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Betadine irrigation and post-craniotomy wound infection

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Abstract

Object—The purpose of this study is to evaluate the efficacy of betadine irrigation in preventing postoperative wound infection in cranial neurosurgical procedures.

Methods—A total of 473 consecutive cranial neurosurgical procedures, including craniotomies and burr hole procedures were retrospectively reviewed. Patients had either antibiotic irrigation or dilute betadine plus antibiotic irrigation prior to skin closure. Infection was determined by purulence noted on reoperation and confirmed with bacterial growth culture. One and three month postoperative infection rates were calculated. Statistical analysis was performed using chi-squared tests.

Results—This study included 404 patients. Betadine was used in 117 (29.0%). At 1 month after surgery, there was no difference in the rate of wound infection between the two groups (1.7% each). However, at 90 days, the betadine group had a 2.6% infection rate compared with 3.8% in the antibiotic group, indicating a 33% decrease in infection rates with the addition of betadine (p=. 527). The small sample size of the study produced a low power and high beta error.

Conclusions—In this small preliminary study, betadine decreased postoperative infection rates compared with antibiotic prophylaxis alone at 90 days but not 30 days. This was not statistically significant, but a larger sample size would lower the beta error and decrease confounding bias associated with group heterogeneity. The potential for betadine, a cheap, low toxicity antimicrobial, to decrease infection rates and reoperations for infection warrants a larger multicenter trial.

Keywords

betadine; infection; craniotomy; therapeutic irrigation

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INTRODUCTION

Deep wound infection following craniotomy can occur in up to 5.8% of all cases. [1] Management of post-craniotomy infection often requires re-admission to the hospital, re-operation, administration of several weeks of antibiotics, and substantial increase in cost to the healthcare system. [2] Prevention of post-operative wound infection is of paramount importance, not only for increasing patient safety and quality of care, but also in decreasing healthcare expenditures. Antibiotic prophylaxis is routinely used by neurosurgeons to avoid postoperative infections in neurosurgical procedures. Several randomized trials have supported the use of antibiotic prophylaxis specifically in craniotomies. [3–9]

More recent studies have demonstrated that povidone-iodine irrigation (betadine, Purdue Pharma, Stamford, CT) of surgical wounds effectively decreased rates of postoperative infection in a variety of surgical procedures with no significant risks.[10, 11] The purpose of this study was to investigate whether the addition of dilute betadine irrigation to antibiotic irrigation would decrease the risk of post-craniotomy wound infection in a consecutive series of patients. Although a single center series might not be expected to find a statistically significant result, we were curious whether our findings would justify a larger multicenter trial and to determine the number of patients that might be required for such a trial.

METHODS

This study was approved by the institutional review board at Weill-Cornell Medical College. A total of 473 consecutive craniotomies and intraoperative burr hole procedures (tumor biopsies and resections, epilepsy electrode implants and resections) performed by a single surgeon (THS) between January 2008 and October 2012 were retrospectively reviewed. These cases were identified from a prospective database of all tumor and epilepsy cases performed. All operative reports were reviewed to determine if antibiotic irrigation only or antibiotic irrigation plus dilute betadine were used after the dura was closed but prior to skin closure. Antibiotic irrigation consisted of 150 cc of gentamycin (80 mg) diluted in 1 liter normal saline. Dilute betadine plus antibiotic irrigation consisted of a 150cc 50:50 mixture of 7.5% povidone iodine and normal saline followed by 150 cc of gentamycin (80 mg) diluted in normal saline. At out institution, the cost of a bottle of betadine and gentamycin was obtained and the additional price per surgery with betadine was calculated.

The groups were historically consecutive since antibiotic only therapy was used prior to the addition of dilute betadine irrigation. Patients were included from a time point chosen to result in at least double the number of control patients compared with study patients. The ratio of control to experimental patients was set greater than 2:1 to increase the chance of capturing a significant change given the small number of patients in the experimental group. Patients were excluded if they were allergic to iodine. All charts were reviewed for demographic and surgical data to ensure parity in both groups. Variables examined included those that have been shown to increase the risk of infection. These variables included age, surgical approach (burr hole versus craniotomy), histology, location of tumor (intraparenchymal versus extraparenchymal), cranial location (supratentorial versus infratentorial), presence of a foreign body (ventricular drain, electrode, brachytherapy), prior surgery, prior radiation therapy, and whether the ventricle was opened during surgery. All wounds were classified as “clean” and not “clean-contaminated” or “contaminated”.

Data was gathered on presence of postoperative wound infection. Post-operative wound infection was defined as any culture-proven infection that occurred within either 30 or 90 days of surgery that required re-operation. All patients were taken for immediate re-

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operation when infection was suspected and none were managed with antibiotics alone. Chi squared tests were used to compare different groups.

RESULTS

General Characteristics

A total of 404 patients were included in this study. Patients were eliminated if the operative report could not be found, if there was no follow up after the surgery, or if the procedure was not a cranial surgery. Patient characteristics, surgical approaches, indications for surgery, and operative variables can be found in Table 1. The average age was 52.0 years with 24 patients under the age of 18. There was a foreign body (ventricular drain, brachytherapy, electrode) in 34 patients (8.4%), 92 patients (22.8%) had a prior operation, and 28 (6.9%) had prior radiation.

The surgical approaches were predominantly craniotomies (378 patients, 93.6%). There were 26 patients (6.4%) who had burr holes without a craniotomy. The indication for surgery was biopsy in 28 (6.9%), resection (for tumor or epileptogenic cortex) in 334 (82.7%), and electrode implant in 42 (10.4%) patients. Histology of surgical specimens were 97 (24.0%) metastasis, 86 (21.3%) glioblastoma multiforme, 20 (5.0%) astrocytoma, 12 (3.0%) oligodendroglioma, and 23 (5.7%) for epilepsy related resections (Table 1). Other types of pathology were involved, but each was much less common. There were 42 cases (10.4%) with electrode implants.

The operative characteristics varied as well. 244 surgeries (60.4%) were for intraparenchymal compared with extraparenchymal tumors and 367 (90.8%) were supra- compared with infratentorial location. The ventricles were opened in 56 (13.9%), a lumbar drain was used in 10 (2.5%), and brachytherapy seeds were left behind in 26 (6.4%) cases.

Betadine Irrigation

Betadine irrigation in addition to antibiotics was administered in 117 patients (29.0%). There were 3 infections with 90 days of the surgery, yielding an infection rate of 2.56% with betadine irrigation. Of the 287 patients with antibiotics but no betadine irrigation, there were 11 infections within 90 days of the procedure and an infection rate of 3.83%. Although these results indicate a 33% reduction in infection rate, a chi-squared test yielded a non-significant p-value of .53. In analyzing the number of infections within 30 days of the surgery, there were 2 infections in the betadine group (1.71%) and 5 infections (1.74%) in the antibiotics only group. This was only a 1.7% decrease with addition of betadine. A chi-squared test again produced a non-significant p-value of .98 (Table 2). The most common pathogen was *S. aureus*. The use of betadine did not appear to clearly influence the type of pathogen (Table 3). The surgical procedures associated with these infections included 9 craniotomies for tumor resection (64.3%), 1 burr hole biopsy (7.1%), 3 epilepsy implants (21.4%), and 1 epilepsy resection (7.1%).

A logistic regression analysis was carried out using betadine use, craniotomy, and presence of foreign body as independent variables and culture confirmed infection within 90 days as the dichotomous variable (Table 4). This analysis yielded an odds ratio of 0.6013 for betadine use. The interpretation is that individuals with betadine irrigation have odds of infection about 0.6× than those with no betadine irrigation controlling for craniotomy being the surgical procedure and presence of a foreign body. The coefficient for betadine was −0.51, but this was non-significant (p=.448).

Although there was a non-significant reduction in infection rates by 33% at 90 days, this may be related to the small sample size of this study. A small sample size decreases the

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statistical power and increases the chance for beta error, which is the percent chance to fail to reject the null hypothesis when it is actually false. With a sample size of 404, the statistical power of this study was only 8.2% which means almost a 90% chance to fail to capture that betadine significantly decreases infection rates compared to just antibiotic irrigation. A sample size calculation showed that to reach a power of 90%, the sample size would have to be almost 3000 patients.

One of the benefits of using betadine is its low cost. At our institution, a 240ml bottle of betadine costs $1.43. In contrast, gentamycin irrigation costs $1.80 per surgery at our institution. Using betadine alone amounts to a 20.5% savings. In this study we added betadine irrigation to our standard of care, namely antibiotic irrigation. Whether betadine irrigation can actually replace antibiotic irrigation, which would ultimately lower costs, warrants further study.

Confounding bias

In order to check for potential bias in calculating the difference in infection rates, we looked for any confounding factors between the betadine plus antibiotics and antibiotic only groups (Table 2). There was a significantly higher percentage of foreign bodies in place in the betadine plus antibiotics group versus the antibiotic only group. A foreign body is a risk factor for infection and thus this could artificially increase the infection rate for the betadine group. In addition, there were higher percentages of craniotomies in the betadine group. An open craniotomy is at higher risk for infection than a burr hole and this could again increase the infection rate seen in the betadine plus antibiotics group in this series. Lastly, age greater than 65 is a risk factor for infection, which was higher in the no betadine group and could have increased the infection rate in that group.

DISCUSSION

Prevention of post-operative wound infection is of paramount importance, not only for increasing patient safety and quality of care, but also in decreasing healthcare expenditures. Guidelines exist to decrease post-operative wound infections that include maneuvers such as treating pre-operative infections and diabetes, decreasing pre-operative length of stay, using closed suction drains, positive pressure ventilation in the operating room, and central sterilization of instruments, among others.[12] Antibiotic prophylaxis is routinely used by neurosurgeons to avoid postoperative infections in neurosurgical procedures. Several randomized trials have supported the use of antibiotic prophylaxis specifically in craniotomies. [3–9] The use of topical antibiotics have also been shown to decrease post-operative infection rates in addition to intravenous antibiotics. [13, 14] More recent studies have demonstrated that povidone-iodine irrigation (Betadine, Purdue Pharma, Stamford, CT) of surgical wounds effectively decreased rates of postoperative infection in a variety of surgical procedures with no significant risks.[10,11] Use for implanting deep brain stimulating electrodes has also been reported. [15] However, efficacy has never been tested in craniotomy patients. This retrospective study of a prospectively acquired database demonstrates a potential benefit for the addition of betadine to antibiotic prophylaxis in cranial neurosurgical procedures at 90 days after surgery. Korinek et al. report a post-craniotomy infection rate of 5.8% with antibiotic prophylaxis and Barker reported a rate of 8.8% in a meta-analysis of 8 studies. [1, 16] The infection rate with prophylactic antibiotics was slightly lower in this study, and even lower with the addition of betadine prophylaxis. We found a 33% decrease in infection rates in patients with betadine plus antibiotic prophylaxis versus solely antibiotic prophylaxis at 90 days, although this was not statistically significant with an alpha value of 5%. However, a major limitation to a study using patients at a single center with a single surgeon is a small sample size and low power of the study, increasing the probability of failing to identify a true difference between the

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two groups. There is the potential for a significant difference between the two groups if the sample size was around 3000 patients, which could be attained with a larger multicenter trial. Sample size limitations also explain the increased efficacy of betadine at 90 compared with 30 days. Prior studies have shown that infection rates increase at 90 days compared with 30 days, thus increasing the "effect size" of the measured parameter.[17]

The intrinsic differences in antimicrobial properties between typical antibiotics and povidone-iodine type antiseptics may help to explain differences in efficacy. Betadine has a broad microbicidal spectrum which includes fungi, protozoans, and viruses. In addition, resistance does not develop.[18] Antibiotics like gentamycin used in this study have limited spectrum and resistance can become a problem. This may be reflected in the fact that each of the two fungal infections happened in the antibiotic only group while there were no fungal infections when betadine was used. The decision to use gentamycin in the irrigation as prophylaxis was made at our institution at an institutional level and is not the choice of the operating surgeon. Whether other antibiotics would be more effective is certainly possible, although our infection rate with antibiotics alone was quite low, likely indicating some degree of efficacy.

A limitation to this study beyond the sample size is the potential for confounding bias associated with the significant group heterogeneity. A certain factor associated with higher infection rates may be more prevalent in one group or another. Indeed, in the betadine group there were more patients with implanted foreign bodies and craniotomies, both of which are known to increase infection rates. [1] However, this potential confounding bias would likely increase infection rates in the betadine group and only further supports the possibility that betadine irrigation may have some efficacy. Likewise, we did not examine the role of diabetes, controlled or poorly controlled, chronic steroid use, obesity and length of surgery to which we did not have accurate and complete records. A limitation to the use of betadine itself is that it cannot be used in patients who are allergic to iodine.

CONCLUSIONS

In this retrospective study we demonstrate a 33% decrease in post-craniotomy infection rates with the addition of betadine to regular antibiotic prophylaxis at 90 days after surgery. Although this was not statistically significant, sample size limitations given the low rate of infections in the antibiotic only group limit the power of the study. In addition, the heterogeneity of the groups may contribute to confounding of the results. The potential for betadine, a cheap, low toxicity antimicrobial, to decrease infection rates and reoperation for infection may warrant a larger multicenter trial. Whether betadine irrigation can replace antibiotic irrigation, which would lower cost, may also warrant further study.

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REFERENCES

1. Korinek AM, Golmard JL, Elcheick A, Bismuth R, van Effenterre R, Coriat P, Puybasset L. Risk factors for neurosurgical site infections after craniotomy: a critical reappraisal of antibiotic prophylaxis on 4,578 patients. Br J Neurosurg. 2005; 19:155–162. [PubMed: 16120519]
2. Hlavin ML, Kaminski HJ, Fenstermaker RA, White RJ. Intracranial suppuration: a modern decade of postoperative subdural empyema and epidural abscess. Neurosurgery. 1994; 34:974–980. discussion 980-971. [PubMed: 7916132]

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3. Geraghty J, Feely M. Antibiotic prophylaxis in neurosurgery. A randomized controlled trial. J Neurosurg. 1984; 60:724–726. [PubMed: 6368765]
4. Bullock R, van Dellen JR, Ketelbey W, Reinach SG. A double-blind placebo-controlled trial of perioperative prophylactic antibiotics for elective neurosurgery. J Neurosurg. 1988; 69:687–691. [PubMed: 3054011]
5. Young RF, Lawner PM. Perioperative antibiotic prophylaxis for prevention of postoperative neurosurgical infections. A randomized clinical trial. J Neurosurg. 1987; 66:701–705. [PubMed: 3553455]
6. Blomstedt GC, Kyttä J. Results of a randomized trial of vancomycin prophylaxis in craniotomy. J Neurosurg. 1988; 69:216–220. [PubMed: 3292719]
7. van Ek B, Dijkmans BA, van Dulken H, van Furth R. Antibiotic prophylaxis in craniotomy: a prospective double-blind placebo-controlled study. Scand J Infect Dis. 1988; 20:633–639. [PubMed: 3222676]
8. Djindjian M, Lepresle E, Homs JB. Antibiotic prophylaxis during prolonged clean neurosurgery. Results of a randomized double-blind study using oxacillin. J Neurosurg. 1990; 73:383–386. [PubMed: 2117055]
9. Gaillard T, Gilsbach JM. Intra-operative antibiotic prophylaxis in neurosurgery. A prospective, randomized, controlled study on cefotiam. Acta Neurochir (Wien). 1991; 113:103–109. [PubMed: 1799151]
10. Cheng MT, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Efficacy of dilute betadine solution irrigation in the prevention of postoperative infection of spinal surgery. Spine (Phila Pa 1976). 2005; 30:1689–1693. [PubMed: 16094267]
11. Chundamala J, Wright JG. The efficacy and risks of using povidone-iodine irrigation to prevent surgical site infection: an evidence-based review. Can J Surg. 2007; 50:473–481. [PubMed: 18053377]
12. Mehta G, Ransjo U. Prevention of postoperative wound infections - what would be worthwhile, and what might be done? Int J Infect Contr. 2008; 4
13. Miller JP, Acar F, Burchiel KJ. Significant reduction in stereotactic and functional neurosurgical hardware infection after local neomycin/polymyxin application. J Neurosurg. 2009; 110:247–250. [PubMed: 19263587]
14. Caroom C, Tullar JM, Benton EG, Jones JR, Chaput CD. Intrawound Vancomycin Powder Reduces Surgical Site Infections in Posterior Cervical Fusion. Spine (Phila Pa 1976). 2013
15. Fenoy AJ, Simpson RK. Management of device-related wound complications in deep brain stimulation surgery. J Neurosurg. 2012; 116:1324–1332. [PubMed: 22404671]
16. Barker FG. Efficacy of prophylactic antibiotics for craniotomy: a meta-analysis. Neurosurgery. 1994; 35:484–490. discussion 491-482. [PubMed: 7646627]
17. Jonkers D, Elenbaas T, Terporten P, Nieman F, Stobberingh E. Prevalence of 90-days postoperative wound infections after cardiac surgery. Eur J Cardiothorac Surg. 2003; 23:97–102. [PubMed: 12493512]
18. Reimer K, Wichelhaus TA, Schäfer V, Rudolph P, Kramer A, Wutzler P, Ganzer D, Fleischer W. Antimicrobial effectiveness of povidone-iodine and consequences for new application areas. Dermatology. 2002; 204(Suppl 1):114–120. [PubMed: 12011534]

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Table 1

General Characteristics

	Betadine n = 117	No Betadine n = 287	Total n = 404
Patient Characteristics			
Age, mean (SD), y	54.4	51.0	52.0 (18.8)
Age < 18 y, No. (%)	5	19	24 (5.9)
Foreign body (ventricular drain, brachytherapy, electrodes)	19	15	34 (8.4)
Prior Operation	22	70	92 (22.8)
Prior Radiation	5	23	28 (6.9)
Surgical Approach (%)			
Burr Hole Only	2	14	26 (6.4)
Craniotomy	115	263	378 (93.6)
Indication (%)			
Biopsy	3	25	28 (6.9)
Resection	114	262	334 (82.7)
Metastasis	28	69	97 (24.0)
Glioblastoma Multiforme	24	62	86 (21.3)
Astrocytoma	9	11	20 (5.0)
Oligodendroglioma	3	9	12 (3.0)
Epilepsy Related	2	21	23 (5.7)
Electrode Implant	8	34	42 (10.4)
Operative Variables (%)			
Intraparenchymal	70	174	244 (60.4)
Extraparenchymal	47	113	59 (14.6)
Supratentorial	103	264	367 (90.8)
Infratentorial	14	23	37 (8.9)
Ventricle Opened	14	42	56 (13.9)
Lumbar Drain	2	8	10 (2.5)
Brachytherapy	9	17	26 (6.4)

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Table 2

Infection Rates with Betadine Irrigation

	Betadine	No Betadine	Total	p-value
Infection rate within 90 days	2.56%	3.83%	3.47%	.5271
Infection rate within 30 days	1.71%	1.74%	1.73%	.9817
Confounding Factors				
Intraparenchymal	70 (59.8)	174 (60.6)		.882
Supratentorial	103 (88.0)	264 (92.0)		.212
Ventricle Opened	14 (12.0)	42 (14.6)		.481
Lumbar Drain	2 (1.7)	8 (.70)		.527
Foreign Body	18 (15.4)	13 (4.5)		.018
Prior Operation	22 (18.8)	70 (24.4)		.225
Prior Radiation	5 (4.3)	23 (8.0)		.179
Craniotomy	115 (98.3)	263 (91.6)		.013
Age > 65	41	73		.052

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Table 3

Pathogens of Infection

Infections Within 90 Days N = 14 (%)	Infections Within 30 Days N = 7 (%)	Betadine N = 3 (%)	Antibiotics N = 11 (%)
Staphylococcus. spp (50.0)	Staphylococcus. spp (42.9)	Staphylococcus. spp (33.3)	Staphylococcus. spp (54.5)
Enterobacter. spp (21.4)	Enterobacter. spp (28.6)	Enterobacter. spp (33.3)	Enterobacter. spp (18.2)
P. acnes (14.3)	P. acnes (14.3)	P. acnes (33.3)	P. acnes (9.1)
C. albicans (7.1)	C. albicans (14.3)		C. albicans (9.1)
Klebsiella (7.1)			Klebsiella (9.1)

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Table 4

Logistic Regression

Variable	Coefficient	SE	P-value	Odds Ratio
Betadine use	−0.5086	0.6695	0.4475	0.6013
Craniotomy	−0.2546	1.0768	0.8131	0.7752
Foreign Body	1.0226	0.5854	0.0807	2.7803

SE= standard error