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SNI: Infection

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*Original Article*

# Role of topical vancomycin in reduction of postoperative infections in head trauma patients: A developing country experience

Ahmed Atallah[1], Mohammad Elbaroody[1], Ahmed A. Aziz N. Hassan[1], Ahmed M. Ali[1], Mohamed E. Elhawary[2]

[1]Department of Neurosurgery, Cairo University Hospitals, Cairo University, [2]Department of Neurosurgery, Benha University, Cairo, Egypt.

E-mail: Ahmed Atallah - ahmed.atallah09@kasralainy.edu.eg; *Mohammad Elbaroody - mohammad.elbaroody@kasralainy.edu.eg; Ahmed A. Aziz N.Hassan-ahmedabdelaziz.neuro@gmail.com; Ahmed M. Ali - ahmed.saad@kasralainy.edu.eg; Mohamed E. Elhawary - dr_hawary1980@yahoo.com

***Corresponding author:**
Mohammad Elbaroody,
Department of Neurosurgery,
Cairo University Hospitals,
Cairo University, Cairo, Egypt.

mohammad.elbaroody@kasralainy.edu.eg

Received : 27 June 2021
Accepted : 05 November 2021
Published : 08 December 2021

**DOI**
10.25259/SNI_640_2021

**Quick Response Code:**

## ABSTRACT

**Background:** Postoperative cranial wound infections are a major cause of morbidity, mortality, and financial burden, especially in developing countries.

**Methods:** We prospectively studied 86 patients in a randomized trial; 39 patients received one gram of topical vancomycin powder in the subgaleal space while 47 matched control patients did not. Both groups received identical intraoperative and post-operative care. The primary outcome variable was the postoperative wound infections rate factored by cohort. Secondary outcomes were the timing of infection and the rate of adverse events.

**Results:** Adding topical vancomycin was associated with a significantly lower rate of infection than the standard of care alone (2.6% [1/39] vs. 14.9% [7/47], *P* =.004). No adverse reactions occurred.

**Conclusion:** Topical vancomycin is safe, and effective in the prevention of surgical site infections following craniotomy. These findings have broad consequences for neurosurgery practice, especially in developing countries with high incidence of head trauma.

**Keywords:** Craniotomy, Head trauma, Surgical-site infection, Vancomycin, Wound

## INTRODUCTION

Surgical site infections (SSIs) are the most common complication encountered in surgically treated patients.[10] The incidence of post-operative infection in cranial surgery varied from 0.7% up to 8.9%.[13,21] Some studies showed that antibiotic prophylaxis lowered the occurrence of incision infections, but did not prevent meningitis.[11,12] The increased blood supply to the scalp is supposed to reduce the risk of infection.[3] Vancomycin has a broad-spectrum action against gram-positive bacteria, especially coagulase-negative staphylococci (e.g., *Staphylococcus epidermis*) and *Staphylococcus aureus*, which are found mainly in skin flora and responsible for most of the SSIs.[8,17] In the literature, there has been a rise in the use of topical vancomycin to guard against infections to include not only cardiothoracic and spine surgery but also cranial surgery.[1,2,9,15,18,19] In this prospective randomized controlled study, we evaluated the role of topical vancomycin powder in the reduction of postoperative wound infections in 86 head trauma patients operated upon in our center.

## MATERIALS AND METHODS

### Study design

We obtained an institutional review board approval for a single-center, prospective, randomized controlled study of patients undergoing cranial surgery after head trauma to determine whether topical vancomycin reduces the risk of postoperative wound infections or not.

### Study population

The study was conducted in the department of neurosurgery, faculty of medicine, Cairo University, Egypt in the period from January 2020 to September 2020 on head trauma patients who needed cranial surgery, and met the inclusion criteria. All procedures performed were approved by Institutional Review Board (MS-193-2020), and informed consent was obtained from each of the patients or their families.

Inclusion criteria were as follows: Head trauma adult patients 13–65 years, Glasgow Coma Score (GCS) (9–15) on admission, and fit for surgery. Exclusion criteria were as follows: Age <13 and >65 years, elective cranial surgery cases, high-risk medical condition, GCS <9.

### Patient selection and study intervention

This study included 86 patients of various age groups who were randomly assigned into two groups: Group A, 39 patients receiving 1 g of topical vancomycin powder in the subgaleal space (case group); and group B, 47 matched patients without application of topical vancomycin.

We gave intravenous cefazolin within 30 min of incision and continued for 48 h, we used betadine to clean the skin after shaving. Patients in the vancomycin cohort received 1 g of vancomycin powder sprinkled evenly in the subgaleal flap over the bone flap after the final wound irrigation before closure. Wounds were closed in layers and covered by dressings. We removed dressings on postoperative day 1, while sutures were removed in the 14$^{th}$ postoperative day.

In the follow-up clinic, we looked for local signs of infection e.g. pus, collection, fever, tenderness; patient with those signs were admitted, then swab from the wound taken for culture and sensitivity followed by empirical intravenous antibiotics. Patients either continue on conservative treatment or surgical debridement could be done according to clinical situation.

### Follow-up and study's outcomes

Patients were then followed up for up to 120 days to assess the study's outcomes. The primary outcome variable SSI was defined as culture-positive wound infection within 120 d of surgery. The secondary outcomes were the timing of infection and the rate of adverse events.

### Sample size calculation

The minimum sample size was calculated by using PASS software (PASS 11 citation: Hintze J (2011). PASS 11. NCSS, LLC. Kaysville, Utah, USA). Based on the previous report by Mallela and colleagues, the addition of topical vancomycin was associated with a significantly lower rate of SSI than the standard of care alone (0.49% [1/205] vs. 6% [9/150], $P = 0.002$).[15] Setting alpha error at 5% and power at 80%.

### Statistical methods

Data were collected, tabulated, statistically analyzed with Statistical Package of Social Science version 20 and Epi Info 2000 programs. Descriptive statistics: in which quantitative data were presented in the form of the mean ($\bar{x}$), standard deviation, range, and qualitative data were presented in the form of numbers (No) and percentages (%). Analytical statistics: Student's *t*-test (t) was used for comparison between two groups having quantitative parameter variables one way, nova test (f) was used for multiple groups comparison with quantitative parameter variables; Chi-squared test ($\chi^2$) was used to study the association between two qualitative variables, Fisher's exact test for 2 × 2 tables when expected cell count of more than 25% of cases was <5; Mann Whitney test (U) was used for comparison between two groups having quantitative non-parameter variables, Kruskal-Wallis test was used for comparison between groups of not normally distributed variables, and Pearson correlation (r) was used to measure the association between two quantitative variables.

## RESULTS

A total of 112 patients of various age groups were involved in traumatic cranial neurosurgical procedures at the neurosurgery department in Cairo University Hospitals. Out of 112 patients, 26 patients were excluded due to either not meeting the inclusion criteria ($n = 17$) or refused to sign the written informed consent ($n = 9$). Thus, a total of 86 patients were included in the present analysis. According to the type of intervention to be used, patients were randomly allocated into 2 groups: Group A: 39 patients receiving 1 g of topical vancomycin powder in the subgaleal space (case group), and Group B: 47 matched patients without application of topical vancomycin. [Figure 1] summarizes the study flowchart.

There was no statistically significant difference between males and females in terms of percentages. The mean age was roughly equal with no significant difference between groups. Regarding patients' factors that could be linked to postoperative infection, there were no statistically significant differences between studied groups regarding the smoking

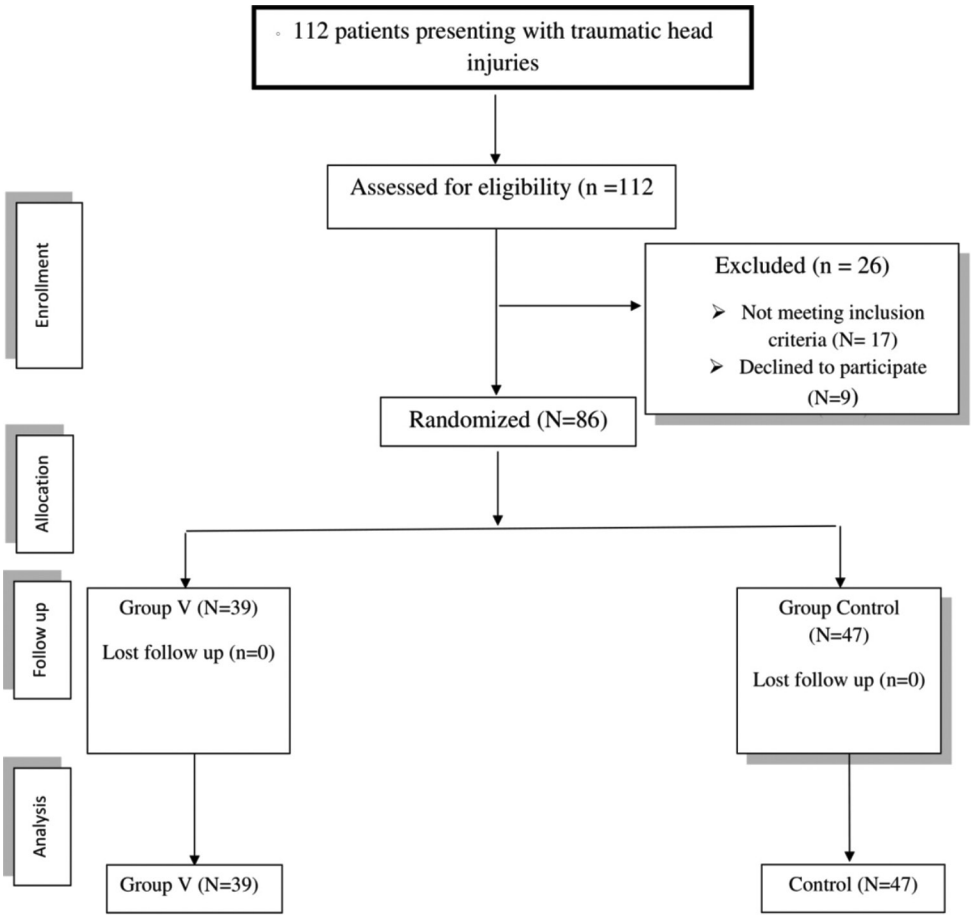


**Figure 1:** The study flow chart.

($P$ = 0.65), hypertension ($P$ = 0.9), and diabetes ($P$ = 0.65). Regarding pathological cause, In the vancomycin group, compound depressed fractures were the most common pathology (58.9%); while in the control group, they were equal to unilateral to extradural hematoma (40.4%). [Table 1] summarizes the clinical data of patients in the vancomycin and control group.

The main outcome which is SSI was lower in the patients in the vancomycin group ($P$ = 0.04), however; There was no statistical difference between the studied groups regarding the interval till infection occurs, complications, and mortality. [Table 2] summarizes the clinical outcomes and complications in both groups.

## DISCUSSION

Topical vancomycin has proved itself as a valuable drug in the decrease of postoperative infection in cranial surgery in many studies.[1,9,15,19] Our prospective series consolidates this evidence, especially in head trauma patients even with compound fractures which have additional risk for infection.

Risk factors for postoperative craniotomy infections include gender, age, emergency procedure, longer procedure duration, and postoperative CSF leakage.[5] In our series, there were no significant differences in any of these risk factors between our two groups.

The incidence of postoperative central nervous system infections varied in the literature from 0.8%,[16] and 1.8%[14] up to 8.60%,[4] and 9.86%.[6] The reported incidence of postoperative infection after use of topical vancomycin in randomized trials was 0%,[19] 0.49%,[15] 1.3%.[1] In our series, postoperative infection in the vancomycin group occurred in a single patient 2.6% while seven patients in the control group 14.9% ($P$ = 0.04).

Serum vancomycin levels stay normal therapeutic or subtherapeutic to undetectable after intrawound vancomycin therapy, although local wound concentrations exceed the least inhibitory concentration required to treat most covered bacteria.[7]

Abdullah *et al*.,[1] analyzed the time to infection in their study with a mean follow-up of more than 7 months, each

**Table 1:** Clinical data of patients in the vancomycin and control group.

| Variables | Vancomycin (*n*=39) | Control (*n*=47) | *P*-value |
|---|---|---|---|
| Age in years | | | |
| Mean±SD | 22.08±15.9 | 21.87±16.7 | 0.9 |
| Median | 18 (4–87) | 19 (1–37) | |
| Gender, No (%) | | | |
| Male | 34 (87.2%) | 39 (83%) | 0.58 |
| Female | 5 (12.8%) | 8 (17%) | |
| Smoking, No (%) | | | |
| Yes | 21 (53.8%) | 25 (53.2%) | 0.56 |
| No | 18 (46.2%) | 22 (46.8%) | |
| Hypertension, No (%) | | | |
| Yes | 4 (10.3%) | 6 (12.8%) | 0.9 |
| No | 35 (89.7%) | 41 (87.2%) | |
| Diabetes, No (%) | | | |
| Yes | 1 (2.6%) | 2 (4.3%) | 0.65 |
| No | 38 (97.4%) | 45 (95.7%) | |
| Diagnosis, No (%) | | | |
| Unilateral extradural hematoma | 8 (20.5%) | 19 (40.4%) | **0.001** |
| Bilateral extradural hematoma | 1 (2.6%) | 2 (4.3%) | |
| Traumatic intracerebral hematoma | 2 (5.1%) | 2 (4.3%) | |
| Compound depressed fractures | 23 (58.9%) | 19 (40.4%) | |
| Simple depressed fractures | 1 (2.6%) | 3 (6.4%) | |
| Acute subdural hematoma | 3 (7.7%) | 1 (2.1%) | |
| Penetrating brain injury | 1 (2.6%) | 1 (2.1%) | |

SD: Standard deviation

**Table 2:** Clinical outcomes, and complications in both groups.

| Variables | Vancomycin (*n*=39) | Control (*n*=47) | *P*-value |
|---|---|---|---|
| SSI, No (%) | | | |
| Yes | 1 (2.6%) | 7 (14.9%) | **0.04** |
| No | 38 (97.4%) | 40 (85.1%) | |
| Interval to SSI in days | | | |
| Mean±SD | 15 | 15.6±3.2 | 0.76 |
| Median | 15 | 14 (12–20) | |
| Pathogens, No (%) | | | |
| *Acinetobacter* | 1 (2.6%) | 1 (2.1%) | 0.27 |
| MRSA | 0 | 3 (6.4%) | |
| MRSA and *Klebsiella* | 0 | 1 (2.1%) | |
| No growth (pus cells) | 0 | 2 (4.2%) | |
| Mortality, No. (%) | | | |
| Yes | 1 (2.6%) | 5 (10.6%) | 0.143 |
| No | 38 (97.4%) | 42 (89.4%) | |

SSI: Surgical site infections, SD: Standard deviation,
MRSA: Methicillin-resistant *Staphylococcus aureus.* Data are presented as mean±SD, median (Range), or number (%)

infection in both groups occurred within 10–34 days of the study, which is consistent with a mean time to occurrence of infection in our series which was 15 days.

Given the broad-spectrum gram-positive coverage provided by vancomycin, there are additional concerns about selecting gram-negative, anaerobic, and vancomycin-resistant bacterial SSIs.[20] In the control group, 4 out 7 cases 57% who developed infection were due to Methicillin-resistant *S. aureus*; while in the vancomycin group, no gram-positive bacteria were cultivated with just a single case of *Acinetobacter cocci*.

In our series, a single patient treated with topical vancomycin experienced an infection postoperatively, whereas seven patients in the control group developed an infection ($P$ = 0.04), mortality occurred in a single patient in the vancomycin group, while occurred in five patients in the control group ($P$ = 0.143).

Thus, while our study represents some guarded initial evidence of the efficacy of topical vancomycin in head trauma patients, we hope it will generate more interest in topical vancomycin for all craniotomy patients, which will lead to larger and more definitive studies on its efficacy. As is the case in many other studies, the data were collected from a patient population at a single institution, and may not be representative of populations across Egypt, to overcome this constraint, future studies could collect data from multiple institutions and combine the results. Also, double-blinded randomized trials would strengthen the findings in this prospective study.

Postoperative cranial wound infections have a substantial cost in terms of both morbidity and patient hospitalization. Deep cranial wound infections can affect the bone flap, dura mater, and brain, requiring repeated operations and antibiotic treatment.[1] Aside from the immediate expense of therapy, the financial burden is compounded by lost earnings and productivity which have more effect in developing countries, hence the beneficial effect of our study.

### Study limitations

There are many limitations in this study, although this study was a prospective randomized study, it was not double-blinded, however; the study cohorts were well balanced in terms of demographics, risk factors, and technical operations. We include all cranial surgeries across head trauma patients, but not all surgeries were performed by a single surgeon. The sample size was small in comparison to other cohorts,[1,15,18,19] however; our practice was in a large, university-based tertiary center.

## CONCLUSION

Topical vancomycin significantly reduces the risk of postoperative cranial wound infections in head trauma patients. The effect of vancomycin against gram-positive was

more obvious than gram-negative bacteria. Nevertheless, large practices with large case volumes are necessary to accrue sufficient sample sizes to detect small differences between groups.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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**How to cite this article:** Atallah A, Elbaroody M, Hassan AA, Ali AA, Elhawary ME. Role of topical vancomycin in reduction of postoperative infections in head trauma patients: A developing country experience. Surg Neurol Int 2021;12:600.