



Original Article

Comparative study of the efficacy of gentamicin-coated intramedullary interlocking nail versus regular intramedullary interlocking nail in Gustilo type I and II open tibia fractures

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ABSTRACT

Purpose: Open tibia fracture is prone to infection, consequently causing significant morbidity and increasing the hospital stay, occupational loss and onset of chronic osteomyelitis. Intramedullary nailing is one choice for treating tibia shaft fractures. To improve the delivery of antibiotics at the tissue-implant interface, many methods have been proposed as a part of prophylaxis against infection. This study was conducted to study the role of gentamicin-impregnated intramedullary interlocking (IMIL) nail in the prevention of infection in Gustilo type I and II open tibia fractures and to compare the results with regular intramedullary nail.

Methods: The study included 28 patients with open tibia fractures (Gustilo type 1 or type 2); of them 14 underwent regular IMIL nailing and the other 14 were treated with gentamicin-coated nailing. Randomization was done by alternate allocation of the patients. Follow-up was done postoperatively (day 1), 1 week, 6 weeks, and 6 months for bone union, erythrocyte sedimentation rate (ESR), hemoglobin and C-reactive protein (CRP). Statistical significance was tested using unpaired *t*-test. A *p* value less than 0.05 was considered significant.

Results: There were 4 cases of infection in controls (regular IMIL nail) and no infection among patients treated with gentamicin-coated nail during the follow up ($\chi^2 = 4.66$, $p = 0.031$). At 6 months post-operatively, CRP ($p = 0.031$), ESR ($p = 0.046$) and hemoglobin level ($p = 0.016$) showed significant difference between two groups. The bone healing rate was better with gentamicin-coated nail in comparison to regular IMIL nail at 6 months follow-up ($p = 0.016$).

Conclusion: Gentamicin-coated IMIL nail has a positive role in preventing infection in Gustilo type I and II open tibia fractures.

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Introduction

Tibia and fibula shaft fractures are common long bone fractures in orthopedic practice and open tibia shaft contributes substantially to such a group.¹ Open tibia fracture is prone to infection which causes a significant morbidity and increases the hospital stay, occupational loss and incidence of chronic osteomyelitis.² Options for treating open tibia fractures are external fixators and intramedullary interlock (IMIL) nailing.³ Early stabilization of open

tibia fractures using IMIL nailing has been proved advantageous for biomechanical stability, soft tissue reconstruction, fracture union and rehabilitation. But there was a potential risk of deep infection.^{4–6} Gaebler et al⁷ found that 13 cases (3.2%) developed infection among 467 patients after tibia IMIL nailing and 5 (1.1%) were deep wound infection. To improve prophylaxis against implant-related infection, various methods have been proposed for the local delivery of antibiotics at the tissue-implant interface.⁵ Antibiotic coated intramedullary nailing is one of the methods. The present study was conducted to observe the role of gentamicin-impregnated IMIL nail in prevention of infection and to compare the outcome with regular intramedullary nail in Gustilo type I and II open tibia fractures.

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Methods

An observational study was conducted on 28 tibia fracture patients coming to the Department of Orthopaedics, Kasturba Medical College Mangalore and its allied hospitals, Government Wenlock Hospital, Mangalore, India over a period of two years from September 2015 to September 2017. Of them, 14 patients underwent regular IMIL nailing (controls) and the other 14 were treated with gentamicin-coated nailing (cases). Randomization was done by alternate allocation of the patients into the groups. Written and informed consent was taken from all patients. Open tibia shaft fractures i.e. Gustilo–Anderson⁸ type I & II, and patient age >18 years were the inclusion criteria. Gustilo type III, pregnant, breast-feeding or planning to become pregnant during the study period, known allergy to aminoglycosides and renal failure patients were excluded. Institutional Ethics Committee clearance was taken before conducting the study.

Indications for the use of gentamicin-coated nails were: (1) open tibia fracture (Gustilo type I, II), (2) open or closed tibia fractures with >2 weeks external fixator prior to intramedullary nailing, and (3) revision of complex tibia fractures (implant-related infections and nonunion). Contraindications included (1) pregnancy and breast feeding, (2) skeletal immaturity, (3) hypersensitivity to aminoglycosides, and (4) implant-related infections without prior debridement.⁵

The antibiotic coated IMIL nail with gentamicin eluting property was procured from the company Matrix Meditec Pvt. Ltd, Ahmedabad, India. The implant was coated with a combination of gentamicin and biodegradable polymeric carrier Poly (D, L-Lactide). The total drug in average sized IMIL nail = 100 mg (1 mg/cm²). The surgical procedure was performed in accordance with standard practices and with the manufacturer's instruction for use of the nail. The surgeon continued standard antibiotic protocol to treat soft tissue injury, fracture pattern and associated injuries.

Patient data were recorded at the time of admission. Data on infections and other adverse events were collected during the follow-up period. Infection was diagnosed clinically (fever, discharge from the surgical wound site), radiologically and using laboratory investigations. Laboratory parameters analyzed were C-reactive protein, erythrocyte sedimentation rate (ESR), leukocyte count and hemoglobin. Follow-up was done immediate postoperative day 1, 1 week, 6 weeks, and 6 months postoperatively.

Radiographic assessment was done at follow-up visits. Conventional radiographs of the fractured limb in two planes (anteroposterior and lateral) with knee and ankle were done for all patients. The radiographs were taken preoperatively, 6 weeks, 3 months and 6 months postoperatively. Consolidated fracture healing was defined as the bridging callus of at least three of four cortices without weight bearing in the anteroposterior and lateral view of the standard radiograph of the tibia. The radiographs were evaluated by two trained orthopedic assistants.

Statistical significance was tested using unpaired *t*-test. SPSS Version 15.0 was used for data analysis. A *p* value less than 0.05 was taken as statistically significant.

Results

Comparison of the case group (antibiotic-coated intramedullary nail, *n* = 14) and control group (regular intramedullary nail, *n* = 14) revealed no significant difference regarding age, fracture type and delay in treatment (all *p* > 0.05, Table 1).

There were 4 cases of infection in controls and no infection in the gentamicin-coated cases, which revealed significant difference ($\chi^2 = 4.66$, *p* = 0.031). All the four patients had low grade fever and

Table 1

Demographic statistics of two groups (*n* = 14 for each group).

Group	Age (year)	Gustilo–Anderson type		Delay in treatment (d)
		I	II	
Antibiotic-coated IMIL nail	35.07	7	7	3
Regular IMIL nail	32.35	7	7	3
<i>p</i> value	0.356	1.00		0.84

discharge from the surgical wound site. Radiological examination showed signs of infection.

At 6 months, 10 cases in the gentamicin-coated implant group healed completely and the other 4 patients showed bridging callus in three cortices on radiographs. The controls with regular IMIL nailing had disadvantaged results: the 4 infected cases had nonunion and only 5 cases achieved complete union at final follow up (Table 2) (Fig. 1). Comparison of the result revealed significant difference at 6 months follow-up ($t = 2.60$, *p* = 0.016). A typical case of a 28 year old male with type II open tibia fracture treated with gentamicin-coated nailing is shown in Fig. 2.

The laboratory analysis for C-reactive protein, ESR and hemoglobin showed significant difference between two groups. Compared with conventional IMIL nailing, CRP (*p* = 0.031) and ESR (*p* = 0.046) reduced at final follow-up in patients with gentamicin-coated implant; while hemoglobin level improved greatly (*p* = 0.016) (Table 3).

Discussion

Infection in the open tibia fractures continues to be the unresolved problem in orthopedic practice.⁹ Recent development of the antibiotic coating of nails with carrier agent which dissolves after certain time without drastically altering the standard procedure has revived the interest in local drug deliver in internal fixation system.¹⁰

Unreamed tibia nail protect nails has been used effectively in more than hundred patients for various indications without infection.⁴ In this study, we investigate the role of gentamicin-coated nail in type I and II open tibia fractures and found gentamicin-coated nails have better results than regular IMIL nail. Fuchs et al.⁴ demonstrated the usefulness of antibiotic-coated nail in both closed and open tibia fractures and suggested further randomized study. In our study, we clinically evaluated infection and chronic osteomyelitis among cases and controls which clearly

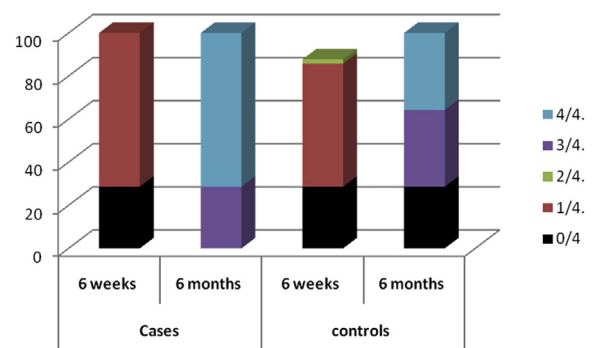


Fig. 1. Fracture healing at 6 weeks and 6 months postoperatively. The numbers in the bars indicate the number of patients with 0, 1, 2, 3 or 4 bridged cortices at each follow-up visit.

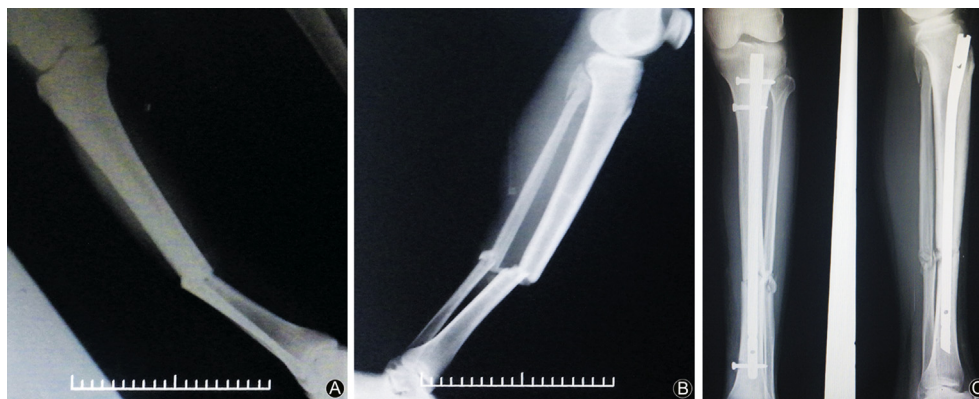


Fig. 2. A 28-year-old male with type II open tibia fractures was treated with gentamicin-coated nail. Preoperative lateral (A) and anteroposterior (B) X-ray and 6 months follow-up X-ray (C) showing fracture healing.

Table 2

Fracture healing in cases and controls at follow up visits ($n=14$ for each group).

Follow-ups	Bone healing					Bone healing rate (Mean $\pm$ SD)	<i>t</i> value	<i>p</i> value
	0/4	1/4	2/4	3/4	4/4			
6 weeks								
Gentamicin-coated IMIL nail	4	10	0	0	0	0.71 ± 0.46	-0.66	0.516
Regular IMIL nail	4	8	2	0	0	0.85 ± 0.66		
6 month								
Gentamicin-coated IMIL nail	0	0	0	4	10	3.71 ± 0.46	2.60	0.016
Regular IMIL nail	4	0	0	5	5	2.5 ± 1.69		

Table 3

Laboratory results of C- reactive protein, ESR and hemoglobin of both groups at each time points ($n = 14$ for each group).

Laboratory parameters	Time points					<i>p</i> value
	Preoperative	Postoperative	7 days	6 weeks	6 months	
C- reactive protein (mg/L)						
Antibiotic-coated IMIL nail	3	3.85	4.14	2.78	3	0.031
Regular IMIL nail	3	8.78	8.78	7.071	7	
ESR (mm/h)						
Antibiotic-coated IMIL nail	9.85	9.4	8.1	7.5	7.7	0.046
Regular IMIL nail	10.6	16.4	25.8	22.02	21.21	
Hemoglobin (g/L)						
Antibiotic-coated IMIL nail	119.3	109.3	112.9	118.6	123.4	0.016
Regular IMIL nail	119.9	111.4	111.1	113.4	121.4	

Statistical significance was tested using student unpaired *t* test.

showed significantly increased occurrence of infection in regular nailing patients ($X^2 = 4.66$, $p = 0.031$).

The lab parameters of chronic infection were also compared, which showed persistently elevated values in clinically infected patients (controls) in contrast to cases treated with antibiotic nails. Radiological union was defined as union of at least three cortices in this study. By the end of 6 months, all the patients in gentamicin-coated group showed union in contrast to delayed or nonunion in the control group ($t = 2.6$, $p = 0.016$).

In our study all the tested parameters of C reactive protein, ESR and hemoglobin showed statistically significant difference between case and controls (all $p < 0.05$), which confirmed the definitive role of gentamicin-coated nail in prevention of infection in open tibia fractures compared with regular nails. Antibiotics-coated nailing has the advantage of not requiring on table preparation or unusual reaming for fitting into medullary cavity since coating will not affect the diameter of the nail (the increase was only by microns). Therefore the procedure of nailing can be conducted as standard without other changes. The release profile of gentamicin as

described by manufacturer is maintained well above the minimum inhibitory concentration of commonly infecting organisms¹¹ and the thermal properties of gentamicin make it suitable for coating and easy sterilization.

Polylactic acid, as a drug carrier agent, has the advantage of self-dissolving without any effect on bone healing¹² and further it has been tested as an osteointegration material.¹³ Polylactic acid will disappear after certain duration allowing the least chance of acting as a nidus of infection which may occur otherwise with polymethyl methacrylate cement. Further studies are recommended comparing different drug delivery system. The limitation of our study was the short follow-up time.

In conclusion, gentamicin-coated IMIL nail has definitive role in preventing infection in Gustilo Type I and II open tibia fractures.

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Ethical statement

Institutional Ethics Committee clearance has been obtained before conduction of this study.

Conflicts of interest

The authors declare no conflicts of interest.

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