Original Article

Study of antibiotic efficacy of topical vancomycin powder in treatment of infected mandibular fractures and soft tissue surgical site infections

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Abstract

Aims and Objective: To study the antibiotic efficacy of topical vancomycin in infected mandibular fracture treatment and its effect in preventing surgical site infections. **Materials and Methods:** The study comprised of 100 subjects of infected mandibular fractures requiring open reduction and internal fixation, randomly categorized into two equal groups of 50 each, that is, vancomycin group ($N = 50$) treated for infected mandibular fractures with topical vancomycin powder used as adjunct and non-vancomycin group ($N = 50$). Clinical parameters like hospital stay, postoperative infections, postoperative fever, abnormal swelling, purulent discharge, and fistula formation at surgical site and radiographic healing was evaluated and compared between the groups. **Results:** Mean age of vancomycin group and non-vancomycin group was 32.5 and 33.2 years, respectively. Demographic factors of the patients like age, sex, and hospital stay (3 ± 0.5 days) did not show significant difference between two groups. Vancomycin group shows 1 hyperthermia, 2 abnormal swelling and discharge, whereas non-vancomycin group shows 6 hyperthermia, 5 postoperative abnormal swelling and discharge with statistically significant ($P < 0.05$). Culture sensitivity of discharged fluid shows staphylococcal + MRSA infection in two patients in vancomycin group and eight patients in non-vancomycin group. Bony healing in vancomycin group shows one patient had non-union and one had graft rejection, whereas five patients had non-union and graft rejection in non- vancomycin group. The comparative results were statistically significant ($P < 0.05$). **Conclusion:** From the result of our study we can conclude that routine use of vancomycin powder in surgical site as a surgical adjunct reduces the incidence of infections at surgical site when it is applied in addition to standard antibiotic prophylaxis. Topical application into a surgical wound also reduces the risk associated with parenteral administration of vancomycin.

Keywords: MRSA (Methicillin resistant Staphylococcus aureus), SSI (surgical site infections), systemic toxicity, vancomycin

Introduction

Infection is one of the most common complication in mandibular fractures. It may be due to negligence on account of patients or may be surgical site infection. Careful aseptic technique is necessary to prevent any surgical site infections. Various treatment modalities had been suggested in literature for management of infected mandibular fractures. The main goals include restoration of pretrauma form and function, elimination of infection and limitation of pain and disability. Prolonged MMF and external fixation was used in the past for management of infected mandibular fractures.[1] Current literature supports use of rigid fixation, debridement and use

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of rigid fixation with bone grafting. Thus, there is decreased need for MMF and less reliance on patient cooperation for favorable outcome.[2]

Surgical guidelines recommend antibiotic prophylaxis in open surgical procedures, especially in cases with implantation. Administration of local antibiotics in conjunction with parenteral antibiotics is gaining popularity among surgeons for reducing the incidence of infection at surgical site.

Topical application of vancomycin was widely used in orthopedic and neurosurgery for prevention of surgical site infection. Local administration of powdered antibiotics with the potential to deliver high doses of antibiotic at surgical with less systemic exposure and hence less adverse effects has gained attention in medical literature. Also in recent year an increase in MRSA infection has been noted. Thus topical vancomycin powder in infected mandibular fractures was used in this study with aim to compare the outcome in patients with infected mandibular fractures treated with rigid fixation with and without the adjunct of topical vancomycin powder.

Materials and Methods

A total of 100 patients were included in this study. Ethical approval was obtained from the institutional ethical committee (Study has been approved from institutional ethical committee dates 22 may 2017). Informed consent from patients was taken. Patients were divided into two groups [Groups 1 and 2] with 50 patients in each group. Healthy men and women between 20 and 65 years with clinically proven infected cases of mandibular fractures requiring open reduction and internal fixation were included in study. Patients with previous history of infections at the surgical site, allergic to vancomycin, pathological fracture, patients with systemic diseases/immuno-compromised (hypertension, diabetes mellitus, respiratory and cardiovascular disease, patient on steroids, bony disorders, smoking habit, etc.) and patients failing to visit postoperative follow-up time of less than 6 month were excluded from the study. All patients were operated by same surgeon and followed up for minimum of 1 year duration.

Surgical procedure

In infected fractures with purulent discharge, specimen of pus was acquired and sent for culture and sensitivity. Empirical antibiotic was started preoperatively after specimen was sent. In all patients, extraoral approach was preferred. Fracture site was exposed. Thorough debridement of the area was done till bleeding bone ensues. Any infected tooth or tooth in the fracture line indicated for removal were extracted. Intraoral irrigation was done. Fracture site was reduced. Rigid fixation was done. Use of bone grafts was done depending on the case. Iliac crest graft was used in most of the cases. Holes were drilled with drill bit corresponding to the diameter of the core diameter of the screw. A minimum of three screw rule with three screws on either side of the fracture site were placed. 1 g of vancomycin powder was applied directly to the wound just prior to closure. Vancomycin powder was sprinkled liberally over the area and suctioning of the area avoided thereafter to soak the vancomycin powder in blood already present at the site. Closure was done by 3-0 vicryl and 4-0 nylon sutures. Patients were discharged on oral antibiotics and recalled at 1 week, 2 weeks, 4 weeks, and 6 weeks after surgery and followed up for at least 1 year. In cases of graft placement closure of graft site was done. Postoperative instructions were given and patient was hospitalized for 2--3 days postoperative [Figures 1-3].

Results

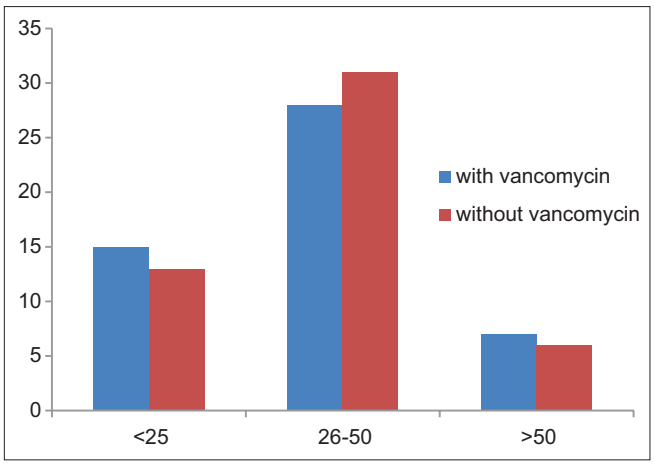
The patients group who underwent surgery and received intrawound vancomycin powder in addition to the standard antimicrobial prophylaxis was categorized as vancomycin group ($n = 50$) and other group who did not receive intrawound vancomycin powder was categorized as non-vancomycin group ($n = 50$).

Among the different age intervals, vancomycin group shows 15 patients are less than 25 years, 28 patients are the age groups between 26 and 50 years, and 7 patients are between 51 and 65 years of age group. Mean age of vancomycin group and non-vancomycin group was 32.5 and 33.2 years, respectively [Graph 1].

There are 40 men and 10 women patients in vancomycin group and 42 men and 8 women patients in non-vancomycin group. Demographic factors of patients did not show significant difference between two groups [Graph 2]. Patients of both the groups show the hospital stay of 3 ± 0.5 days and comparative results was not significant [Table 1].

Clinical evaluation and healing

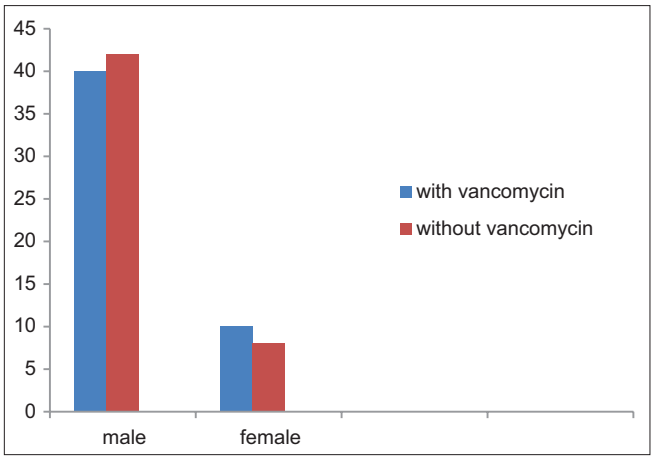
Both the groups were evaluated clinically for postoperative fever, abnormal swelling, any purulent discharge, and fistula formation at surgical site. Out of 50 patients, 1 patient shows hyperthermia and 6 patients in vancomycin and non-vancomycin group respectively. Two patients had abnormal swelling and



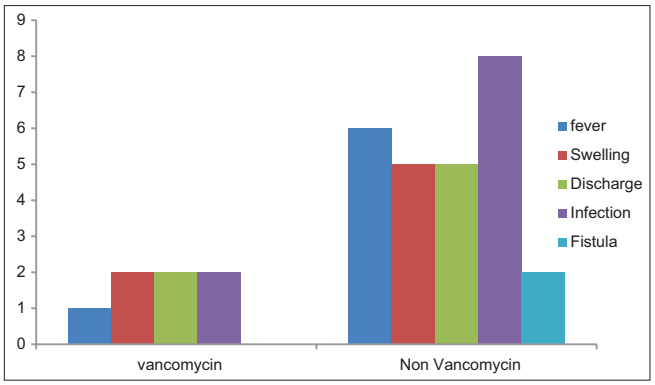
Graph 1: Age distribution between the two groups

discharge in vancomycin group and 5 had swelling and discharge in non-vancomycin group. Two patients in non-vancomycin group had chronic postoperative fistula which was managed by debridement and culture directed antibiotics. Culture sensitivity of discharged fluid shows staphylococcal + MRSA infection in two patients in vancomycin group and 8 patients in non-vancomycin group. The comparative results was statistically significant ($P < 0.05$) [Graph 3].

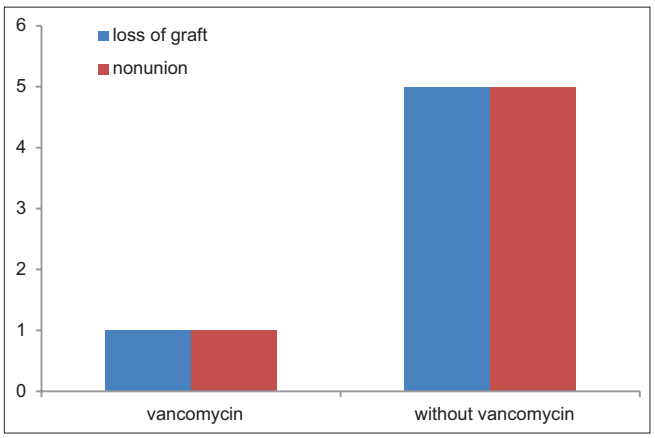
In late postoperative period, bony healing was assessed through radiographs and the result shows one patient had non-union and one had graft rejection in vancomycin group. In non-vancomycin group, 5 patients had non-union and graft rejection. The comparative results was statistically significant ($P < 0.05$) [Graph 4].



Graph 2: Sex distribution between the two groups



Graph 3: Comparison of clinical parameters between the two groups



Graph 4: Comparison of bony healing with non-union and graft rejection between two groups

Discussion

Surgical site infections (SSIs) are currently the most frequent hospital-acquired infections accounting for 31% of all infections among hospitalized patients.[3] SSIs are also one of the most common complications in operated cases of maxillofacial trauma especially mandibular fractures despite of use of prophylactic antibiotics. Staphylococcus epidermidis and *Staphylococcus aureus* are the common bacteria associated with SSIs and are resistance to antibiotics that bind penicillin-binding proteins. SSI is thought mainly to arise from wound contamination occurring from small inoculums during the operation. 10^3-10^5 bacteria may be necessary to initiate a bone infection, however 10 organisms may be sufficient in the presence of an implant to cause infection.[4]

Local administration of topical powdered antibiotics was first popularized in the late 1960s for prevention of wound infection in abdominal surgery prior to the existence of effective systemic prophylaxis.[5]

Topical antibiotics have also been applied locally in irrigation solutions, ointments, pastes, beads, sponges, and fleeces.[6] Local administration of powdered antibiotics is a potential method to deliver exceptionally high doses of antibiotic to the surgical site with less systemic exposure and adverse systemic effects. The vancomycin was first isolated by Eli Lilly from Streptomyces orientalis and was renamed vancomycin due to its ability to kill penicillin resistant *Staphylococcus aureus*. This glycopeptides is highly effective against gram-positive bacteria. It acts as a bactericidal agent against most gram-positive bacteria by inhibiting cell wall synthesis.[7]

The main aim of locally applied powdered antibiotics is to achieve substantially higher and long-lasting antibiotic concentrations at the surgical site without exposing the systemic circulation to toxic drug levels. This pharmacokinetics is based on studies evaluating both serum drug levels and surgical site levels excreted into surgical drains. After administration of 2 g of vancomycin, surgical site levels during the first day postoperatively reached nearly 1,500 mg/L and remained elevated above 100 mg/L through the third day. Serum levels were undetectable (<0.6 mg/L) in 80% of patients.[8] 1 g of vancomycin topically in pediatric spine patients, with surgical drain levels reaching above 400 mg/L and serum concentrations peaking at a mean of only 2.5 mg/L postoperatively.[9]

Vancomycin has been selected as prophylactic topical antibiotic of choice due to its cost-effectiveness, easy-to-use powdered form, and its effective broad coverage against organisms such

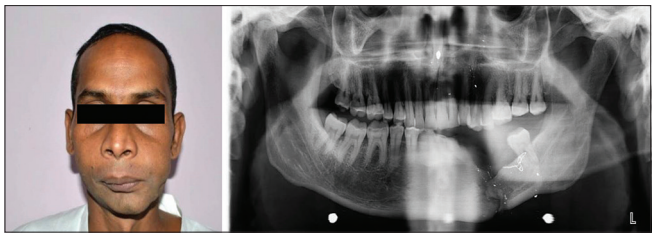


Figure 1: Preoperative clinical and radiological images

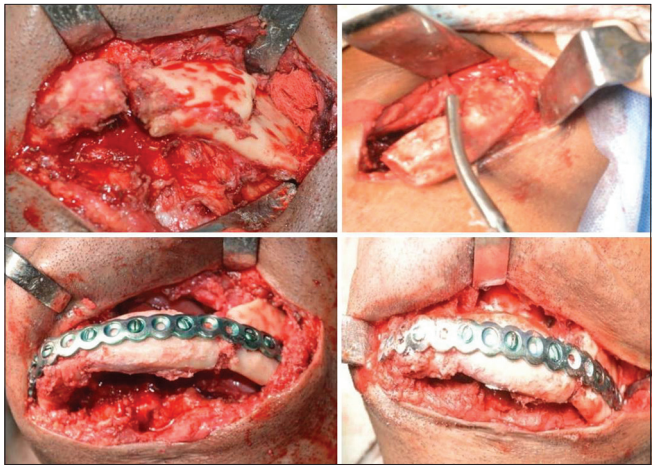


Figure 2: Intraoperative images showing vancomycin powder sprinkled over surgical site

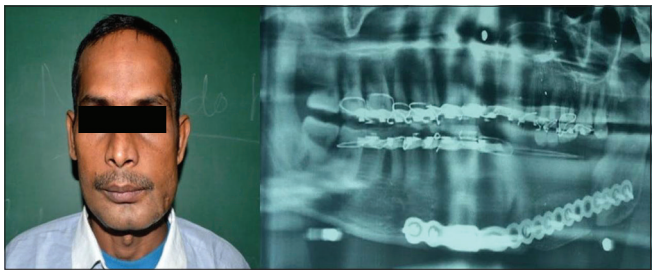


Figure 3: Postoperative clinical and radiological images

as MRSA. Intrawound topical vancomycin powder is not readily absorbed into the systemic circulation, but rather stays in the wound and acts locally to prevent infection.

Systemic level of vancomycin is lower than 2.0 μg/mL required to cause systemic toxicity. This may be largely due to large molecular size of vancomycin, thus interrupting vancomycin from absorbed systematically. Study comparing vancomycin and control group which injected *S. aureus* into the wound after surgery and concluded that intrawound vancomycin concentration was high enough to defeat known staphylococcal infection.[10]

Persistent systemic exposure to sub-inhibitory levels of vancomycin may cause resistant strains. The development of vancomycin intermediate-resistant *Staphylococcus* was demonstrated in an *in vitro* model with persistent vancomycin exposure above 10 mg/L.[11] However, the emergence of vancomycin resistance has not been reported in studies on the use of topical vancomycin in spine surgery[12]

Table 1: Showing demographic and operative data

Characteristics	Vancomycin group (*n*=50)	Non-Vancomycin group (*n*=50)	*P*
Age (years)	32.5	33.2	>0.05
Sex (M:F)	40:10	42:8	>0.05
Hospital stay (days)	2-3 days	3-4 days	>0.05
Infections (Staphylococcal + MRSA)	2	8	<0.05
Bony healing (Radiographically)	1 non-union	5 non-union	>0.05
	1 graft rejection	5 graft rejection	

One of the main attention of local antibiotics is low systemic toxicity. 16 studies including 6,701 patients shows only 23 complications including culture-negative seromas, ototoxicity resulting in transient hearing loss, nephropathy, and super-therapeutic exposure. One case of circulatory collapse following an anaphylactic reaction to intrawound vancomycin has been reported.[13] Study shows topical vancomycin is safe for use in pediatric patients with no reported anaphylaxis, nephrotoxicity, red man syndrome, thrombophlebitis, or rash.[14]

Topical vancomycin and healing

In an experiment, the use of local vancomycin shows no significant effect on fracture healing at typical levels achieved with systemic therapy.[15] Concentrations (>2,000 mg/L) may be attained when using local antibiotics. Studies on osteoblast-like cells have demonstrated that concentrations of vancomycin below 1,000 mg/L had little or no detrimental effect, but concentrations of 10,000 mg/L caused osteoblast cell death.[16] The relative risk for pseudoarthrosis with the use of topical vancomycin in was shown to 0.87.[17] Different studies shows that there is no increased risk of wound dehiscence at surgical site with the use of topical vancomycin, although one study reported n increased dehiscence and herniation.[18-22]

Topical application of vancomycin powder over surface wounds and suturing sites can be good method in treatment of SSI at primary healthcare centres. Primary care centres, rural areas where MRSA infections prevails more, vancomycin continues to be the drug of choice for treating most MRSA infections caused by multidrug-resistant strains with low side effects.

Conclusion

Vancomycin is a well-known antibiotic against gram-positive bacteria. Its topical use is well studied in spine surgery, orthopedic surgery, and cranial surgery to reduce SSIs. The result of our study also shows decreased SSIs with its topical use when it is applied in addition to standard antibiotic prophylaxis. Topical application into a surgical wound also reduces the risk associated with parenteral administration. Also, there is no data and observation that routine single-use vancomycin powder leads to antibiotic resistance. So we can conclude that routine use of vancomycin powder in surgical site as a surgical adjunct reduces the incidence of infections at surgical site. Small sample size

was our main limitation of our study and it requires larger study samples in randomized controlled trials for conclusive results.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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