The efficacy and risks of using povidone-iodine irrigation to prevent surgical site infection: an evidence-based review

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Introduction: Surgical site infection is a serious complication of surgery. This evidence-based review sought to determine the efficacy and risks of using povidone-iodine irrigation to prevent surgical site infection. **Methods:** We searched MEDLINE and EMBASE for randomized controlled trials (RCTs) or comparative studies only (level of evidence I–III). **Results:** Of the 15 included studies, all of which were level I or level II evidence (11 RCTs and 4 prospective comparative studies), 10 found povidone-iodine irrigation to be significantly more effective at preventing surgical site infection than the comparison interventions of saline, water or no irrigation. No significant risks were associated with the use of povidone-iodine irrigation other than increased postoperative serum iodine. **Conclusion:** Povidone-iodine irrigation is a simple and inexpensive solution with the potential to prevent surgical site infection.

Objectif : L'infection du site de l'intervention constitue une complication sérieuse de la chirurgie. Cette critique factuelle voulait déterminer l'efficacité et les risques de l'utilisation de l'irrigation par solution de povidone-iode pour prévenir l'infection du site opératoire. **Méthodes :** Nous avons effectué dans MEDLINE et EMBASE une recherche portant uniquement sur des études contrôlées randomisées (ECR) ou des études comparatives (niveaux de preuve I–III). **Résultats :** Des 15 études incluses, qui présentaient toutes un niveau de preuve I ou II (11 ECR et 4 études comparatives prospectives), 10 ont révélé que l'irrigation au moyen d'une solution de povidone-iode avait été beaucoup plus efficace pour prévenir l'infection du site d'intervention que autres mesures comparées (application de solutions salines ou d'eau, ou l'absence d'irrigation). Aucun risque significatif n'a été associé à l'utilisation de l'irrigation à la povidone-iode, sauf l'élévation de la concentration sérique d'iode après l'intervention. **Conclusion :** L'irrigation au moyen d'une solution de povidone-iode est un moyen simple et peu coûteux de prévenir l'infection du site d'intervention.

Surgical site infection is an infrequent but serious complication of surgery.[1] Postoperative infection often requires repeat surgery and prolonged hospitalization, and it may compromise ultimate surgical outcomes.[1] In addition to sterile procedures and patient warming, prophylactic antibiotics have been shown to reduce surgical site infection.[1,2] Despite the widespread use of prophylactic antibiotics, however, surgical site infection continues to occur and is devastating for patients.[1] Many different wound irrigation solutions, including soaps, antibiotics and antiseptics, have been used to reduce surgical site infection.[3,4] Wound irrigation with povidone-iodine, an antiseptic solution, may be useful for reducing infection, but it is of uncertain efficacy and risk.

Povidone-iodine (Betadine) is an antiseptic solution consisting of polyvinylpyrrolidone with water, iodide and 1% available iodine; it has bactericidal ability against a large array of pathogens.[5] Although a vast amount of literature exists regarding its use as a topical antibacterical agent in surgery, its use as a prophylactic irrigation solution against surgical site infection has been examined to a lesser degree. This evidence-based review sought to determine the efficacy and risks of using povidone-iodine irrigation to prevent surgical site infection.

Methods

We conducted a search of MEDLINE (1966–2006) and EMBASE

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(1980–2006). The following search string was used in MEDLINE: (povidone-iodine / or betadine.mp.) and irrigation / and surgical wound infection/. In EMBASE, the following search string was used: (povidone iodine / or betadine.mp.) and (lavage / or irrigation.mp.) and surgical infection/. The search was limited to human beings and to articles published in English. The results from both searches were exported to EndNote (The Thompson Corp., Philadelphia, Pa.) where duplicate results were removed. Articles mentioned in the reference lists of these results were also retrieved.

To be eligible, studies had to be focused on the efficacy or risks, or both, of povidone-iodine irrigation to prevent surgical site infection; to have a sample size greater than 1; and to be either a randomized controlled trial (RCT) or a comparative study. Studies were excluded if they dealt with the treatment of surgical site infection instead of its prevention or if they used povidone-iodine topically rather than as an irrigation solution to prevent surgical site infection. Studies were also excluded if they focused on eye, oral, breast or gynecological surgery. The 15 studies that met all the inclusion criteria could be divided into 4 surgical areas: general, cardiovascular, orthopedic and urologic. These 15 studies in 4 surgical disciplines formed the basis of our review.

We extracted the following information from the studies: author, year, country, study design, patient age, surgical procedure, sample size, concentration and amount of povidone-iodine, comparison intervention used, outcome and risks. When provided by the studies, the following information was also extracted: antibiotics used in addition to povidone-iodine irrigation, definition of wound infection and bacterial contamination of patients (clean, dirty, etc.).

We also classified the studies according to the levels of evidence described by Wright and colleagues,[6] who categorize therapeutic studies from level I (stronger evidence) to level V (weaker evidence) on the basis of study design. In our review, only level I–III evidence was considered. Level I evidence derives from high-quality RCTs and systematic reviews of level I studies with consistent results. Level II evidence comprises RCTs of lesser quality (i.e., those with no blinding or improper randomization), prospective comparative studies, systematic reviews of level II studies or level I studies with inconsistent results. Level III evidence encompasses case–control studies, retrospective comparative studies and systematic reviews of level III studies.[6]

Findings

The 15 included studies are summarized in Table 1. The years of publication ranged from 1977 to 2006. Two examined the efficacy of povidone-iodine irrigation to prevent surgical site infection in multiple types of surgery, whereas 8 focused on general, 2 on cardiovascular, 2 on orthopedic and 1 on urologic surgery. Of the 15 studies, 11 were RCTs, 3 of which were single-blind (none were double-blind); 4 were prospective comparative studies. Three of the 15 studies were considered level I evidence, 12 level II evidence and none level III evidence.

Efficacy of povidone-iodine irrigation in surgery in general

As noted, 2 studies investigated the use of povidone-iodine irrigation in multiple types of surgery. Sindelar and Mason[3,4] conducted an RCT at the University of Maryland Hospital where patients ranged in age from 9 to 80 years and had surgery that included general (abdominal and gastrointestinal) and urologic (genitourinary) procedures. Of the 500 patients enrolled, 242 were randomly allocated to 10% povidone-iodine (1% available iodine) irrigation of the subcutaneous tissue for 60 seconds at operation, and 258 were randomly allocated to an equivalent amount of saline irrigation. Patients were classified as clean, potentially contaminated, contaminated or dirty. Patients in the latter 3 groups received combined clindamycin and gentamicin as antibiotics preoperatively to 48 hours postoperatively. When possible renal impairment or allergy was present, doxycycline was used instead. Infection was defined as pus from the incision site within 12 weeks after surgery along with bacteria recovered from a wound culture. The infection rate was 2.9% in the treatment group and 15.1% in the control group ($p < 0.001$). The treatment group did not experience any interference with wound healing or adverse reactions.

In a prospective comparative study, Singh and colleagues[7] examined 90 patients undergoing clean-contaminated operations who were divided into 3 equal groups. Group A patients received irrigation of the operative wound with 5% povidone-iodine. Group B patients received irrigation with 5% povidone-iodine and 5 mg/mL of metronidazole. Group C patients received irrigation with sterile normal saline. The infection rate was 30% in Group C and 10% in Group A and Group B ($p = 0.056$). No antibiotics were used in this study. Participants' age and adverse effects were not identified.

Efficacy of povidone-iodine irrigation in general surgery

Of the 8 studies related to general surgery, 1 was a prospective comparative study and 7 were RCTs. In the prospective comparative study, Barr[8] examined patients undergoing gastrointestinal surgery, 35 of whom received 2-minute lavage with Betadine solution (age range 8–92 yr) and 60 of whom did not (age not provided). Patients were classified as

Table 1

Summary of findings for povidone-iodine irrigation to prevent surgical site infection

Study	Year	Country	Level	Study design	Population: Age, yr	Population: Surgical procedure	Population: PA	Definition of infection	Intervention	Comparison	Out-come (+/–)*
Surgery in general											
Sindelar and Mason[3,4]	1977; 1979	United States	II	RCT	9–80	Included general and urologic procedures (*n* = 500)	Y	Pus from incision site within 12 wk after surgery along with bacteria recovered from wound culture	10% povidone-iodine irrigation (*n* = 242)	Saline irrigation (*n* = 258)	+
Singh et al[7]	1988	India	II	Prospective comparative study	NA	Various clean or contaminated operations (*n* = 90)	N	NA	5% povidone-iodine irrigation (*n* = 30)	5% povidone-iodine irrigation + 5 mg/mL of metronidazole (*n* = 30)	–
										Sterile normal saline irrigation (*n* = 30)	–
General surgery											
Barr[8]	1978	United States	II	Prospective comparative study	NA	Gastrointestinal	N	NA	Betadine lavage (*n* = 35)	No lavage (*n* = 60)	+
Sindelar and Mason[9]	1979	United States	II	RCT		Laparotomy (*n* = 168)	Y	Abscess formation	1% povidone-iodine irrigation	Saline irrigation	+
de Jong et al[10]	1982	The Netherlands	II	RCT	≥ 5	Intra-abdominal or inguinal hernia operations	N	Discharge from wound within 4 wk after surgery or a positive culture of fluid from wound	1% povidone-iodine irrigation (*n* = 154)	No irrigation (*n* = 142)	–
									10% povidone-iodine irrigation (*n* = 149)	No irrigation (*n* = 137)	–
Tighe et al[11]	1982	Ireland	II	RCT	3.5–74	Appendectomy (*n* = 131)	Y	Presence of pus with or without probing	1% Betadine irrigation (*n* = 49)	Sterile water irrigation (*n* = 31)	–
										No irrigation (*n* = 51)	–
Rogers et al[12]	1983	United States	II	RCT	Mean 60.2	General surgery (*n* = 187)	Y	Pus from wound within 1 mo of surgery	10% povidone-iodine (1% available iodine) irrigation (*n* = 86)	Normal saline irrigation (*n* = 101)	–
Johnson et al[13]	1985	United Kingdom	II	RCT	Intervention group: mean 68.3 (range 48–86) Comparison group: mean 67.2 (range 52–80)	Abdomino–perineal excision of the rectum for carcinoma or proctectomy for carcinoma (*n* = 56)	N	Purulent wound discharge or wound discharge with bacteria cultured	1% povidone-iodine irrigation (*n* = 28)	Sterile normal saline irrigation (*n* = 28)	+

Continued on next page

Table 1 continued

Study	Year	Country	Level	Study design	Population: Age, yr	Population: Surgical procedure	PA	Definition of infection	Intervention	Comparison	Out-come (+/–)*
Parker et al[14]	1985	United Kingdom	II	RCT	Intervention group: mean 69 Comparison group: mean 68	Major resection for large bowel carcinoma (*n* = 45)	Y	Pus discharging from wound	10% aqueous povidone-iodine irrigation (*n* = 22)	Water irrigation (*n* = 23)	+
Sindelar et al[15]	1985	United States	II	RCT	Intervention group: mean 51.5 (range 19–75) Comparison group: mean 51.7 (range 20–69) Overall: mean 51.4 (range 19–75)	intra-abdominal (*n* = 75)	Y	NA	1% povidone-iodine (0.1% available iodine) irrigation (*n* = 37)	Saline irrigation (*n* = 38)	+
Cardiovascular surgery											
Angelini et al[16]	1990	United Kingdom	II	Prospective comparative study	Intervention group: mean 61 Comparison group: mean 58	Early repeat sternotomy for postoperative hemorrhage (*n* = 43)	Y	Presence of purulent discharge along with a positive culture for bacteria	Aqueous povidone-iodine irrigation (*n* = 22)	No irrigation (*n* = 21)	+
Ko et al[17]	1992	United States	I	Single-blind RCT	NA	Cardiopulmon-ary bypass surgery with sternotomy incision (*n* = 1980)	Y	Unusual pain, fever, tenderness, induration, drainage or erythema	Povidone-iodine (0.5% in NaCl) irrigation (*n* = 990)	Saline (0.9% in NaCl) irrigation (*n* = 990)	–
Orthopedic surgery											
Cheng et al[18]	2005	Taiwan	I	Single-blind RCT	intervention group: mean 64 Comparison group: mean 61	Spinal surgery (*n* = 414)	Y	Unusual pain, fever, tenderness, induration, drainage or erythema	0.35% povidone-iodine irrigation (*n* = 208)	Normal saline irrigation (*n* = 206)	+
Chang et al[19]	2006	Taiwan	I	Single-blind RCT	Intervention group: mean 67.1 (range 20–82) Comparison group mean 65.4 (range 22–89)	Primary instrumental lumbosacral posterolateral fusion due to degenerative spinal disorder with segmental instability (*n* = 244)	Y	NA	0.35% povidone-iodine irrigation (*n* = 120)	Normal saline irrigation (*n* = 124)	+
Urologic surgery											
Richter et al[20]	1991	Israel	II	Prospective comparative study	mean 64 (range 55–90)	Open prostatectomy (*n* = 156)	Y	Redness, swelling, pus with a positive culture	NA	No irrigation (*n* = 76)	+

PA = prophylactic antibiotics; Y = yes; N = no; RCT = randomized controlled trial; NA = not available; NaCl = sodium chloride;
*+ = intervention was significantly more effective than comparison; – = intervention was not significantly more effective than comparison.

clean-contaminated or contaminated. In the group that received Betadine lavage, 2 of 35 (5.7%) developed wound infection; in the group that did not receive Betadine lavage, 23 of 60 (38.3%) developed wound infection ($p < 0.001$). No significant changes in triiodothyronine (T3) or thyroxine (T4) levels, which were assessed in 12 patients in the Betadine lavage group, were observed. In addition, no deleterious effects to the wounds occurred from Betadine lavage, and wounds healed without evidence of induration or inflammation except when infection occurred. The use of antibiotics was not mentioned in this study.

Sindelar and Mason[9] carried out an RCT of 168 patients undergoing laparotomy at the University of Maryland Hospital. The age of patients was not identified. Patients were classified as contaminated or dirty. All the patients received combined clindamycin and gentamicin as antibiotics preoperatively to 48 hours postoperatively. When possible renal impairment or allergy was present, doxycycline was used instead. The treatment group ($n = 80$) received irrigation of the peritoneal cavity for 60 seconds before closure of the abdomen with 1 L of 1% povidone-iodine (1:9 dilution of stock povidone-iodine aqueous solution with saline solution giving 0.1% available iodine in diluted form). The control group ($n = 88$) received irrigation for 60 seconds with saline. Infection was defined as abscess formation. In the treatment group, 1 of 80 patients (1.3%) developed an abscess, whereas in the control group 9 of 88 patients (10.2%) developed an abscess ($p < 0.05$). A total of 5 patients in the treatment group had their serum iodine and thyroxine levels measured. A significant rise in serum iodine levels was found in these patients 24 hours after surgery. However, the levels returned to preoperative levels 72 hours after surgery. No significant changes occurred in serum thyroxine levels and no untoward effects of elevated serum iodine levels occurred in these patients.

In yet another RCT, de Jong and colleagues[10] examined all patients ≥ 5 years of age undergoing intra-abdominal and inguinal hernia operations from April 1, 1980, to February 1, 1981. Patients were classified as clean, clean-contaminated, contaminated or dirty. Infection was defined as discharge from the wound within 4 weeks after surgery or a positive culture of fluid from the wound. No antibiotics were used in this study. The study was divided into 2 phases. In phase 1, the study group ($n = 154$ wounds) received 1% povidone-iodine irrigation at the end of the operation and the control group ($n = 142$ wounds) did not. In phase 2, the study group ($n = 149$ wounds) received 10% povidone-iodine irrigation at the end of the operation and the control group ($n = 137$ wounds) did not. No significant between-group difference in wound infection was found in phase 1: 17 of 154 study group wounds (11%) developed infection, whereas 21 of 142 control group wounds (15%) developed infection ($p = 0.335$). Similarly, no significant between-group difference in wound infection was found in phase 2: 22 of 149 study group wounds (15%) developed infection, whereas 15 of 137 control group wounds (11%) developed infection ($p = 0.337$). No risks were identified.

In another RCT, Tighe and colleagues[11] enrolled 131 patients ranging in age from 3.5 to 74 years and undergoing appendectomies at Limerick Regional Hospital. Antibiotics were used in 53 of the 131 patients distributed evenly across 3 study groups. The first group ($n = 49$) received irrigation with 1% Betadine solution (150 mL intraperitoneally and 50 mL on the wound following closure of the peritoneum). The second group ($n = 31$) received irrigation with sterile water. The third group ($n = 51$) received no irrigation. Infection was defined as the presence of pus with or without probing. Overall, 17 wound infections, or a 12.97% infection rate, occurred. There were no significant differences between the 3 groups; however, the authors did not supply the p value, nor did they provide enough data to calculate it. The authors did not identify any risks.

Rogers and colleagues[12] undertook an RCT of 187 patients (mean age 60.2 yr) undergoing general surgery at Nashville Veterans Administration Hospital during a 6-month period from July 1, 1979, to December 31, 1979. Patients were categorized as clean, clean-contaminated, or dirty. Antibiotics were used in the latter 2 groups perioperatively. The treatment group ($n = 86$) received 1-minute irrigation of the subcutaneous tissue with saline followed by the instillation of about 60 mL of 10% povidone-iodine (1% available iodine). The control group ($n = 101$) received 1 minute irrigation of the subcutaneous tissue with normal saline alone. Infection was defined as pus from the wound within 1 month after surgery. The wound infection rate was 4.6% (4/86) in the treatment group and 10.9% (11/101) in the control group ($p = 0.117$). No risks were identified.

Between 1975 and 1980, Johnson and colleagues[13] performed an RCT with 56 patients undergoing abdomino-perineal excision of the rectum for carcinoma. No antibiotics were used in this study. Patients were classified as contaminated or non-contaminated. The treatment group (mean age 68.3 yr, range 48–86 yr) received irrigation of the perineal space with 50 mL of 1% povidone-iodine every 8 hours for 5 days immediately following surgery; the control group (mean age 67.2 yr, range 52–80 yr) received an equivalent amount of irrigation with sterile normal saline. Infection was defined as purulent wound discharge or wound discharge with bacteria cultured. The treatment group had significantly

fewer wound infections than the control group ($p < 0.01$) even when wound contamination occurred during surgery ($p < 0.05$). In addition, primary wound healing was significantly better in the treatment group than in the control group ($p < 0.02$) even when contamination occurred during surgery ($p < 0.005$). Although fewer patients in the treatment group had a persistent sinus at 6 months after surgery, this was not statistically significant ($p = 0.051$). No risks were identified.

Parker and colleagues[14] carried out an RCT of 45 patients undergoing major resection for large bowel carcinoma. The study group consisted of 22 patients with a mean age of 69 years who received preoperative irrigation with 500 mL of 10% aqueous povidone-iodine; the control group consisted of 23 patients with a mean age of 68 years who received an equivalent amount of irrigation with water. All the patients received antibiotics consisting of intravenous ampicillin 500 mg, or erythromycin if allergic to penicillin, and metronidazole 500 mg. Infection was defined as pus discharging from the wound. Only 1 patient (4.5%) in the study group developed wound infection, whereas 9 patients (39.1%) in the control group developed infection ($p < 0.01$). No risks were identified.

Sindelar and colleagues[15] undertook an RCT of 75 patients undergoing contaminated or dirty intra-abdominal surgery at the National Institutes of Health in Bethesda, Maryland (mean age 51.5 yr, range 19–75 yr). Of these, 37 patients were randomized to the treatment group (mean age 51.4 yr, range 19–75 yr) and 38 patients were randomized to the control group (mean age 51.7 yr, range 20–69 yr). The treatment group received intraperitoneal irrigation with 1000 mL of low molecular weight povidone-iodine mixed in saline to a 10% dilution (1% povidone-iodine; 0.1% available iodine). They received the irrigation 3 times, with the final irrigation occurring immediately before closure and the peritoneal cavity suctioned 30–60 seconds after each irrigation. The control group received intraperitoneal irrigation with saline. Patients in the study received perioperative antibiotics according to the operating surgeon's preference, which consisted of no antibiotics, cephalosporin, cephalosporin-aminoglycoside, clindamycin-aminoglycoside or other antibiotics. The incidence of primary closure of the surgical incision was higher in the treatment group (35/37) than in the control group (30/38). In addition, 3 patients in the treatment group and 12 patients in the control group developed postoperative complications related to wound healing or infection. In each group, 3 patients also experienced abnormalities of wound healing. Wound infection occurred in 1 treatment group patient and 3 control group patients. However, no significant difference in wound healing complications was observed. Three treatment group patients and 11 control group patients developed intra-abdominal complications ($p < 0.05$). Moreover, among patients with only peritonitis or intra-abdominal abscesses, control group patients had a significantly higher incidence of intra-abdominal infectious complications (9/38) than treatment group patients (2/37) ($p < 0.05$) even after exclusion of patients who developed peritonitis or intra-abdominal abscesses from surgical technical complications (control group, 7/38 patients; intervention group, 1/37 patients; $p < 0.05$). Compared with preoperative levels, median serum iodine levels measured in 19 treatment group patients significantly increased about 9-fold at 24 hours after surgery ($p < 0.001$) but returned to preoperative levels by 7 days after surgery. Median serum iodine levels measured preoperatively in 18 control group patients did not significantly differ at 24 hours and 7 days after surgery. No clinical signs of iodine toxicity were observed in any of the patients.

Efficacy of povidone-iodine irrigation in cardiovascular surgery

Of the 2 identified studies on povidone-iodine irrigation in cardiovascular surgery, 1 was a prospective comparative study and 1 was a single-blind RCT. Angelini and colleagues[16] undertook a prospective comparative study of 43 patients undergoing early repeat sternotomy for postoperative hemorrhage at the University Hospital of Wales. Between October 1987 and September 1988, 22 patients (mean age 61 yr) received irrigation of the pericardial cavity and median sternotomy wound layers with 250–500 mL of aqueous povidone-iodine before reclosure; between October 1986 and September 1987, 21 patients (mean age 58 yr) did not receive povidone-iodine irrigation. The concentration of povidone-iodine solution used was not provided. Patients received antibiotics consisting of cefuroxine 750 mg and gentamicin 1.5 mg/kg at their initial operation. Infection was defined as the presence of purulent discharge along with a positive culture for bacteria. No median sternotomy infections occurred in the irrigation group, and 5 median sternotomy infections occurred in the no-irrigation group ($p < 0.05$).

Over a 2-year period from July 1987 to June 1989, Ko and colleagues[17] conducted a single-blind RCT of 1980 adult patients undergoing cardiopulmonary bypass surgery with a sternotomy. The age of study participants was not specified. All patients received perioperative antibiotics consisting of cefazolin in simple cases and vancomycin for penicillin-allergic patients. While the treatment group received povidone-iodine (0.5% in sodium chloride) intraoperative irrigation, the control group received saline (0.9% sodium chloride) intraoperative irrigation. Infection was characterized by un-

usual pain, fever, tenderness, induration, drainage or erythema. In the treatment group 11/990 patients (1.1%) developed infection, and in the control group, 6/990 patients (0.6%) developed infection ($p = 0.16$).

Efficacy of povidone-iodine irrigation in orthopedic surgery

Two single-blind RCTs were identified on povidone-iodine irrigation in orthopedic surgery. In one single-blind RCT, Cheng and colleagues[18] assessed 414 patients undergoing spinal surgery. Of these, 208 patients (group 1) were randomized to have their surgical wounds irrigated with 10% povidone-iodine (100 mg of povidone-iodine per 1 mL of solution) before wound closure (5 mL of the povidone-iodine solution was diluted with normal saline to achieve a concentration of 0.35% povidone-iodine or 3.5% Betadine). The remaining 206 patients (group 2) were randomized to have their surgical wounds irrigated with 2000 mL of normal saline. In group 1, the average age was 64 years, and in group 2, the average age was 61 years. All patients received intravenous antibiotics consisting of cefazolin 1000 mg and gentamicin 60 mg 1 hour before surgery as well as cefazolin 1000 mg every 6 hours and gentamicin 60 mg every 12 hours for 48 hours after surgery. After this, 500 mg of oral cefazolin was given every 6 hours for 3 days. Infection was characterized by unusual pain, fever, tenderness, induration, drainage or erythema. No wound infection occurred in group 1. One superficial infection (0.5%) and 6 deep infections (2.9%) occurred in group 2. The between-group differences in the deep infection rate and the total infection rate were statistically significant at a level of $p = 0.015$ and $p = 0.007$, respectively. No allergic or hypersensitive reactions occurred in group 1.

From January 2002 to August 2003, in another single-blind RCT, Chang and colleagues[19] examined 244 patients undergoing primary instrumental lumbosacral posterolateral fusion with segmental instability due to degenerative spinal disorder. Of these, 120 patients (mean age 67.1 yr, range 20–82 yr) received 0.35% povidone-iodine wound irrigation for 3 minutes, followed by irrigation with 2000 mL of normal saline to remove the povidone-iodine. The remaining 124 patients (mean age 65.4 yr, range 22–89 yr) received wound irrigation with 2000 mL of normal saline. All patients received intravenous antibiotics consisting of cefazolin 1000 mg and gentamicin 60 mg 1 hour before surgery as well as cefazolin 1000 mg every 6 hours and gentamicin 60 mg every 12 hours for 48 hours after surgery. After this, 500 mg of oral cefazolin was given every 6 hours for 3 days. Wound dehiscence occurred in 1 patient in the treatment group and 2 patients in the control group. A significantly higher infection rate occurred in the control group than in the treatment group ($p < 0.05$). No adverse effects were identified in the treatment group. Overall, no significant between-group differences were found in fusion rate, wound healing, improvement of pain score, function score and ambulatory capacity.

Efficacy of povidone-iodine irrigation in urologic surgery

A prospective comparative study by Richter and colleagues[20] investigated povidone-iodine irrigation in urologic surgery. The study enrolled 156 patients with a mean age of 64 years (range 55–90 yr) undergoing open prostatectomy during the 12-month study period. Patients undergoing surgery during the first 6 months of the study did not receive preoperative bladder irrigation (control group). Patients undergoing surgery during the last 6 months of the study received preoperative bladder irrigation with 50–60 mL of nondiluted povidone-iodine containing 1% available iodine (treatment group). Preoperative intravenous antimicrobial prophylaxis was given according to bacteria sensitivity and minimum inhibitory concentration. Infection was indicated by redness, swelling or pus along with a positive wound culture. Wound infection occurred in 17 of 76 patients (22.4%) in the control group and in 4 of 80 patients (5%) in the treatment group ($p < 0.001$). No risks were identified.

Risks of povidone-iodine irrigation

A case report by Strife and colleagues[21] reported a possible complication with povidone-iodine irrigation. A 15-year-old girl with a pelvic mass undergoing exploratory laparotomy for severe pelvic inflammatory disease was copiously washed with 550 mL of a 1/10 povidone-iodine solution. One day later, her serum glutamic-oxaloacetic transaminase level was elevated and she presented with mild proteinuria and microscopic hematuria. Serum and urine free iodine levels at 54 hours after surgery were higher than normal at 195 μg/dL and 170 μg/dL, respectively (normal levels were not stated). Although it was suspected that povidone-iodine toxicity had occurred, other factors seemed to explain these findings, including the presence of hepatitis B antigen and high-dose antibiotic therapy consisting of cephalothin sodium and gentamicin sulfate. Povidone-iodine's toxicity could not therefore be established in this case.

In a case series of 4 premature infants (age range 38–130 d; gestation 27–34 wk) undergoing bowel reanastomosis, Ryan and colleagues[22] assessed thyroid function after 15–40 mL lavage of the ostomy site with 10% povidone-iodine at the time of surgery. T4, thyroid-stimulating hormone (TSH), total serum iodine and 24-hour urine excretion of iodine levels were all measured. T4 levels significantly decreased from a mean of 112 μmol/L to a mean of 90 μmol/L within 24 hours

of surgery ($p < 0.05$), but no significant changes occurred in mean TSH levels. Total serum iodine levels increased from a mean of 1.5 μmol/L before surgery to a mean of 61.6 μmol/L 24 hours after surgery. During the same period, 24-hour urine excretion of iodine increased from 2.5 μmol/L to 160 μmol/L. However, by 2 weeks after surgery, mean T4, TSH and 24-hour urine excretion of iodine levels returned to presurgery levels. Total serum iodine levels remained elevated at 4.0 μmol/L. In one infant's case, povidone-iodine was aspirated from the stomach and showed a total iodine concentration of 12 400 μmol/L. Neither renal failure nor metabolic acidosis occurred in any of the infants, and the highest serum sodium level found in the first 48 hours after surgery was 142 mmol/L. None of the infants developed goiters and all survived. The authors concluded that because povidone-iodine may cause transient suppression of thyroid function in premature infants undergoing bowel reanastomosis, their thyroid levels should be measured about 2 weeks after the repeated or widespread use of povidone-iodine.

Kovacikova and colleagues[23] assessed the thyroid function of 18 pediatric cardiac patients with a median age of 8 months (range 18 d–5.3 yr) who received mediastinal irrigation with povidone-iodine for the treatment of deep sternal wound infection (DSWI). After extensive sternal débridement, the patients received repeated irrigation with 0.5% povidone-iodine, followed by 20 mL/h continuous postoperative irrigation. On postoperative day (POD) 1, they received 0.05% povidone-iodine irrigation. On POD 2, they received 0.01% povidone-iodine irrigation, followed on POD 3 by 0.005% povidone-iodine irrigation. If reinfection was suspected, they underwent débridement again, followed by povidone-iodine irrigation for 6 days (0.05% povidone-iodine irrigation on POD 1–2, 0.01% povidone-iodine irrigation on POD 3–4 and 0.005% povidone-iodine irrigation on POD 5–6). The use of povidone-iodine irrigation to treat DSWI in these patients did not produce any significant changes in thyroid function.

Discussion

Povidone-iodine irrigation is a simple and inexpensive solution with the potential to reduce surgical site infection. A total of 15 studies, summarized in Table 1, evaluated the efficacy or risk, or both, of povidone-iodine irrigation to prevent surgical site infection. Of these, 11 were RCTs that provided level I (3 studies) or level II (8 studies) evidence. The remaining 4 studies were prospective comparative studies that provided level II evidence. Of the 15 studies, 5 did not find povidone-iodine irrigation to be significantly more effective at preventing surgical site infection than the comparison interventions of saline, water or no irrigation.[7,10–12,17] Of these 5 studies, 1 examined patients undergoing surgery in general, 3 focused on patients undergoing general surgery procedures specifically, and 1 was related to patients undergoing cardiovascular surgery. The remaining 10 studies found povidone-iodine irrigation to be significantly more effective at preventing surgical site infection than the comparison interventions of saline, water or no irrigation.[3,4,8,9,13–16,18–20] Although povidone-iodine demonstrated efficacy in all the surgical disciplines evaluated, the heterogeneity of the types of surgery and concentrations of povidone-iodine used precluded combining the studies in a meta-analysis.

The main risks associated with povidone-iodine irrigation were primarily related to thyroid function. Varying findings were reported, but no serious harms occurred. Because contamination of the povidone-iodine solution has been associated with infections, precautions should be taken to ensure its sterility before use.[24,25] Although not directly relevant to this review, the use of 10% topical povidone-iodine ointment (1% available iodine) in burn patients has resulted in severe metabolic acidosis due to the absorption of iodine or acidic povidone-iodine. Thus care should be taken when using it in patients with burns covering more than 20% of the body surface or when renal failure is present.[26] In general, povidone-iodine irrigation should not be used in patients with iodine sensitivity, burns, thryroid disease or renal disease until more research has been conducted.

This review has several limitations. First, because many of the studies did not include pediatric patients in their sample, the appropriateness of using povidone-iodine irrigation in children is unknown. Second, the studies included in this review vary in both quality and design, which precludes summing the results in a meta-analysis. Third, the amount, frequency, concentration and type of povidone-iodine solution used were inconsistent across studies. Further, the formulation of povidone-iodine solutions may vary by manufacturer, which does not allow the "optimal" irrigation solution to be delineated. However, the studies demonstrated effectiveness even at low concentrations, and therefore, concentrations less than 5% would seem appropriate. Finally, many of the studies had methodological limitations, including heterogeneous patient populations with no classification of patient bacterial contamination, lack of blinding, and inconsistent or nonstandardized definitions of wound infection. Many of the older studies did not classify wound types and included a heterogeneous mixture of patients. However, randomization should, on average, balance prognostic factors such as wound type between the 2 treatment groups. Although definitions of surgical site infection were not standardized, we included only controlled studies so that at least the same definition was used in both

treatment groups. In addition, prophylactic antibiotics were not used consistently throughout the studies, so whether povidone-iodine solution would show efficacy in conjunction with antibiotics is unknown. However, several of the recent RCTs demonstrated that, even with routine prophylactic antibiotics, irrigation with povidone-iodine further reduced surgical site infection rates.

In conclusion, the evidence suggests that povidone-iodine irrigation may be effective in preventing surgical site infection. However, more studies, especially double-blind RCTs, should be conducted to determine the "ideal" solution of povidone-iodine irrigation as well as specific risks associated with its use.

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