ORIGINAL ARTICLE

Effect Of Topical Vancomycin Powder on the prevention of surgical site infections in craniotomy surgeries

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ABSTRACT

Background: One of the most common complications of craniotomy is an infection at the surgical site. The use of different antibiotics to prevent infection has been studied in various studies, and vancomycin is one of these antibiotics.
Aim: To examine the effect of topical vancomycin powder on the prevention of operative infections in craniotomy surgeries.
Methods: This is a case-control study on patients undergoing craniotomy. All patients received standard systemic prophylactic antibiotics, including one gram of intravenous cefazolin before surgery. In the case group, at the end of the operation, one gram of vancomycin powder was applied locally to ulcers. All patientswere re-examined two weeks postoperatively, and wound status was evaluated based on surgical site infection criteria. Data were analyzed by SPSS-22.
Result: Two-hundred (126 male) patient enrolled to study.There was no significant statistical difference between the two groupsbased on age and gender (P>0.05). Surgical site infection between two groups was not statistically significant (P=0.157). In women, there was no infection in the vancomycin group, whereas in the control group, 5 cases (12.5%) were observed and were statistically significant (P=0.033). Between infection with wound dehiscence, age, and wound size have positively and significantly correlated.
Conclusion: The results of this study showed that increasing age, increasing length of incision, and the occurrence of surgical wound dehiscence are more likely to be associated with wound infection. Another result was that increased wound length was associated with increased wound dehiscence.
Keywords: Craniotomy, Vancomycin, Infection, Surgery

INTRODUCTION

The craniotomy is a type of brain surgery that removes part of the skull bone for easy access to brain tissue. In craniotomy, anesthesiais generally performed, but in some cases, local anesthesia is used. Like other surgeries, this type of surgery is associated with some complications; one of the most common complications is an infection at the surgical site[1,2]. Surgical site infection is associated with many complications, including increased morbidity, increased hospitalization, increased hospital costs, antibiotic resistance, and even increased patient mortality[3,4].

The incidence of these infections in patients undergoing clean extra-abdominal such as craniotomy is much lower than in patients undergoing internal abdominal surgery, with a reported infection rate of about 2 - 5%[5]. Many studies have been done on the risk factors of surgical site infection in neurosurgery, and the identification of these factors in the prevention of these infections is critical, but the underlying causes remain unclear. For this reason, prophylaxis methods are essential to prevent surgical site infections[6-10].

The source of most surgical site infections are bacteria that enter the wound at the time of surgery. Different microorganisms can cause endemic and epidemic nosocomial infections that are subject to conditions such as underlying disease, use of immunosuppressive drugs, and prior antibiotic use. Any strain of bacteria in the hospital can cause nosocomial infections, but the most common bacteria are E. coli. In a study in the United States, among the infectious agents, gram-positive Staphylococcus aureus, Staphylococcus coagulase-negative, and Enterococcus were identified as the most infectious organisms[8,11,12]. Vancomycin is a glycopeptide antibiotic used against Staphylococcus, the most common pathogenic bacterial strain in surgical infections. The antibacterial function of vancomycin is to limit cell wall biosynthesis in Gram-positive bacteria. The use of different antibiotics to prevent infection has been studied in different studies, and vancomycin is one of these antibiotics. For example, in a survey by Rivikumar et al. on 350 patients to evaluate the rate of infection after craniotomy after vancomycin powder use, the results showed that vancomycin powder reduced the rate of craniotomy postoperative infection less than 2.2%[13]. In another study, Abdullah et al. studied 150 patients who underwent craniotomy and concluded that vancomycin powder significantly reduced the rate of surgical site infection compared to the control group[14]. On the other hand, a study by Ghobrial et al. concluded that using the powder of vancomycin during surgery did not affect the incidence of spinal cord infections caused by gram-negative organisms

or the incidence of polymicrobial infections[15]. In a systematic review of the efficacy of topical vancomycin powder in craniotomy surgery, they concluded that there was currently insufficient evidence for topical vancomycin use to prevent surgical infections. Still, many surgeons use this method to control infection[4].As can be seen, the data and results in this field are minimal and different, and no study has been conducted in Iran. This study aimed to examine the effect of topical vancomycin powder on the prevention of operative infections in craniotomy surgeries.

MATERIALS AND METHODS

This is a case-control study on patients undergoing craniotomy in Imam Khomeini Hospital in Sari, Iran, from March 2019 to March 2020. The study population consisted of all patients over 18 years of age undergoing craniotomy. Exclusion criteria were patients who needed general surgical procedures, orthopedics, urology, or had a previous history of infection at the surgical site. Finally, 200 people were enrolled in the study using statistical methods and considering the sample size of other studies. Patients were randomly divided into two groups (case and control) after randomization.

Intervention: All patients received standard systemic prophylactic antibiotics, including one gram of intravenous cefazolin before surgery and then every 8 hours to one day after surgery. The controlled dose was injected if the procedure was longer than 4 hours. In the case group, at the end of the surgery, 1 g of vancomycin powder was applied locally to ulcers below 10 cm and 1.5 g for ulcers higher than 10 cm. All patients were re-examined two weeks postoperatively, and wound status was evaluated based on surgical site infection criteria(5). Wound remission, inflammatory markers (ESR, CRP, and white blood cell count) were also assessed.

Ethical Consideration: This study was conducted after approval by the Vice-Chancellor for Research and Technology of Mazandaran University of Medical Sciences and approved by the Ethics Committee (Code: IR.MAZUMS.IMAMHOSPITAL.REC.1397.057). First, the purpose of the study and how it was implemented for patients and their companions were explained, and consent to participate in the survey was given.

Statistical analysis: For descriptive data, mean standard deviation and frequency tables were used. In order to analyze the data and compare in two groups, independent t-test and chi-square test were used. Spearman Rho's coefficient was used to investigate the correlation. All data were analyzed by Statistical Package for the Social Sciences (SPSS) version 22.

RESULTS

A total of 200 patients were enrolled in this study. Sixty-six cases (66%) in the vancomycin-treated group and 60 cases in the control group (60%) were male. There was no significant statistical difference between the two groups. (P-Value=0.380). The mean age and standard deviation of patients in the vancomycin group were 48.97 ±13.89 years old and in control group were 51.08 ±14.45 old years, which had no significant difference (P-Value = 0.295). The type of surgery was evaluated between the two groups, and the results are shown in the diagram below. It should be noted that the cause or type of surgery did not show a statistically significant difference between the two groups (P-Value = 0.928). The general causes of surgery were evaluated in patients (Figure 2).

Mean and standard deviation of laboratory findings, bleeding rate, wound size, and duration of surgery in vancomycin and control groups Were investigated; the CRP and WBC levels were slightly higher in the vancomycin group. However, there was no significant difference between the two groups in all variables (p>0.05) (Table1).

Surgical site infection was 7 (7%) cases in the vancomycin group and 13 (13%) cases in the control group, but it was not statistically significant (P-Value=0. 157). Furthermore, The rate of surgical site infection in the two study groups was evaluated by age and sex, the results of which are shown in the following table. In terms of gender, these results were significant, and in women, there was no infection in the vancomycin group. In contrast, in the control group, 5(12.5%) were observed and were statistically significant (P-Value = 0.033). This condition was not significant in male gender (P-Value = 0.673). Dehiscence was also evaluated in patients in both groups according to age and gender. Only in the age group over 53 years, the rate of separation was significantly higher in the vancomycin group (18.6% vs 7.5%, P-Value = 0.044). (Table 2).

Figure 1. Frequency of type of surgery performed in vancomycin and control group

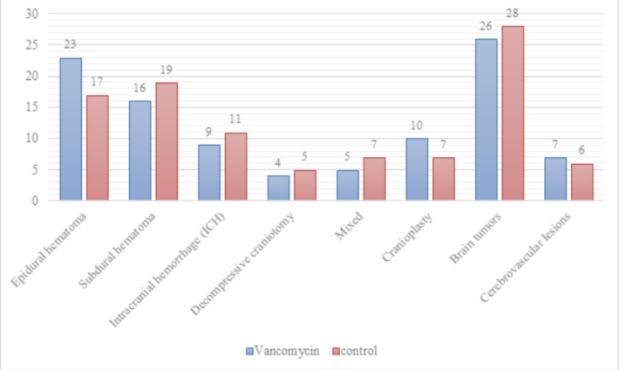
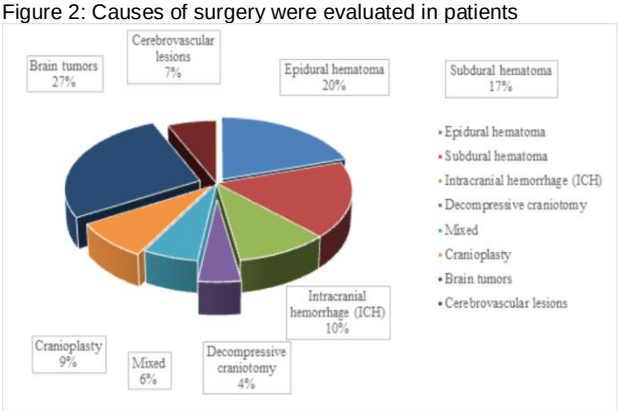


Figure 2: Causes of surgery were evaluated in patients



Duration of surgery, size of the wound, amount of bleeding, and laboratory findings were evaluated based on

the presence or absence of infection. The results showed that wound length was significantly higher in cases of infection (16.57 vs 10.62 and P-Value = 0.044). There was no difference in bleeding between cases with and without infection (P-Value = 0.314). There was also no significant difference between the duration of surgery and the incidence of wound infection (P-Value = 0.975). On the other hand, laboratory findings of CRP, ESR, and WBC were significantly higher in cases of wound infection ($p < 0.05$), which are shown in the following table.

Correlations between demographic variables wound variables, and laboratory variables with infection and detachment were evaluated. According to the results between infection with wound Dehiscence (cc = 0.622, P =0.0001), Infection with age (cc = 0.356, P = 0.0001), Wound size with infection (cc = 0.417, P = 0.0001) and Wound size with Dehiscence (cc = 0.559, P = 0.0001) have positively and significantly correlated. That is to say, with the increase of the abundance of another, it also increases. Among laboratory variables, CRP and WBC were positively and significantly correlated with infection and wound Dehiscence ($P < 0.05$).

Table1.Mean (SD) of laboratory findings, bleeding rate, wound size and duration of surgery in vancomycin and control groups

Variable	Groups		P-Value
	Vancomycin	Control	
Duration of surgery	2.98 (0.93)	3.06 (0.98)	0.554
Wound Size	11.04 (2.78)	10.76 (2.52)	0.456
Hemorrhage	288.2 (78.92)	292.5 (84.48)	0.710
CRP	0.46 (0.8)	0.52 (0.88)	0.257
ESR	38.17 (16.26)	43.17 (22.75)	0.075
WBC	8176 (3143.64)	8347 (3252.86)	0.158

Table 2: The rate of surgical site infection and dehiscence in the two study groups based on age and gender. N (%)

Variables		Dehiscence	Group		P-Value	Infection	Group		P-Value
			Vancomycin	Control			Vancomycin	Control	
Gender	Male	No	57 (86.4)	57 (95)	0.099	No	59 (89.4)	52 (86.7)	0.637
		Yes	9 (13.6)	3 (5)		Yes	7 (10.6)	8 (13.3)	
	Female	No	31 (91.2)	39 (97.5)	0.231	No	34 (100)	35 (87.5)	0.033
		Yes	3 (8.8)	1 (2.5)		Yes	0	5 (12.5)	
Age	≤ 53	No	53 (93)	47 (100)	0.064	No	57 (100)	47 (100)	NS
		Yes	4 (7)	0		Yes	0	0	
	> 53	No	35 (81.4)	49 (92.5)	0.044	No	36 (83.7)	40 (75.5)	0.322
		Yes	8 (18.6)	4 (7.5)		Yes	7 (16.3)	13 (24.5)	

Table 3: Duration of Surgery, size of the wound, amount of bleeding and laboratory findings based on the presence or absence of infection. Mean (SD)

Variable	Infection	Vancomycin		Control	P-Value
		Mean	P-Value	Mean	
Duration of surgery	No	2.98 (0.95)	0.842	3.06 (0.99)	0.975
	Yes	2.91 (0.59)		3.05 (0.9)	
Wound Size	No	10.62 (2.34)	0.0001	10.14 (1.95)	0.0001
	Yes	16.57 (2.22)		14.92 (1.8)	
Hemorrhage	No	287.20 (77.70)	0.648	289.19 (84.31)	0.314
	Yes	301.43 (99.9)		314.61 (85.6)	
CRP	No	0.45 (0.6)	0.0001	0.29 (0.57)	.0001
	Yes	2.86 (0.38)		2 (1.15)	
ESR	No	37.7 (15.31)	0.293	39.86 (18.66)	.0001
	Yes	44.43 (26.82)		65.31 (34.1)	
WBC	No	8240.86 (2581.89)	0.0001	7635.63 (2023.98)	.0001
	Yes	17285.71 (5219.01)		13107.69 5451.06)	

DISCUSSION

This study aimed to evaluate the effect of topical vancomycin powder on the prevention of operative infections in craniotomy surgeries. Surgical wound infection (SSI) is one of the major complications after surgery that, despite the use of prophylactic antibiotics and aseptic methods, accounts for about 22% of all patients' health-related infections(6). SSIs are the second health-care-related infection in the United States, imposing between $ 1 and $ 10 billion annually on the health system(4, 7, 16, 17). The prevalence of SSI is increasing following the use of current treatments such as prophylaxis with intravenous antibiotics due to increased bacterial resistance. As a result, other preventive strategies, such as the use of topical antibiotics that could theoretically reduce area bacterial burden, even those with moderate resistance, have been suggested, including the application of vancomycin powder(18, 19). However, studies using vancomycin powder to prevent surgical site infection continue to be controversial, as studies in this area have reported conflicting results(20-22).

There was no significant difference between the two groups in terms of age and sex, which indicates a good match between the two groups. The results of this study showed that the rate of wound infection in craniotomy

surgery in the vancomycin group 2 weeks after surgery was almost half lower than in the control group, but this was not statistically significant. On the other hand, in the evaluation of gender, the rate of infection in the vancomycin group was significantly lower in women. Still, it was not significantly different in the men group. The results of our study also showed that the rate of dehiscence was higher in 53 years, and the older group, which was statistically significant.

Also, in our study, correlational research showed that the infection rate had a significant positive correlation with age, wound dehiscence, and wound size. These can be considered as risk factors for infection. Also, ulcer dehiscence had a positive and significant correlation with wound size. In this regard, studies have been carried out that will be discussed below and compared. Chiang et al[17].. In their meta-analysis study, evaluated the efficacy of topical vancomycin powder for reducing surgical site infection. Collected evidence showed that vancomycin powder had a significant protective effect against surgical site infection.

This study is less valuable than our study because our research is a clinical trial, but the results were not consistent with the results of our research. In another meta-analysis study on the efficacy of topical vancomycin powder to reduce surgical site infection, the collected evidence showed that vancomycin powder had a significant protective effect against surgical site infection[19]. This study has not only examined craniotomy procedures, but also other surgical procedures were evaluated. In another study, Emohare et al[12] Designed and implemented a survey aimed at cost-effectiveness analysis using vancomycin powder in craniotomy surgery. The study showed that vancomycin powder, combined with other common antibiotics, might be useful in reducing the rate of surgical infection.

Also, in a retrospective study by Neill et al[23], the control group included 54 patients who received normal systemic prophylactic only, and the treatment group included 56 patients who received vancomycin powder in addition to normal systemic preventive. During this study, it was found that the use of vancomycin powder in surgical wounds of traumatic patients who underwent surgery reduced the rate of surgical site infection. The difference between this study and our study was that this study only examined traumatic patients, while in our different operations of craniotomy were evaluated. In a study investigating the use of vancomycin powder to reduce surgical site infections following craniotomy, a case-control study was performed on five patients who had undergone craniotomy. The results of their research showed that vancomycin powder significantly reduced the rate of surgical site infection compared to the control group following craniotomy (1 case in the intervention group and 5 cases in the control group, respectively[24]. The results of these studies were not consistent with our research, however, in contrast to those reported in the survey by Ghobrial et al[15]., Which examined the use of vancomycin in craniotomy infection. After completion of treatment, 66 patients (6.71%) had surgical site infection, and 51 patients (5.02%) had a positive culture. Finally, the study found that vancomycin powder during surgery had no significant effect on the incidence of spinal cord infections caused by gram-negative organisms or the occurrence of polymicrobial infections.

Similarly, Tubaki et al[21]. studied 907 patients undergoing craniotomy. The results of their study showed that vancomycin powder during surgery did not reduce the rate of infection compared to the control group (28). Also, Kang et al[18]. in a systematic review study reviewing existing databases, investigated the efficacy of topical vancomycin powder in craniotomy surgery. They concluded that there is currently insufficient evidence for topical vancomycin use to prevent surgical infections. But despite this, many surgeons use this method to control infection.

As can be seen, the results of the studies are very different and contradictory and require further investigation with larger sample size and these differences could be due to differences in sample size and population, type of study design, and patients' baseline conditions. It is recommended that a more extensive population study, longer follow-up, and more focus on only one type of surgical procedure and one type of surgical complication need to be designed and implemented in the future to evaluate the efficacy of vancomycin powder.

CONCLUSION

According to the results of our study, although the infection rate was lower in the vancomycin group, the results were not statistically significant. The results of this study showed that increasing age, increasing length of incision, and the occurrence of surgical wound dehiscence are more likely to be associated with wound infection. Another result was that increased wound length was associated with increased wound dehiscence.

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Conflict of Interest: None.

REFERENCES

1. Gerometta A, Olaverri JCR, Bitan F. Infections in spinal instrumentation. International orthopaedics. 2012;36(2):457-64.
2. .Godil SS, Parker SL, O'Neill KR, Devin CJ, McGirt MJ. Comparative effectiveness and cost-benefit analysis of local application of vancomycin powder in posterior spinal fusion for spine trauma. Journal of Neurosurgery: Spine. 2013;19(3):331-5.
3. Abdullah KG, Attiah MA, Olsen AS, Richardson A, Lucas TH. Reducing surgical site infections following craniotomy: examination of the useof topical vancomycin. Journal of neurosurgery. 2015;123(6):1600-4.
4. Bakhsheshian J, Dahdaleh NS, Lam SK, Savage JW, Smith ZA. The use of vancomycin powder in modern spine surgery: systematic review and meta-analysis of the clinical evidence. World neurosurgery. 2015;83(5):816-23.
5. Leaper D. Surgical-site infection. British journal of Surgery. 2010;97(11):1601-2.
6. Abdul-Jabbar A, Takemoto S, Weber MH, Hu SS, Mummaneni PV, Deviren V, et al. Surgical site infection in spinal surgery: description of surgical and patient-based risk factors for postoperative infection using administrative claims data. Spine. 2012;37(15):1340-5.
7. Burke JP. Infection control--a problem for patient safety. The New England journal of medicine. 2003;348(7):651.

8. Chiang H-Y, Herwaldt LA, Blevins AE, Cho E, Schweizer ML. Effectiveness of local vancomycin powder to decrease surgical site infections: a meta-analysis. The Spine Journal. 2014;14(3):397-407.
9. Sabzghabaei F, Akhtar M, Hashemi SMR, Mollahoseini R. Adipsic diabetes insipidus: A single-center case series. Nephro-Urology Monthly. 2018;10(1.(
10. Moradi A, Sabzghabaei F, Kalantar M. The Available Clinical Approaches to the Management of Patients with Acute and Chronic Hypernatremia. Open Access Macedonian Journal ofMedical Sciences. 2020;8(F):1-10.
11. Ducel G, Fabry J, Nicolle L, Organization WH. Prevention of hospital-acquired infections: a practical guide. 2002.
12. Emohare O, Ledonio C, Hill B, Davis R, Polly D, Kang M. Cost savings analysis of intrawound vancomycin powder in posterior spinal surgery. The Spine Journal. 2014;14(11):2710-5.
13. Ravikumar V, Ho AL, Pendhakar AV, Sussman ES, Chow K-h, Li G. The Use of Vancomycin Powder for Surgical Prophylaxis Following Craniotomy. Neurosurgery. 2017;80(5):754-8.
14. Kang DG, Holekamp TF, Wagner SC, Lehman RA. Intrasite vancomycin powder for the prevention of surgical site infection in spine surgery: a systematic literature review. The Spine Journal. 2015;15(4):762-70.
15. Ghobrial G, Thakkar V, Andrews E, Lang M ,Chitale A, Oppenlander M. Intraoperative Vancomycin Use in Spinal Surgery: Single Institution Experience and Microbial Trends. Spine. 2014;39(7):550-5.
16. .Berríos-Torres SI, Sarah HY, Bratzler DW, Ma A, Mu Y, Zhu L, et al. Activity of commonly used antimicrobial prophylaxis regimens against pathogens causing coronary artery bypass graft and arthroplasty surgical site infections in the United States, 2006–2009. Infection Control & Hospital Epidemiology. 2014;35(3):231-9.
17. Chiang H, Harwaldt L, BlevinsA, Cho E, Schweizer M. Effectiveness of local vancomycin powder to decrease surgical site infections: a meta-analysis. spine. 2014;14(3):397-407.
18. Kang D, Holekamp T, Wagner S, Lehman R. Intrasite vancomycin powder for the prevention of surgical siteinfection in spine surgery: a systematic literature review. The Spine Journal. 2015;15(4):762-70.
19. Martin ET, Kaye KS, Knott C, Nguyen H, Santarossa M, Evans R, et al. Diabetes and risk of surgical site infection: a systematic review and meta-analysis .infection control & hospital epidemiology. 2016;37(1):88-99.
20. Tjeertes EE, Hoeks SS, Beks SS, Valentijn TT, Hoofwijk AA, Stolker RJR. Obesity–a risk factor for postoperative complications in general surgery? BMC anesthesiology. 2015;15(1):112.
21. Tubaki VR, Rajasekaran S, Shetty AP. Effects of using intravenous antibiotic only versus local intrawound vancomycin antibiotic powder application in addition to intravenous antibiotics on postoperative infection in spine surgery in 907 patients. Spine. 2013.55-2149:(25)38;
22. Xiang J, Guo W, Wan Y, Zhao Y. Therapeutic efficacy of combined Vancomycin infusion and continuous lumbosacral cerebrospinal fluid drainage in the treatment of staphylococci-induced intracranial infection after craniotomy. Journal ofTropical Medicine (Guangzhou). 2009;9(9):1038-43.
23. Neill K, Smith J, Abtahi A, Archer K, Spengler D, McGirt M, et al. Reduced surgical site infections in patients undergoing posterior spinal stabilization of traumatic injuries using vancomycin powder .The Spine Journal. 2011;11(7):641-6.
24. Graf K, Ott E, Vonberg R-P, Kuehn C, Schilling T, Haverich A, et al. Surgical site infections—economic consequences for the health care system. Langenbeck's archives of surgery. 2011;396(4):453