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Intrawound application of vancomycin reduces wound infection after open release of post-traumatic stiff elbows: a retrospective comparative study

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Background: With the improvements in wound healing through the use of intravenous prophylactic antibiotics and technical refinements, postoperative elbow infections have become less common but still occur in certain elective elbow surgeries. The objective of this study was to evaluate the safety and efficacy of prophylactic application of vancomycin into the operative site to reduce the incidence of infection after the open release of post-traumatic stiff elbows.

Methods: A retrospective review of 272 such patients during a 4-year period was performed. In the control group (93 patients), simple prophylaxis with standard intravenous antibiotics was performed; in the vancomycin group (179 patients), vancomycin powder was applied directly into the wound before closure along with standard intravenous prophylaxis.

Results: After a follow-up of at least 6 months, the control group was found to have 6 infections (6.45%; confidence interval: 2.40%-13.52%) compared with none (0%; confidence interval: 0-2%.04%) in the vancomycin group, which was a statistically significant difference ($P = .0027$). No adverse effects were documented from the direct use of the vancomycin powder.

Conclusions: The local application of vancomycin powder may be a promising means of preventing postoperative elbow infections after elbow release in patients with post-traumatic elbow stiffness.

Level of evidence: Level III, Retrospective Cohort Design, Treatment Study.

Keywords: Post-traumatic stiff elbow; elbow stiffness; open release; wound infection; vancomycin; local application

Despite advances in the treatment of injuries around the elbow, approximately 12% of patients develop elbow stiffness, which is a common problem that can be associated with significant morbidity, posing a challenging dilemma for the surgeon, therapist, and patient.[6,25] A variety of nonoperative treatments have been described, and surgical arthrolysis may be indicated for those patients with

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persistent impairment of the functional range of motion despite adequate conservative treatment.[4,15,17,30,36]

Despite the prophylactic use of systemic antibiotics and improved surgical technique, surgical site infections remain a serious concern, especially in joint surgery.[1] Such infections have a profound impact on patients as they often require additional surgery and prolonged systemic administration of antibiotics; rehabilitation is delayed, surgical outcome is poor, and significant additional medical expense is incurred.[34] An open release of the post-traumatic stiff elbow with extensive dissection and arthrolysis often produces local hematoma or seroma that is inaccessible to systemically administered antibiotics, resulting in an increased potential for infection. A review of the literature suggests that the incidence of wound infection after surgical release of the stiff elbow is about 1.3% to 6.5%.[8,15,16,21,36]

Local delivery of antibiotics is attractive for wound infection prophylaxis because high concentrations are achieved directly at the wound site and systemic toxicity is limited.[11] Recent studies have examined the efficacy of intrawound application of vancomycin powder and have shown decreased infection rates with no adverse events in diverse populations.[2,5,9,26,35] To our knowledge, local application of vancomycin after operative release of the stiff elbow has not been reported. The purpose of this retrospective study was to evaluate the safety and efficacy of adding prophylactic vancomycin into the operative site during the open release of a post-traumatic stiff elbow as an adjuvant to standard intravenous (IV) prophylaxis.

Patients and methods

This is a retrospective case-control study of evaluating the safety and efficacy of prophylactic application of vancomycin into the operative site to reduce the incidence of infection after the open release of post-traumatic stiff elbows. We reviewed all patients undergoing open release of stiff elbows during a 4-year period from February 2009 through March 2013. All the operations were performed by a single surgeon (C.F.) at our institution. Inclusion criteria consisted of patients who had suffered from a stiff elbow after trauma and had undergone open release of the elbow combined with a hinged external fixator. Exclusion criteria included patients with a previous history of elbow infections, elbow stiffness due to nontraumatic causes (such as rheumatoid arthritis and burns), and postoperative follow-up time of less than 6 months. Baseline demographics, clinical characteristics, and operative details were obtained from the medical records. Patient demographics (age and sex), body mass index, hypertension, smoking history, steroid use, presence of diabetes, and original injury types were recorded. In addition, the details of surgical intervention were also noted for comparison.

Standard systemic antibiotic prophylaxis consisting of 1 g IV cefazolin within 1 hour before incision followed by 1 g IV cefazolin every 8 hours for 1 day was used for all patients. If the patient was allergic to penicillin, 900 mg IV clindamycin was administered instead. For children, the weight-based same prophylactic antibiotic was adopted. Patients who received preoperative systemic antibiotics alone were assigned to the control group, and those with additional wound application of 1 g of vancomycin powder intraoperatively were designated the vancomycin group.

All of the patients had a standard povidone-iodine (Betadine) preparation and were treated with similar surgical techniques as described in our previous reports.[18,19,28,29,33] All of the releases were performed by approaches that were based on the source of the elbow stiffness and previous surgeries. Arthrolysis was accompanied by reconstruction with anchors and radial head replacement as needed. Absorbable suture was used to close the fascia and subcutaneous layers; silk suture was used for skin closure. A hinged external fixator was used for 6 weeks in most of the patients based on the elbow stability for the assistance of postoperative rehabilitation. Double drains were kept in place for 2 to 4 days, depending on the drainage volume. Operative time, surgical approach, estimated blood loss, and materials used intraoperatively were obtained from the chart. In the vancomycin group, the powder was placed directly around the coronoid fossa anteriorly and olecranon fossa posteriorly before wound closure (Fig 1).

The primary outcome evaluated was the incidence of wound infection, but the incidence of pin site infection was excluded from the study. Superficial wound infections were identified by wound inspection, whereas deep infections were confirmed during exploration and débridement. Cultured organisms and subsequent treatments were recorded. Superficial infections were treated with local wound care and 5 to 7 days of oral antibiotics; deep infections were managed with serial surgical débridement, IV antibiotics, and consultation with infectious disease specialists.

Statistical analysis

A 2-tailed Fisher exact test was used to compare characteristics for categorical variables and a 2-tailed t test for normally distributed continuous variables. Fisher exact tests were also performed to evaluate differences in infection between groups, and 95% confidence intervals (CIs) were determined. All values were calculated as mean $\pm$ standard deviation unless otherwise noted. Statistical significance was considered at the 5% level.

Results

Between February 2009 and August 2010, 127 consecutive open releases of stiff elbows were performed; 110 met the inclusion criteria, and 93 were available for follow-up and review in the control group with an average follow-up of 14 months (range, 6-37 months). Starting in September 2010, 209 patients were treated routinely with adjunctive vancomycin powder applied to the local wound in addition to the IV antibiotics; 179 patients met the inclusion criteria as the vancomycin group with an average 13-month follow-up (range, 6-28 months). Overall, the 2 groups were statistically similar ($P > .05$) with regard to all patient parameters (Table I). The surgical approach, estimated blood loss, preoperative mean active range of motion, and materials used were statistically similar between the control group and the vancomycin group. The operative time was

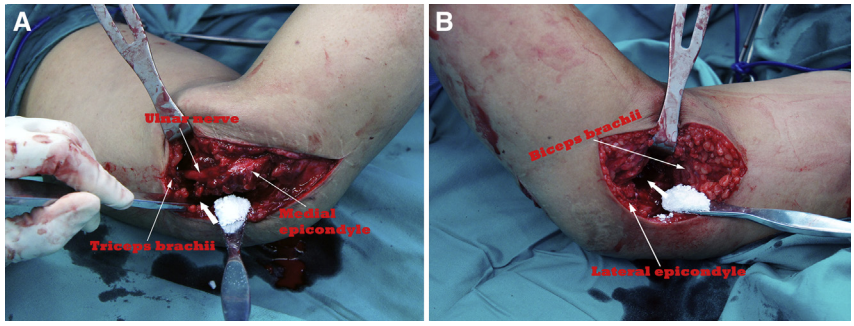

Figure 1 Demonstration of the local application of vancomycin. (**A**) Vancomycin was applied under the triceps brachii around the olecranon fossa posteriorly. (**B**) Vancomycin was applied under the biceps brachii around the coronoid fossa anteriorly.

Table I Patient demographic and clinical characteristics

Variable	Control group (N = 93)	Vancomycin group (N = 179)	*P* value
Gender, male/female	57/36	101/78	.517
Age composition, N (%)			.595
Pediatric patients (≤16 years)	13 (14)	21 (11.7)	
Adult patients (>16 years)	80 (86)	158 (88.3)	
Diabetes mellitus, N (%)	5 (5.4)	12 (6.7)	.795
Hypertension, N (%)	17 (18.3)	35 (19.6)	.872
Smoking (>6 months), N (%)	24 (25.8)	41 (22.9)	.653
Systemic steroids (preoperatively), N (%)	2 (2.2)	2 (1.1)	.608
Body mass index, range (mean), kg/m^2	19-30 (22.9)	19-31 (23.4)	.214
Original injury type, N (%)			.844
Radial head fracture	9 (9.7)	15 (8.4)	
Monteggia fracture	17 (18.3)	31 (17.3)	
Terrible triad injury of elbow	26 (28.0)	49 (27.4)	
Distal humerus fracture	38 (40.9)	72 (40.2)	
Olecranon fracture	3 (3.2)	12 (6.7)	
Number of previous surgery, N (%)			.834
0	26 (28.0)	47 (26.3)	
1	39 (41.9)	82 (45.8)	
≥2	28 (30.1)	50 (27.9)	
Preoperative mean active range of motion, degrees			
Extension-flexion	36 (0-73)	40 (0-75)	.195
Supination	32 (0-65)	31 (0-67)	.763
Pronation	29 (0-71)	31 (0-66)	.328
Mayo Elbow Performance Score, mean (range)	57 (45-70)	56 (40-75)	.292

statistically longer in the control group, with an average duration of 176 minutes, compared with the treatment group, with an average duration of 154 minutes ($P < .001$) (Table II).

The control group was found to have 6 infections (6.45%; CI, 2.40-13.52%) compared with none (0%; CI, 0%-2.04%) in the vancomycin group, which was a statistically significant difference ($P = .0027$). The infected cases were all adult patients, and no pediatric ones were involved. Two superficial infections were diagnosed at 4 and 18 days postoperatively and treated with local wound care and antibiotics. Four deep infections were diagnosed at 6 to 32 days (mean, 21 days) and required operative débridement and IV antibiotics. Methicillin-resistant *Staphylococcus aureus* was cultured from 3 of the 4 deep infections. In addition, no late infections occurred at more than 6 months of follow-up in this series. With use of an α level of 1% (chance of a type I error), the statistical power of this study was 86.5%. In terms of the 6 infected cases, the mean preoperative active range of motion was 16° (range, 0°-40°), which was much lower than the mean range of motion of the control group (mean, 36°; range, 0°-73°) and the vancomycin group (mean, 40°; range, 0°-75°). The mean operative time of the infected cases was 3.1 hours (range, 2-4 hours), which was a bit longer compared with 2.9 hours on average (range, 1.9-4.1 hours) of the control group and 2.6 hours on average (range, 1.5-4.0 hours) of the vancomycin group. In addition, only 25.3% of noninfected patients (22 of 87) in the control group and 27.9% of patients in the vancomycin group (50 of 179) had

Table II Operative variables

Variable	Control group (N = 93)	Vancomycin group (N = 179)	*P* value
Operative time, mean (range), minutes	176 (116-251)	154 (98-243)	<.001
Estimated blood loss, mean (standard deviation), mL	123 (90-312)	127 (85-328)	.270
Surgical approach, N (%)			.292
Lateral approach	11 (11.8)	14 (7.8)	
Medial approach	24 (25.8)	55 (30.7)	
Lateral and medial approach	49 (27.4)	82 (45.8)	
Posterior approach	9 (9.7)	28 (15.6)	
Radial head implant, N (%)	5 (5.4)	6 (3.4)	.519
Anchor used, N (%)			.555
0	23 (24.7)	47 (26.3)	
1	39 (41.9)	63 (35.2)	
2	31 (33.3)	69 (38.5)	
Hinged external fixator, N (%)	79 (84.9)	156 (87.2)	.710

more than 2 previous surgeries, whereas the 6 infected patients all sustained at least 2 operations before open release of the elbow (Tables I and III).

Pin track infections with purulent pin site drainage occurred in 1 patient (2 pins) in the control group and 2 patients (2 pins) in the vancomycin group; however, no pin track infections progressed concurrently to wound infection in these patients, and all were cured by pin removal, oral antibiotics, and local wound care. There were no fractures around the pin sites or radial nerve injuries associated with pin placement.

No significant difference was seen regarding the good-excellent rate of the Mayo Elbow Performance Score (MEPS) between the 2 groups ($P = 0.855$) on the basis of the results at the last follow-up (more than 6 months in both groups). Fisher exact test showed that the noninfected cases had a much higher good-excellent rate (85%; 226 of 266) than that in the infected cases (33.3%; $P = .007$) (Table IV).

After surgery, there was no notable difference in regard to perioperative complications, such as neuritis of peripheral nerves, or narcotic requirements between the 2 groups. Hypotension and renal toxicity were not observed in patients undergoing local adjunctive prophylaxis with vancomycin powder. In general, there were no adverse effects attributed to the local vancomycin powder.

Discussion

Nowadays, local antibiotics in cement and beads have been widely accepted in the treatment of infected open fractures and osteomyelitis.[23,27,32] Recently, a series of studies have shown that the occurrence of surgical site infection is significantly decreased after the prophylactic application of vancomycin powder to surgery sites in elective spine surgeries.[2,9,10,22,26] Thus, this treatment modality has been gradually established as a means of prophylaxis rather than treatment. As reported, vancomycin is a bactericidal glycopeptide that inhibits cell wall synthesis by binding to a D-alanyl-D-alanine cell wall precursor necessary for peptidoglycan cross-linking[24]; it achieves very high doses in the local environment with drug levels that are up to a 1000-fold higher than the mean inhibitory concentration for methicillin-resistant *S. aureus* and coagulase-negative staphylococcus. In addition, because of the poor absorption of vancomycin from the surgical site, most patients have undetected blood levels and subsequently should be at a lower risk for development of resistant organisms and adverse effects.[35]

Most cases of open release of a stiff elbow require extensive release, osteophyte removal, and relatively complicated soft tissue reconstructions with extended operative time, resulting in potential infection risks after surgery.[8,36] On the basis of a preliminary review of the literature, the incidence of postoperative infection can be as high as 6.5% (5 of 77). Once infection occurs, the consequences to the elbow are usually catastrophic, and satisfactory outcomes are difficult to achieve. In our series, between February 2009 and October 2010, patients (the control group) encountered an infection rate of 6.5% (6 of 93), which is consistent with previous studies. In comparison, since then, with the addition of vancomycin to the surgical wound, no infections occurred in the following 179 cases (vancomycin group). As expected, no significant differences in surgical outcomes based on the MEPS were noted in noninfected patients from both groups, whereas the infected cases had a much lower MEPS than that of the noninfected ones.

The concern of vancomycin powder directly applied to the surgical site is its safety. A hypersensitivity reaction, either anaphylactic or anaphylactoid, is a well-known adverse effect after IV and oral administration of

Table III Patients from control group with postoperative infections

Case No.	Sex/age, years	Original injury pattern	Preoperative ROM		Operation duration, hours	Comorbidities	No. of previous surgery	Culture	Treatment	ROM at last follow-up	
			E/F	S/P						E/F	S/P
1	M/51	TTI	20/50	0/45	3.5	HBP	3	MRSA	Multiple débridements + IV vancomycin	10/90	45/70
2	M/45	DHF	40/40	0/0	3.0	—	4	MRSA	Multiple débridements + IV vancomycin	0/90	30/90
3	F/31	TTI	20/60	30/45	4.0	—	4	—	Local wound care + oral cefixime	0/140	70/80
4	F/57	DHF	30/40	70/70	2.0	HBP DM	3	MRSA	Multiple débridements + IV vancomycin	5/125	45/90
5	M/49	TTI	0/0	0/0	2.5	DM	2	—	Local wound care + IV clindamycin	20/110	30/60
6	M/39	MF	45/60	0/0	4.0	HBP DM	3	Polymicrobial	Multiple débridements + implant removal + oral rifampin + IV vancomycin	15/110	40/45

DHF, distal humerus fracture; *DM*, diabetes mellitus; *E/F*, extension/flexion; *HBP*, high blood pressure; *IV*, intravenous; *MF*, Monteggia fracture; *MRSA*, methicillin- resistant *Staphylococcus aureus*; *RHF*, radial head fracture; *ROM*, range of motion; *S/P*, supination/pronation; *TTI*, terrible triad injury of elbow.
Six patients from the control group developed postoperative wound infection with the characteristics described. Two patients had superficial infections (cases 3 and 5), and no surgical intervention was required. The other 4 cases sustained deep infections requiring operative interventions and IV antibiotic treatment. MRSA was detected in 3 of these 4 deep infections.

vancomycin.[20] In the present study, hypotension, renal toxicity, and allergy-related conditions were not seen in any of the patients in the vancomycin group. Furthermore, no neuritis of peripheral nerves or other local irritations to the surrounding tissues were observed in this group. The similarity in outcome measures and postoperative complications between the 2 groups suggests that direct application of vancomycin powder in the elbow is a safe procedure. Moreover, an additional potential benefit of topical vancomycin is that high concentrations of antibiotics have been shown to inhibit bone formation in vitro.[7,12,14,31] The peak concentration of gentamicin after powder application in an animal model has been revealed to briefly exceed the threshold for affecting osteoblasts.[13,34] It is not clear whether this would benefit the inhibition of heterotopic ossification, which is a common post-traumatic complication around the elbow and a major cause of elbow stiffness.[3] If so, this would be an extra advantage for this treatment modality in the management of post-traumatic stiff elbow. However, we have not focused on this aspect in the present study. Further investigations are warranted to demonstrate whether local application of vancomycin powder could also be effective in preventing heterotopic ossification.

Six patients from the control group developed postoperative wound infections. Two patients had superficial infections and did not require operative irrigation and débridement. The other 4 patients sustained deep infections requiring operative interventions and IV antibiotic treatment. Methicillin-resistant *S. aureus* was identified in 3 of these 4 deep infections. Because of the limited number of cases, factors associated with an increased risk of wound infection have not been statistically analyzed. However, the severity of elbow stiffness with less active range of motion, relatively longer operative time, presence of diabetes, and increased previous operation times seem to be risk factors in our group. More important, no infection was seen in the pediatric patients in this study, indicating that wound infection may not be a problem in the pediatric patients in comparison with the adults in the open release of stiff elbows. Therefore, considering the cost-effectiveness, local application of vancomycin powder is highly suggested in the patients with these increased risks of wound infection in this scenario, but it may be unnecessary for the pediatric patients.

There are some limitations to this study. It is a retrospective study, and therefore bias and confounding factors were likely to be present. Also, not all factors known to contribute to postoperative infections were evaluated. Factors such as nutritional status, limited mobility, and various medical comorbidities can contribute to infection and were not controlled for in this study as we were unable to obtain all the information in a retrospective fashion. In addition, because all operations were performed by a single surgeon, there may be some bias in that all surgical procedures in the vancomycin group occurred chronologically

Table IV Results at follow-up

Group	Cases n	Postoperative MEPS			
		Excellent N (%)	Good N (%)	Fair N (%)	Poor N (%)
Control group					
Noninfected cases	87	38 (43.7)	37 (42.5)	7 (8.0)	5 (5.7)
Infected cases	6	0	2 (33.3)	3 (50)	1 (16.7)
Vancomycin group	179	77 (43.0)	74 (41.3)	16 (8.9)	12 (6.7)
Total	272	115 (38.6)	113 (41.5)	26 (9.6)	18 (6.6)

MEPS, Mayo Elbow Performance Score.
No significant difference was seen regarding the good-excellent rate of MEPS between the two groups ($P = .855$). Fisher exact test showed that the noninfected cases had a much higher good-excellent rate than that in the infected cases ($P = .007$).

after those in the control group. There is a possibility that the surgeon may have used improved techniques that were not recognized or controlled for. This concern may partly account for a statistically longer operative time in the control group and may have contributed to the increased infection rate observed in the control group. Specially, serum vancomycin levels were not monitored in our patients; thus, the rate of absorption and bioavailability cannot be determined for specific wound beds.

Conclusion

Intrawound application of vancomycin powder was found to significantly decrease postoperative infections in patients undergoing open release of a post-traumatic stiff elbow. There were no identified complications or adverse outcomes from the local application of vancomycin in the surgical wound. Additional prospective studies are suggested to further substantiate the effectiveness and to weigh the advantages and disadvantages of this new method as a routine protocol to reduce postoperative elbow infection after stiff elbow release with local application of vancomycin powder.

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