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A randomized trial that compared povidone iodine and chlorhexidine as antiseptics for vaginal hysterectomy

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KEY WORDS
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Objective: The purpose of this study was to compare the efficacy of chlorhexidine and povidone iodine for cleansing the operative field for vaginal surgery.

Study design: This was a randomized controlled trial that compared 10% povidone iodine and 4% chlorhexidine gluconate as surgical scrubs. Our primary end point was the proportion of contaminated specimens (defined as total bacterial colony counts of ≥ 5000 colony-forming units) per group found throughout the surgical procedures. All patients received standard infection prophylaxis that included preoperative intravenous antibiotics. Immediately before antibiotic administration and baseline aerobic and anaerobic cultures of the vaginal flora were obtained, which were followed by cultures at 30 minutes after the surgical scrub and hourly thereafter throughout each patient's surgery.

Results: A total of 50 patients were enrolled between October 2002 and September 2003. There were no differences between the povidone iodine (n = 27) and chlorhexidine (n = 23) groups with respect to age, race, exogenous hormone use, body mass index, gravity, parity, preoperative mean colony counts, or operative time. Among the first set of intraoperative specimens (which were obtained 30 minutes after the surgical scrub), 63% of the cultures (17/27) from the povidone iodine group and 22% of the cultures (5/23) from the chlorhexidine group were classified as contaminated ($P = .003$; relative risk, 6.12; 95% CI, 1.7, 21.6). Subsequent cultures failed to demonstrate significant differences.

Conclusion: Chlorhexidine gluconate was more effective than povidone iodine in decreasing the bacterial colony counts that were found in the operative field for vaginal hysterectomy.

Before the widespread use of aseptic techniques and prophylactic antibiotics, the rate of wound infection after vaginal hysterectomy was an unacceptably high 30% to 40%.[1] Eventually, evidence from dozens of randomized controlled trials prompted the American College of Obstetricians and Gynecologists

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to recommend antimicrobial prophylaxis for all vaginal hysterectomies.[2]

In addition to antibiotic prophylaxis, preparation of the surgical field with povidone iodine has been recommended widely.[3,4] Although the exact mechanism by which iodine destroys bacteria is unknown, it has been postulated that iodine reacts with bacterial amino acids and fatty acids resulting in the destruction of their cellular structures and enzymes.[5]

Another surgical antiseptic, chlorhexidine gluconate, causes the destruction of bacterial cell membranes leading to leakage of cellular constituents and coagulation of cell contents.[5] Both agents have been shown to decrease cutaneous and mucosal bacterial counts in the vagina.[6-8] However, there have been no prospective, randomized trials that have compared these 2 agents' efficacy for vaginal surgery.

Therefore, our objective was to compare the efficacy of chlorhexidine and povidone iodine for cleansing the operative field for vaginal surgery.

Material and methods

This was a randomized controlled trial that was approved by the University of Louisville Health Sciences Center Human Studies Committee that compared povidone iodine and chlorhexidine gluconate to prepare the surgical field before vaginal hysterectomy with or without reconstructive pelvic surgery. We had no outside funding source for this study; therefore, it was paid for by the University of Louisville Urogynecology Divisional account.

In preparation for this randomized trial, our group first carried out a pilot study that described the bacterial colony counts that were found throughout the course of vaginal surgery.[9] In that study, we obtained serial vaginal cultures before and during 31 vaginal hysterectomies. Each of those patients received standard infection prophylaxis that included intravenous antibiotics and a standardized surgical scrub with povidone iodine. For the purposes of that study, our definition of *contaminated* included any specimen culture that yielded $\geq$5000 colony-forming units per milliliter. Pilot study results were as follows[9]: The first set of intraoperative cultures were obtained 30 minutes after the completion of the scrub; 52% of the cultures (16/31) were contaminated. In the next set of cultures (which were obtained 90 minutes after the initial scrub), 41% of the cultures (12/29) were contaminated. The remaining sets of cultures showed progressively fewer contaminated specimens, which prompted us to conclude that future investigations regarding bacterial colony counts during vaginal surgery should focus on the initial 30 to 90 minutes of the procedure.

Using that pilot data, we performed a sample size estimate for our randomized trial. In doing so, we decided that a reduction in the contaminated specimens from 52% to 10% may be clinically significant. Therefore, we needed 22 patients in each arm of the study to have an 80% power to detect that difference (α = .05). All patients who underwent vaginal hysterectomy through our institution between October 2002 and September 2003 were offered enrollment. Patients were assigned randomly to receive a standardized preoperative scrub with either 10% povidone iodine (Medline Prep Solution; Medline Industries, Mundelein, Ill) or 4% chlorhexidine gluconate (Dynahex 4; Xttrium Laboratories Inc, Chicago, Ill). Randomization was performed immediately after enrollment on the day of surgery. A blocked random assignment technique was used to determine the allocation sequence, and opaque sealed envelopes were used to conceal the group assignments.

Our primary end point was the proportion of contaminated specimens per group that were found throughout the surgical procedures.

All patients received standard infection prophylaxis that included preoperative intravenous antibiotics within 30 minutes of the surgical start time. Cefazolin (1 g) was used, unless a patient reported an allergy to this medication. In those cases, clindamycin (900 mg) and gentamicin (120 mg) were used. Our only exclusion criterion was patient-reported allergy to iodine.

Immediately before the administration of the preoperative antibiotics, baseline aerobic and anaerobic cultures of the vaginal flora were obtained with a combined aerobic/anaerobic collection and transport system (CultureSwab Plus; Becton Dickinson, Franklin Lakes, NJ). A standard technique was used to obtain all cultures[9]: With the patient in the dorsal lithotomy position, a swab was placed in the posterior fornix and agitated throughout the length and circumference of the vagina for 1 minute. Care was taken to include the entire surface area of the vagina, but the cervix was avoided.

The same technique was used to obtain cultures of the vaginal field 30 minutes after the completion of the surgical scrub and hourly thereafter throughout each surgery. Exact time intervals between cultures were determined with a stopwatch.

Immediately after each operation, the culture transport tubes were taken to the University of Louisville Hospital Microbiology Laboratory for processing, as previously described.[9] The laboratory personnel were blinded to the patient group assignments. A sterile, calibrated (0.01 mL) loop was used to inoculate the specimen onto 5% sheep blood agar and chocolate agar plates that were incubated at 35°C in 5% to 10% carbon dioxide (aerobic cultures). Cultures for anaerobic micro-organisms were inoculated quantitatively on *Brucella* blood agar, phenylethyl alcohol, kanamycin vancomycin agar, and *Bacteroides* bile esculin agar. Manual colony counts were reported for all positive

Table Demographics and baseline colony counts

Variable	Povidone iodine group (n = 27)	Chlorhexidine group (n = 23)	*P* value
Mean preoperative colony count (n)	172,296 ± 74,866	211,956 ± 94,204	.10
Mean age (y)*	42.6 ± 7.8	45.0 ± 11.5	.47
Mean body mass index (kg/m^2)*	30.4 ± 6.4	29.9 ± 7.8	.82
Mean gravidity (n)*	3.0 ± 1.7	3.1 ± 1.2	.77
Mean parity (n)*	2.6 ± 1.5	2.5 ± 1.0	.84
Hormone replacement therapy (%)†	0 (0/27)	13 (3/23)	.053
White (%)†	82 (22/27)	78 (18/23)	.78

* Data are given as means ± SD, compared with the use of independent samples *t*-test; proportions compared with the use of Pearson chi-squared test.
† Data in parentheses represent number/total.

cultures; the identification was performed according to standard biochemical methods. The approach to quantifying microbial flora involved a 0.01-mL calibrated loop. Using this technique, 1 colony is equivalent to 100 colony-forming units per milliliter of specimen. For each specimen, the "total colony count" was determined by adding all colony counts (regardless of bacteria type). For any specimen, a total colony count of $\geq$5000 colony-forming units per milliliter was classified as contaminated.

To detect any clinical infections, routine postoperative office visits that included a pelvic examination were carried out between 2 and 6 weeks after surgery.

Statistical analyses were performed with SPSS software (version 11.0; SPSS Inc, Chicago, Ill). Demographic characteristics of the 2 groups were compared with the Pearson chi-squared test (for proportions) or the independent samples *t*-test (for continuous variables). At each time interval, the proportions of contaminated specimens were compared between groups with the Pearson chi-squared test.

Results

Fifty patients were enrolled between October 2002 and September 2003. Only 1 eligible patient refused enrollment, citing no specific reason. The entire study protocol was completed for all 50 patients. No protocol deviations occurred. As expected in a randomized trial, there were no differences between the povidone iodine (n = 27 patients) and chlorhexidine (n = 23 patients) groups with respect to age, race, exogenous hormone use, body mass index, gravity, parity, or preoperative mean colony counts (Table).

All but 4 patients (2 in each group) received cefazolin; the remaining patients received clindamycin and gentamicin. There was no difference between the 2 groups with respect to mean surgical duration. The mean operative times for the chlorhexidine and iodine groups were 95 ± 74 minutes and 74 ± 65 minutes, respectively (P = .3). All patients returned for at least 1 visit between 2 and 6 weeks after the operation; no patient in either group had evidence of an operative site infection.

At the first postoperative interval (30 minutes after the surgical scrub), 63% of the cultures (17/27) from the povidone iodine group and 22% of the cultures (5/23) from the chlorhexidine group were classified as contaminated (P = .003; relative risk, 6.12; 95% CI, 1.7, 21.6). The mean colony counts at 30 minutes were 10,743 ± 28,906 for the povidone iodine group and 15,730 ± 28,559 for the chlorhexidine group (P = .54).

At the second postoperative interval (90 minutes after the surgical scrub), 36% of the povidone iodine cultures (4/11) and 14% of the chlorhexidine (2/14 cultures) groups were classified as contaminated (P = .12; relative risk, 3.4; 95% CI, 0.5, 23.8). The mean colony counts at 90 minutes were 20,472 ± 40,058 for the povidone iodine group and 1221 ± 2857 for the chlorhexidine group (P = .001).

At the third postoperative interval (150 minutes after the surgical scrub), 50% of the povidone iodine group (3/6 cultures) and 14% of the chlorhexidine group (1/7 cultures) were classified as contaminated (P = .17; relative risk, 6.0; 95% CI, 0.4, 85.3).

Comment

Despite the widespread use of aseptic techniques and prophylactic antibiotics, infection remains the most common complication that is associated with vaginal hysterectomy, occurring between 2.1% and 9.5% of cases.[10] These infections arise primarily from the ascending spread of micro-organisms from the upper vagina.[11] The obvious ideal strategy for lowering these infection rates would incorporate only randomized controlled trials, with operative site infections as their primary outcome measure. However, such studies would require large numbers of patients to detect a clinically significant difference in postoperative infections. For example, a randomized controlled trial with 80% power to detect a reduction in infection rates from 6% to 3% would require 814 patients in each arm. Given the

difficulty and expense of such a study, we chose to carry out this trial using a surrogate end point for infection.

While planning the protocol for this study, we encountered several operating room nurses who had been taught not to use chlorhexidine as a vaginal preparation. We performed a literature search on this subject through MEDLINE using the key words *vagina* and *chlorhexidine*. We found no evidence to support the idea that chlorhexidine is unsafe as a vaginal preparation. On the contrary, before enrolling any patients, we found 3 randomized trials in which a chlorhexidine vaginal preparation was performed on nearly 4500 patients (among the 3 studies) with no adverse events.[11-14] Although a recent case report (published after completion of our study) suggests that some women can have a desquamating reaction after vaginal scrub with chlorhexidine,[15] we believe the incidence of that problem must be extremely small.

Our study was the first randomized trial to compare povidone iodine and chlorhexidine in the preparation of the vaginal field for hysterectomy. Based on cultures that were obtained 30 minutes after the surgical scrubs, chlorhexidine was clearly superior. In fact, cultures from the povidone iodine group at 30 minutes were >6 times as likely to be contaminated as those from the chlorhexidine group. Although a similar trend existed in the culture sets that were obtained at 90 minutes, no statistical significance was found at that time interval.

Although the exact clinical significance of this information is unclear, our findings suggest that the widespread use of chlorhexidine rather than povidone iodine might reduce the risk of operative site infections after vaginal hysterectomy.

Clearly, the purpose of a surgical scrub is to reduce the number of pathogens that are present in the operative field. Assuming that there are equivalent costs and effort associated with the use of the 2 antiseptics, our study raises 1 simple question: Why not use the antiseptic that seems to make the operative field cleaner?

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