI (25 °C) n = 55	Warm PI (37 °C) n = 55	CH (25 °C) n = 55	Warm CH (37 °C) n = 54	
Age (years)[a]	54.4 (12.4)	51.6 (11.6)	51.9 (12.3)	54.6 (13.1)	0.420
Weight (kg)[b]	73 (65–85)	72 (63–89)	70 (65–79)	69 (63–78)	0.482
Height (cm)[b]	162 (157–166)	162 (155–165)	163 (158–167)	162 (159–163)	0.622
Body mass index (kg/m^2)[b]	27.6 (24.9–33.9)	29.1 (23.4–34.2)	26.6 (24.3–30.8)	26 (24.6–30.1)	0.559
Gravidy (*n*)[b]	3 (2–4)	3 (2–5)	3 (1–4)	3 (2–5)	0.196
Parity (*n*)[b]	3 (2–4)	2 (1–3)	2 (1–3)	3 (2–4)	0.117
Abortus (*n*)[b]	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0.279
ASA score[b]	2 (1–2)	2 (1–2)	2 (2–2)	2 (1–2)	0.490
Operation time (min)[b]	125 (93–153)	118 (88–132)	102 (86–148)	120 (97–168)	0.229
Intensive care stay (days)[b]	0	0	0	0	0.076
Hospitalization (days)[b]	4 (4–7)	4 (3–6)	5 (4–7)	5 (4–7)	0.321
Preoperative haemoglobin (gr/dl)[a]	11.9 (1.7)	11.8 (1.2)	12.1 (1.5)	12.3 (1.5)	0.252
Postoperative haemoglobin (gr/dl)[a]	11.3 (1.5)	11.0 (1.3)	11.2 (1.5)	11.5 (1.7)	0.316
Packed red cell transfusion[b]	0	0	0	0	0.907

ASA, American Society of Anesthesiologists; PI, povidone-iodine; CH, chlorhexidine gluconate.
[a] Mean (standard deviation).
[b] Median (25th percentile–75th percentile).

Table 2
Distribution of categorical variables by group.

		Group				Total	p
		n (%)					
		PI (25 °C) n = 55	Warm PI (37 °C) n = 55	CH (25 °C) n = 55	Warm CH (37 °C) n = 54	219	
Incision	Pfannenstiel	16 (29.1)	29 (52.7)	10 (18.2)	5 (9.3)	60 (27.4)	0.008
	Supraumblical vertical	12 (21.8)	8 (14.5)	20 (36.4)	20 (37.0)	60 (27.4)	
	Infraumblical vertical	27 (49.1)	18 (32.7)	25 (45.5)	29 (53.7)	99 (45.2)	
Indication	Endometrial cancer	25 (45.5)	31 (56.4)	17 (30.9)	24 (44.4)	97 (44.2)	
	Cervical cancer	0	3 (5.5)	2 (3.6)	4 (7.4)	9 (4.1)	
	Ovarian cancer	9 (16.4)	7 (12.7)	14 (25.5)	9 (16.6)	39 (17.8)	
	Peritoneal carcinomatosis	2 (3.6)	0	2 (3.6)	1 (1.9)	5 (2.3)	
	Sarcoma of the uterus	0	1 (1.8)	1 (1.8)	1 (1.9)	3 (1.4)	
	Ovarian borderline tumour	2 (3.6)	1 (1.8)	3 (5.5)	3 (5.6)	9 (4.1)	
	Endometrial intra-epithelial neoplasia	12 (21.8)	3 (5.5)	6 (10.9)	2 (3.7)	23 (10.5)	
	Benign tumours of ovary	5 (9.1)	8 (14.5)	9 (16.4)	9 (16.6)	31 (14.2)	
	Cervical dysplasia	0	1 (1.8)	1 (1.8)	1 (1.9)	3 (1.4)	
Medical history	None	29 (52.7)	30 (54.5)	18 (32.7)	23 (42.6)	100 (45.6)	
	Hypertension	11 (20.0)	14 (25.5)	9 (16.4)	12 (22.2)	46 (21.0)	
	Diabetes	3 (5.5)	4 (7.3)	6 (10.9)	3 (5.6)	16 (7.3)	
	Hypertension + diabetes	9 (16.4)	4 (7.3)	6 (10.9)	3 (5.6)	22 (10.0)	
	Thyroid disease	1 (1.8)	1 (1.8)	7 (12.7)	2 (3.7)	11 (5.0)	
	Rheumatic disease	0	0	0	1 (1.8)	1 (0.5)	
	Cardiac disease	1 (1.8)	1 (1.8)	1 (1.8)	3 (5.6)	6 (2.7)	
	Deep venous thromboembolism	0	1 (1.8)	2 (3.6)	1 (1.8)	4 (1.8)	
	Asthma	0	0	6 (10.9)	3 (5.6)	9 (4.1)	
	Cancer (other)	1 (1.8)	0	0	1 (1.8)	2 (1.0)	
	Renal disease	0	0	0	2 (3.7)	2 (1.0)	
Operation history	None	28 (50.9)	34 (61.8)	23 (41.8)	29 (53.7)	114 (52.1)	
	Pfannenstiel incision	15 (27.3)	15 (27.3)	17 (30.9)	11 (20.3)	58 (26.4)	
	Vertical incision	4 (7.3)	1 (1.8)	2 (3.6)	1 (1.9)	8 (3.7)	
	Appendectomy	4 (7.3)	1 (1.8)	6 (10.9)	4 (7.4)	15 (6.8)	
	Laparoscopy	1 (1.8)	0	3 (5.5)	1 (1.9)	5 (2.3)	
	Vaginal	1 (1.8)	1 (1.8)	2 (3.6)	0	4 (1.8)	
	Nephrectomy	1 (1.8)	0	0	0	1 (0.5)	
	Cholecystectomy	1 (1.8)	3 (5.5)	2 (3.6)	8 (14.8)	14 (6.4)	
Intestinal surgery	No	52 (94.5)	52 (94.5)	50 (90.9)	54 (100)	208 (94.9)	
	Yes	3 (5.5)	3 (5.5)	5 (9.1)	0	11 (5.1)	
Re-admission to hospital	No	46 (83.6)	50 (90.9)	50 (90.9)	49 (90.7)	195 (89.0)	
	Yes	9 (16.4)	5 (9.1)	5 (9.1)	5 (9.3)	24 (11.0)	
Postoperative complication	None	48 (87.3)	51 (92.7)	42 (76.4)	46 (85.1)	187 (85.3)	
	Evisceration	1 (1.8)	0	1 (1.8)	0	2 (0.9)	
	Wound dehiscence	1 (1.8)	0	4 (7.3)	0	5 (2.2)	
	Lymphocele	1 (1.8)	2 (3.6)	1 (1.8)	2 (3.7)	6 (2.7)	
	Ileus	3 (5.5)	1 (1.8)	5 (9.1)	3 (5.5)	12 (5.5)	
	Pneumonia	0	0	0	1 (1.9)	1 (0.5)	
	Deep venous thromboembolism	0	0	1 (1.8)	0	1 (0.5)	
	Pancreatitis	0	1 (1.8)	0	0	1 (0.5)	
	Pelvic abscess	0	0	1 (1.8)	0	1 (0.5)	
	Atalectasis	0	0	0	1 (1.9)	1 (0.5)	
	Haematoma	1 (1.8)	0	0	1 (1.9)	2 (0.9)	
Intraoperati-ve complication	None	53 (96.4)	55 (100.0)	53 (96.4)	53 (98.1)	214 (97.7)	
	Urinary tract	0	0	0	1 (1.9)	1 (0.5)	
	Gastrointestinal	0	0	1 (1.8)	0	1 (0.5)	
	Vascular	2 (3.6)	0	1 (1.8)	0	3 (1.3)	

PI, povidone-iodine; CH, chlorhexidine gluconate.

and quality of life in these patients. With perioperative bundles containing a preoperative shower with 4% chlorhexidine gluconate and intraoperative use of 2% chlorhexidine gluconate and 70% isopropyl alcohol solution, the overall SSI rate declined from 6.0% to 1.1% in patients with gynaecologic cancer [30]. The most common decrease in SSI was observed in patients who did not undergo intestinal surgery. SSI rates were reduced from 20% to 3% (OR 0.13, 95% CI 0.037–0.53, $p = 0.001$) in patients with ovarian cancer with five-point SSI prevention bundles [31]. SSI reduction was greatest in patients who underwent colon resection, from 33% to 7% (OR 0.14, 95% CI 0.037–0.53, $p = 0.001$). In a study of patients with gynaecologic cancer undergoing colon surgery, the incidence of SSI was reduced from 37% to 12% with bundles using 4% chlorhexidine antibacterial solution [32]. In the present study, there was no significant difference between povidone-iodine and chlorhexidine solutions in general. When different solutions were compared at different temperatures, SSI rates were reduced by warming povidone-iodine. However, this effect could not be obtained by warming chlorhexidine.

Hypothermia reduces tissue oxygenation by causing vasoconstriction [33]. Impaired oxygenation delays wound healing and

Table 3
Surgical site infection correlations between groups.

	PI (25 °C) n = 10 (18.2%)	Warm PI (37 °C) n = 2 (2.6%)	CH (25 °C) n = 7 (12.7%)
Warm PI (37 °C) n = 2 (2.6%)	$p = 0.032$		
CH (25 °C) n = 7 (12.7%)	$p = 0.598$	$p = 0.161$	
Warm CH (37 °C) n = 5 (9.3%)	$p = 0.266$	$p = 0.438$	$p = 0.760$

PI, povidone-iodine; CH, chlorhexidine gluconate.

Table 4
Distribution of identified micro-organisms by group.

Identified micro-organism	Group				Total
	PI (25 °C) n = 55	Warm PI (37 °C) n = 55	CH (25 °C) n = 55	Warm CH (37 °C) n = 54	219
Enterococcus faecalis	1	NI	2	NI	3
Staphylococcus epidermidis	1	NI	1	NI	2
Staphylococcus lugdunensis	2	NI	NI	NI	2
Escherichia coli	NI	1	NI	1	2
Klebsiella pneumoniae	NI	1	NI	1	2
Dyphteroid bacilli	NI	NI	1	1	2
Acinetobacter baumannii	1	NI	NI	NI	1
Staphylococcus hominis	1	NI	NI	NI	1
Staphylococcus aureus	1	NI	NI	NI	1
Pseudomonas aeruginosa	NI	NI	1	NI	1
Morganelli morganii	1	NI	NI	NI	1

NI, not identified.

creates a suitable microenvironment for the development of infection. Pre- and perioperative warming can help to prevent these complications [34,35]. In addition, pre-anesthetic skin warming will help to reduce the initial postinduction hypothermia and could prevent intraoperative hypothermia and postoperative shivering [36]. Wistrand et al. compared preheated (36 °C) and room temperature (20 °C) chlorhexidine solutions on patients with pacemaker device implantation but did not find any difference in bacterial colonization or SSI rates [37]. The same authors investigated heat loss, bacterial growth and patient experiences with warm and cold chlorhexidine alcohol, and reported heat loss of 1.4 °C and 2.5 °C from baseline skin temperature, respectively. The experience of unpleasantness was reduced after disinfection at 38 °C without a difference in bacterial growth [38].

In the present study, no factors were associated with SSI except older age. Peripheral vascular disease, which reduces tissue blood flow, is a risk factor for the development of SSI [39]. In a study containing 1369 patients with endometrial cancer, predictors of superficial incisional SSI were smoking, obesity, intraoperative transfusion, laparotomy and American Society of Anesthesiologists score >2. In addition, older age, greater estimated blood loss, prior infection with meticillin-resistant *Staphylococcus aureus*, and lymphadenectomy or bowel resection were defined as predictors for organ/space SSI [40]. Increased BMI [41,42] and subcutaneous fat thickness [43] have been identified as risk factors for SSI in other studies. Similarly, with BMI, the percentage of body fat can predict SSI [44]. Mahdi et al. found that surgical complexity was an independent risk factor for SSI [11].

A strength of this study is its randomized controlled design, comparing povidone-iodine with chlorhexidine alcohol in patients with gynaecologic cancer. There are insufficient comparative studies in gynaecologic oncology. Available studies are SSI prevention bundle studies comparing a historical cohort with a postintervention cohort. To the authors' knowledge, this is the first study to compare different antiseptic solutions at different temperatures in gynaecologic oncologic patients. The limitations of this study include its single-centre design, and the inclusion of both premalignant and malignant patients may have affected the study population. This may have caused selection bias because premalignant patients were younger and this was the only factor found to be relevant to SSI in this study.

Conclusions

SSI remains a major factor contributing to perioperative morbidity and mortality, and high costs of care for surgical patients. This study showed that SSI rates can be reduced by warming povidone-iodine, but this effect could not be demonstrated with chlorhexidine solutions. There is a clear need for further studies comparing povidone-iodine with chlorhexidine alcohol at different temperatures for skin preparation in patients with gynaecologic cancer.

Declaration of Competing Interest

None declared.

Funding

None.

Acknowledgements

The authors wish to thank Barış Yıldırım for his contribution.

References

[1] Bratzler DW, Hunt DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. Clin Infect Dis 2006;43:322–30.
[2] De Lissovoy G, Fraeman K, Hutchins V, Murphy D, Song D, Vaughn BB. Surgical site infection: incidence and impact on hospital utilization and treatment costs. Am J Infect Control 2009;37:387–97.
[3] Monge Jodra V, Sainz de Los Terreros Soler L, Diaz-Agero Perez C, Saa Requejo CM, Plana Farras N. Excess length of stay attributable to surgical site infection following hip replacement: a nested case–control study. Infect Control Hosp Epidemiol 2006;27:1299–303.
[4] Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization and extra costs. Infect Control Hosp Epidemiol 1999;20:725–30.
[5] Whitehouse JD, Friedman ND, Kirkland KB, Richardson WJ, Sexton DJ. The impact of surgical-site infections following orthopedic surgery at a community hospital and a university hospital: adverse quality of life, excess length of stay, and extra cost. Infect Control Hosp Epidemiol 2002;23:183–9.
[6] Coello R, Charlett A, Wilson J, Ward V, Pearson A, Borriello P. Adverse impact of surgical site infections in English hospitals. J Hosp Infect 2005;60:93–103.
[7] Erekson EA, Yip SO, Ciarleglio MM, Fried TR. Postoperative complications after gynecologic surgery. Obstet Gynecol 2011;118:785–93.
[8] Colling KP, Glover JK, Statz CA, Geller MA, Beilman GJ. Abdominal hysterectomy: reduced risk of surgical site infection associated with robotic and laparoscopic technique. Surg Infect (Larchmt) 2015;16:498–503.
[9] Matsuo K, Prather CP, Ahn EH, et al. Significance of perioperative infection in survival of patients with ovarian cancer. Int J Gynecol Cancer 2012;22:245–53.
[10] Gerestein CG, Damhuis RA, de Vries M, Reedijk A, Burger CW, Kooi GS. Causes of postoperative mortality after surgery for ovarian cancer. Eur J Cancer 2009;45:2799–803.
[11] Mahdi H, Gojayev A, Buechel M, Knight J, Sanmarco J, Lockhart D, et al. Surgical site infection in women undergoing surgery for gynecologic cancer. Int J Gynecol Cancer 2014;24:779–86.
[12] Nugent EK, Hoff JT, Gao F, Massad LS, Case A, Zighelboim I, et al. Wound complications after gynecologic cancer surgery. Gynecol Oncol 2011;121:347–52.
[13] Tran CW, McGree ME, Weaver AL, Martin JR, Lemens MA, Cliby WA, et al. Surgical site infection after primary surgery for epithelial ovarian cancer: predictors and impact on survival. Gynecol Oncol 2015;136:278–84.

[14] Mahner S, Eulenburg C, Staehle A, Wegscheider K, Reuss A, Pujade-Lauraine E, et al. Prognostic impact of the time interval between surgery and chemotherapy in advanced ovarian cancer: analysis of prospective randomised phase III trials. Eur J Cancer 2013;49:142–9.
[15] Hofstetter G, Concin N, Braicu I, Chekerov R, Sehouli J, Cadron I, et al. The time interval from surgery to start of chemotherapy significantly impacts prognosis in patients with advanced serous ovarian carcinoma-analysis of patient data in the prospective OVCAD study. Gynecol Oncol 2013;131:15–20.
[16] Nishihara Y, Kajiura T, Yokota K, Kobayashi H, Okubo T. Evaluation with a focus on both the antimicrobial efficacy and cumulative skin irritation potential of chlorhexidine gluconate alcohol-containing preoperative skin preparations. Am J Infect Control 2012;40:973–8.
[17] Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 1999;20:250–78 quiz 279–80.
[18] Leung MP, Bishop KD, Monga M. The effect of temperature on bactericidal properties of 10% povidone-iodine solution. Am J Obstet Gynecol 2002;186:869–71.
[19] Maloney T, O'Neill B. Stability of povidone-iodine antiseptic solution stored at 37° C. Med J Aust 1986;144:389.
[20] Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgicalwound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med 1996;334:1209–15.
[21] National Healthcare Safety Network, Centers for Disease Control and Prevention. Surgical site infection (SSI) event. Atlanta, GA: CDC; 2019 Available at: http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf (last accessed 22 March 2019).
[22] Uppal S, Bazzi A, Reynolds RK, Harris J, Pearlman MD, Campbell DA, et al. Chlorhexidine-alcohol compared with povidone-ıodine for preoperative topical antisepsis for abdominal hysterectomy. Obstet Gynecol 2017;130:319–27.
[23] Privitera GP, Costa AL, Brusaferro S, Chirletti P, Crosasso P, Massimetti G, et al. Skin antisepsis with chlorhexidine versus iodine for the prevention of surgical site infection: a systematic review and meta-analysis. Am J Infect Control 2017;45:180–9.
[24] Lee I, Agarwal RK, Lee BY, Fishman NO, Umscheid CA. Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antisepsis to prevent surgical site infection. Infect Control Hosp Epidemiol 2010;31:1219–29.
[25] Noorani A, Rabey N, Walsh SR, Davies RJ. Systematic review and meta-analysis of preoperative antisepsis with chlorhexidine versus povidone-iodine in clean-contaminated surgery. Br J Surg 2010;97:1614–20.
[26] Dumville JC, McFarlane E, Edwards P, Lipp A, Holmes A. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. Cochrane Database Syst Rev 2013;28:CD003949.
[27] Ayoub F, Quirke M, Conroy R, Hill A. Chlorhexidine-alcohol versus povidone-iodine for pre-operative skin preparation: a systematic review and meta-analysis. Int J Surg Open 2015;1:41–6.
[28] Swenson BR, Hedrick TL, Metzger R, Bonatti H, Pruett TL, Sawyer RG. Effects of preoperative skin preparation on postoperative wound infection rates: a prospective study of 3 skin preparation protocols. Infect Control Hosp Epidemiol 2009;30:964–71.
[29] Levin I, Am-Alshiek J, Avni A, Lessing JB, Satel A, Almog B. Chlorhexidine and alcohol versus povidone-iodine for antisepsis in gynecological surgery. J Womens Health (Larchmt) 2011;20:321–4.
[30] Johnson MP, Kim SJ, Langstraat CL, Jain S, Habermann EB, Wentink JE, et al. Using bundled ınterventions to reduce surgical site ınfection after major gynecologic cancer surgery. Obstet Gynecol 2016;127:1135–44.
[31] Lippitt MH, Fairbairn MG, Matsuno R, Stone RL, 3rd. Tanner EJ, Wick EC, et al. Outcomes associated with a five point surgical site infection prevention bundle in women undergoing surgery for ovarian cancer. Obstet Gynecol 2017;130:756–64.
[32] Schiavone MB, Moukarzel L, Leong K, Zhou QC, Afonso AM, Iasonos A, et al. Surgical site infection reduction bundle in patients with gynecologic cancer undergoing colon surgery. Gynecol Oncol 2017;147:115–9.
[33] Seamon MJ, Wobb J, Gaughan JP, Kulp H, Kamel I, Dempsey DT. The effects of intraoperative hypothermia on surgical site infection: an analysis of 524 trauma laparotomies. Ann Surg 2012;255:789–95.
[34] Kurz A, Sessler DI, Narzt E, Bekar A, Lenhardt R, Huemer G, et al. Postoperative hemodynamic and thermoregulatory consequences of intraoperative core hypothermia. J Clin Anesth 1995;7:359–66.
[35] Melling AC, Ali B, Scott EM, Leaper DJ. Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomised controlled trial. Lancet 2001;358:876–80.
[36] Just B, Trevien V, Delva E, Lienhart A. Prevention of intraoperative hypothermia by preoperative skin-surface warming. Anesthesiology 1993;79:214–8.
[37] Wistrand C, Söderquist B, Magnusson A, Nilsson U. The effect of preheated versus room temperature skin disinfection on bacterial colonizationduring pacemaker device implantation: a randomized controlled non-inferiority trial. Antimicrob Resist Infect Control 2015;4:44.
[38] Wistrand C, Nilsson U. Effects and experiences of warm versus cold skin disinfection. Br J Nurs 2011;20(148):150–1.
[39] van Walraven C, Musselman R. The Surgical Site Infection Risk Score (SSIRS): a model to predict the risk of surgical site infections. PLoS One 2013;8:e67167.
[40] Bakkum-Gamez JN, Dowdy SC, Borah BJ, Haas LR, Mariani A, Martin JR, et al. Predictors and costs of surgical site infections in patients with endometrial cancer. Gynecol Oncol 2013;130:100–6.
[41] Suidan RS, He W, Sun CC, Zhao H, Fleming ND, Ramirez PT, et al. Impact of body mass index and operative approach on surgical morbidity and costs in women with endometrial carcinoma and hyperplasia. Gynecol Oncol 2017;145:55–6.
[42] Khavanin N, Lovecchio FC, Hanwright PJ, et al. The influence of BMI on perioperative morbidity following abdominal hysterectomy. Am J Obstet Gynecol 2013;208: 449e1–6.
[43] Soper DE, Bump RC, Hurt WG. Wound infection after abdominal hysterectomy: effect of the depth of subcutaneous tissue. Am J Obstet Gynecol 1995;173:465–9 discussion 469–71.
[44] Waisbren E, Rosen H, Bader AM, Lipsitz SR, Rogers Jr SO, Eriksson E. Percent body fat and prediction of surgical site infection. J Am Coll Surg 2010;210:381–9.