

Can Antibiotic-mixed Polymethyl Methacrylate-wrapped Intramedullary Nail be used for Post Nailing Infected Tibial Non-union as Definitive Treatment?

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Abstract

Introduction: Standard protocol for the management of intramedullary infected ununited fracture of tibial shaft is implantation of suitable antibiotic-impregnated bone cement-coated nail to eradicate infection followed by definitive interlocking intramedullary fixation within 6 weeks. In this study we investigate the utility of antibiotic cement coated nail to the end point.

Materials and Methods: A total of 23 (M = 17, F = 6) unilateral cases of mean age 32.6 years (ranges 15-68 years) are included in this prospective study. Initially, 14 had closed and 9 had open fractures. Pre-operative culture showed *Staphylococcus aureus* in 21 cases, and two had mixed infection of *S. aureus* and *Pseudomonas aeruginosa*. All were sensitive to Vancomycin. About 6 mm V nail with Herzog bend was used. 4 g vancomycin in 40 g methyl methacrylate polymer was used to wrap the nail after mixing. Medullary canals are reamed and thoroughly washed and prepared nails are introduced in the medullary canal. After 2 weeks, patients are permitted to bear weight with patellar tendon bearing cast. Nails are removed with union usually 4 months after insertion.

Results: Average follow-up was 30 months (range 7-63 months), and results at 1 year are produced. 20 achieve control of infection within 5 weeks, and in 2 cases, the same procedure was repeated and infection controlled. One case who failed to achieve control of infection was subjected to distraction histogenesis. Eventually, by this technique 21 of the 23 infection-free non-unions are united. However, in one case, larger-sized interlocking nail was applied. Ankle and knee joint movements show terminal 10% restrictions. According to Klemm and Borner scoring protocol, results are finally graded as 9, 12, 0, and 2 for excellent, good, fair, and poor, respectively. In initial 3 cases, final cement nail removal was a problem.

Conclusion: This cost-effective protocol is very simple and can be done in any setup. Further study is proposed.

Key words: Antibiotic mixed bone cement, Infection, Nail, Non-union, Tibia

INTRODUCTION

Infection after intramedullary nailing is reported as 1-7.9% in closed fractures in low- and middle-income Delete ‘-’ after low and middle countries and up to 25%

in type III open tibial fractures.¹⁻⁵ Methicillin-resistant *Staphylococcus aureus* is the most common organism.⁶ One of the methods of treatment for post-nail implanted infected non-union of tibial diaphyseal fractures is use of antibiotic-impregnated polymethyl methacrylate (PMMA)-wrapped intramedullary non-locking nail placement to eradicate intramedullary and overall regional infection control, and long-duration retention of cement nail has been used in some situation.⁶⁻⁸ Secondary procedure such as definitive interlocking intramedullary nailing (ILIMN) and more cumbersome Ilizarov technique do also yield satisfactory success rate.⁸⁻¹¹ We investigate the usefulness of antibiotic-mixed PMMA

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bone cement-wrapped nail as method of definitive treatment in such situation to avoid two more operations.

MATERIALS AND METHODS

In this prospective case series, a study conducted in a newly recognized rural Murshidabad Medical College of eastern India during January 2011-June 2017 includes 23 (M = 17, F = 6) unilateral cases. Mean age being 32.6 years (ranges 15-68 years) where right side was affected in 14 cases. Ethical committee approval and informed consent of participants are obtained duly. 11 of them was smoker, and 3 and 5 had diabetes and hypertension, respectively, and of them, 2 had combined diabetes and hypertension. Multiple ununited fractures of lower limbs, significant bone loss, and associated vascular or renal complications of diabetes are excluded from this study. 15 patients received initial treatment with ILIMN in other center. In 9 patients, initial injury was open fracture. Of them, 3 had reamed nail insertion during debridement within 24 h and other 6 had external fixation followed by ILIMN application within 5-21 days also from different centers. Two cases presented with broken nail (Table 1). Pre-operative pus culture isolated *S. aureus* in 19 cases, whereas in two cases, it was mixed infection with *Pseudomonas aeruginosa*. All were

sensitive to vancomycin and 17 were sensitive to cefuroxime also. In remaining two cases, no organism can be isolated with repeated culture. Perioperative medullary material isolates *S. aureus* in 11 cases.

Technique

All the patients were subjected to prophylactic pre-operative cefuroxime 1500 mg intravenous twice daily since 1 day before operation. Previously, applied intact or broken nails are removed (Figure 1). Thorough intramedullary debridement is done in all cases. Canal is washed with normal saline during every increment of reaming up to 10.5 except the last. Extramedullary debridement was also added in 4 cases. The powder of a 40 g PMMA combination is mixed with 4 g vancomycin and prepared manually. In moldable state, it is wrapped to a "V"-shaped nail of appropriate length and allowed to harden and cooled (Figure 2). Thus, it became a cylindrical nail of 9-10 mm diameter which is confirmed by passing through a gauge. Surface irregularities are removed using rasp. The prepared nail is then placed in medullary canal with firm pressure but without hammering. Wound is then closed in layers, and affected limb is placed in bivalve above knee slabs for 2 weeks. After 2 weeks, the anterior slab is opened to remove stitches and reapplied for another 1-2 weeks when PTB cast is put and permitted to

Table 1: Patient-related demographic data including course of treatment

Sex-age	Side	Close/open	Comorbid conditions	Date of injury	Date of IM nailing	Date of PMMA nailing	Date of PTB	Date of removal of PTB
M-32	L	Close	Smoker	27.02.11	03.03.11	17.04.12	07.05.12	09.07.12
F-15	L	Open		14.04.11	14.04.11	12.11.11 and 10.12.11	11.01.12	06.03.12
M-22	R	Close		11.09.11	17.09.11	14.04.12	04.05.12	01.08.12
M-37	R	Close	Smoker	21.06.12	02.07.12 (open)	28.08.13	12.09.13	11.12.13
M-68	R	Open	DM/H'tensive	07.09.12	12.09.12	20.09.13	19.10.13	06.01.14 Leg guard 16.02.14
F-39	R	Close	H'tensive	10.10.12	14.03.12	02.06.12	26.06.12	15.09.12
F-41	R	Close		22.05.13	23.05.13	20.12.13	05.01.14	09.03.14
M-27	L	Open	Smoker	08.09.13	24.09.13 (nail broke)	26.03.14 + (surface beads BG)	10.05.14	01.07.14
M-22	R	Close	Smoker	01.12.13	03.12.13	21.06.14	11.07.14	13.09.14; (leg guard 13.10.14)
M-24	L	Open	Smoker	12.03.14	02.04.14 (nail broke)	13.07.14 + (surface beads BG)	28.08.14	02.10.14
F-29	L	Open		21.07.14	09.08.14	26.01.15	20.02.15	19.05.15 non-union; exchange nailing 0
M-53	L	Close	H'tensive	13.01.15	15.01.15	16.10.15	30.10.15	20.01.16
M-32	R	Close	Smoker	11.03.15	14.03.15	12.10.15	26.10.15	03.01.16
F-20	R	Close		19.03.15	23.03.15	08.08.15	27.08.15	04.12.15
M-31	R	Open	Smoker	10.06.15	10.06.15	13.09.15 + (surface beads BG)	27.10.15	13.12.15
M-25	L	Close	Smoker	17.06.15	19.06.15	18.01.16	03.02.16	21.04.16
F-28	L	Open		27.08.15	27.08.15	22.01.16	10.02.16	21.04.16
M-24	R	Open		03.09.15	13.09.15	03.01.16	15.01.16	30.03.16
M-33	R	Close	Smoker	09.11.15	12.11.15	11.06.16	23.06.16	30.08.16
M-55	R	Close	H'tensive	02.12.15	03.12.15	07.06.16	21.06.16	20.09.16
M-23	L	Close	Smoker	03.03.16	06.03.16	05.08.16	19.08.16	14.10.16

PMMA: Poly methyl methacrylate, PTB: Patellar tendon bearing, M: Male, F: Female, R: Right, L: Left, BG: Bone graft, DM: Diabetes mellitus, H'tensive: Hypertensive

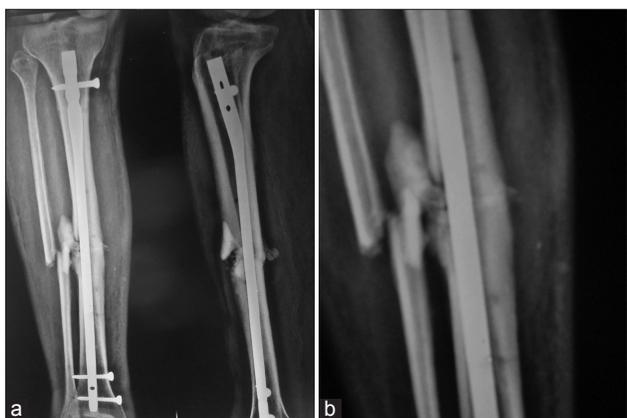


Figure 1: X-ray of interlocking nailing done for open mid shaft tibial fracture, (a) anteroposterior and lateral views with features of intramedullary and surface infection, (b) focused view of the same



Figure 2: V-shaped nail with proximal Herzog bend, (a) before preparation, (b) after wrapping with antibiotic-mixed polymethyl methacrylate bone cement

bear weight from partial to full at 2 months post-operatively. Cast discarded after 2-3 months, and ankle mobilizing exercises started (Figure 3). The PMMA-impregnated nail is removed after 3-5 months when the fracture adequately consolidated (Figure 4). In two cases, after 4 and 5 weeks, same procedure was repeated to control infection. Another 4 cases with more aggressive stage II osteomyelitis with soft-tissue infection surface debridement as well as removal of sequestrum and antibiotic cement beads are placed. Surface beads were removed after 4 weeks with control of infection, and at that time, cancellous autologous bone grafts were applied where there was partial cortical bone loss. In 2 cases with delayed consolidation beyond 3 months of PTB application, it is replaced with a leg guard for additional 4-6 weeks (Table 1).

RESULTS

Patients are followed up with removal of PTB, once in every 6 months for 1 year and then once yearly. Assessment done using “Klemm and Borner” protocol in a modified way.¹² Mean follow-up was 30 months (range 7-63 months). In this series, overall infection is controlled in 22 (95.7%)



Figure 3: X-ray after insertion of antibiotic-mixed polymethyl methacrylate bone cement-wrapped nail when 3 cortices union is complete, (a) anteroposterior and lateral views, (b) focussed view



Figure 4: Clinical photography showing (a) knee flexion, (b) ankle planter flexion

cases, but supplementary procedures were adopted in five. Of which in two cases, second, antibiotic-mixed cement nail was repeated after 5 week and surface antibiotic cement beads and bone grafting were combined in 3 cases. Union achieved in 21 (91%) cases in average of 13.3 weeks (range 10-20 weeks). One case, who was persistent smoker and diabetic infection, cannot be eradicated and failed to unite. Subsequently, he was treated using ring fixator. In another case, infection was controlled but failed to achieve union where PMMA-impregnated nail was replaced with larger diameter locking nail using exchange nailing technique.

Finally, the overall results were rated as 9, 12, 0, and 2 for excellent, good, fair, and poor, respectively, as per modifies Klemm and Borner scoring criteria (Table 2).

DISCUSSION

Conventionally, antibiotic-mixed PMMA nail was used to control infection, and subsequent stabilization with ILIMN is to achieve union. After union, most often that nail requires removal also. The treatment method of this study thus avoids two operations for the same purpose. Apart from morbidity and mortality, economic issue is a concern. Although cumbersome Ilizarov distraction technique is a good option particularly with quiescent infection. Same is

Table 2: Results of the study and rating as per Klemm and Borner criteria with little modification

Total cases	Infection control (%)	Union (%)	Average time of infection control (Wk)	Average time of union (Wk)	Grading of results (number and %)			
					Excellent (%)	Good (%)	Fair	Poor (%)
23	22 (95.7)	21 (91)	4.5	13.3	9 (39)	12 (62.2)	0	2 (8.7)

Wk: Week

also applicable for the exchange nail technique.^{13,14} We had to follow corticotomy and distraction histogenesis in one case and adopted exchange nailing technique in another case. Hence, those options are always applicable in any stage where indicated.

Combined application of vancomycin with gentamycin or tobramycin has been used by many authors with convincing results.^{7,15-17} Whereas Vatia *et al.* (2017) used vancomycin and teicoplanin combination with good clinical outcome.¹¹ In this study, vancomycin is used only as in 21 of 23 cases organisms, were sensitive to it. It worked also in those two cases where no organism can be isolated. Longer duration of antibiotic-mixed PMMA nail is not of much problem in terms of tissue response; moreover, it is evident that it can elude antibiotics as long as 5 years though in low quantity but above MIC level.¹⁸⁻²²

In the present series, infection developed in 14 cases of close fractures and 9 cases with open fractures. All were treated initially with interlocking intramedullary nail mostly using closed technique. More problems are faced to control infection and to achieve union in open fracture group. Possible reason may be deep intramedullary infection combined with bone surface and soft-tissue infection associated with some bone loss and some local vascular compromise.⁵ It appears that the use of “self-releasing antibiotic fixation endomedullary nail(SAFE nail)” application as initial treatment may be thought of. This is a dual core, multiple perforated intra medullary nail with locking facility. There is in built antibiotic impregnated cement inside where antibiotics are permitted to elude through the perforations.²³ Additional procedures such as extraosseous debridement, application of cement beads, and bone grafting are relatively simple procedures with low morbidity.

Natarajan *et al.*²⁴ and Yang *et al.*²⁵ found that average union time is 24.9 weeks and 22.6 weeks, respectively. In the present study, the average union time is 13.3 weeks which is much faster than other techniques. Possible reasons are (1) as there is no locking compression is permitted at non-union site, (2) partial weight bearing with PTB cast stimulates union, (3) reaming improves vascularity at target site, and (4) reamed material acts as bone graft. To ensure the last one, we did not wash after last reaming. PMMA nail do not produce stable fixation. However, PTB cast

supplements stability, fracture stability, and early weight-bearing hastens union.

Klemm and Borner assessment system included union time, range of motions of knees and ankle, wasting of muscles of leg, pain at fracture site, and alignment.¹² Infection control is not a criterion in it. This is more applicable in non-infected situations. We have modified it by allowing 3 points for different states of infection in place of wasting of leg muscles. In all patients, we found wasting at presentation, persists during treatment. However, at 1-year follow-up, all improved to the presentation state and 5 cases achieved similar girth like that of the sound side.

2-3 months application of PTB is likely to develop stiffness of ankle. We did not see it in the present study. Itching sensation was experienced by all patients but could manage to continue.

During removal of PMMA nail of the first case, we faced a lot of difficulties and continued in other two cases also. This was because of early application of PMMA nail during hot stage. Subsequently, putting them after complete cooling, there is no such problem in remaining cases.

CONCLUSION

In active intramedullary infection with non-union following intramedullary nailing of tibial shaft fracture, antibiotic-mixed PMMA-impregnated nail use is the best option and is to be put in after complete polymerization. Continuing the same nail till union and augmented with PTB cast will significantly reduce the union time without causing much problem to the ankle joint. Although inconvenience of plaster application is a concern for a small subset of patients.

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