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Outcome of treating osteomyelitis and infected non-union of long bones with antibiotic coated bone cement nails

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Abstract
Introduction: Nonunion in the presence of infection poses the combined dilemma of infection management and stability. The purpose of this research was to determine the function of antibiotic cement coated nailing in infection management and bony union of infected non-union of long bones.
Methodology: This prospective observational study was conducted in the Department of Orthopedics, Janki Medical College, Janakpur, Nepal from August 2016 till August 2021. In this study, we included patients aged 18 years or above, who were treated with antibiotic cement coated nailing for infected non-union post-operative fractures of tibia or femur. 2 g of vancomycin and 2 g of gentamycin were put into every 40 g of bone cement. Clinical, radiographic, and haematological markers were used to assess infection control and osseous union.
Results: In the present study, 50 patients were included, with a mean age of 37.3 ± 6.2 years, and 72% of the patients were males (n=36) and rest being females (28%, n=14). Tibia was involved in 60% of the cases and rest had their femur involved. Wound culture revealed staphylococcus aureus in 60% of the patients and Enterobacter in 20% of the patients. At 6 months, bone union was achieved by 92% of the patients, infection control was achieved in 94% and 90% had no complications. Reinfection was observed in four cases (4%), nail break, nail migration and malunion was observed in one patient each.
Conclusions: Based on the results, it appears that antibiotic cement coated nailing in the therapy of infected non-union of long bones is a good method for achieving early infection control.

Keywords: Non-union, infection, antibiotic coated nail, long bone, femur

Introduction
One of the complications that may emerge as a consequence of fractures is delayed union. Delayed union happens when a sufficient period of time has elapsed after the initial injury without attaining bone union. The fact that a bone's union is delayed does not always mean that it will be called non-union. One of the consequences of a delayed union is non-union, and differentiating between the two may be difficult at times [1]. A delayed union or non-union of the fracture occurs in 5% to 10% of long-bone fractures. In the presence of infection, nonunion creates a conundrum of infection control and stability. There are various casuses of non-union of factures, like open fractures, infection post-internal fixation, chronic case of osteomyelitis with pathological fractures, and surgical debridement of pathological fracture. Interactions between the pathogen, the biomaterial, and the human immune response to both complicate implant infection [2]. The most common bacteria found in orthopaedic prosthesis infections are Gram-positive cocci, coagulase-negative staphylococci (CNS), and enterococci [3]. Several authors have recommended for the use of antibiotic cement impregnated intermedullary nails as a simple, low-cost, and very effective single-stage surgery for treating infected nonunion. Antibiotic cement nails are implants that provide intramedullary antibiotic delivery while also providing fracture stability. Paley and Herzenberg were the first to describe the device's use in the treatment of intramedullary osteomyelitis [4]. The goal of this study was to see if antibiotic cement coated nailing helped with infection control and bony union in infected non-union of long bones.

Methodology

Study Design and Sampling

From August 2016 to August 2021, the Department of Orthopedics at Janki Medical College in Janakpur, Nepal, performed this prospective observational research. In this research, we included patients aged 18 and above who had antibiotic cement coated nailing for infected non-union post-operative tibia or femur fractures. Patients with history of allergy to vancomycin, had chronic osteomyelitis, a pathological or tumor-related fracture, polytrauma, an additional fracture that might impair functional outcome, presented with distal neurovascular deficit, and were lost to follow-up were excluded from the research. Pruthi *et al*. reported infection control in 90% of the patients using antibiotic coated intramedullary nail in treatment of infected non-union of long bones [5]. The sample size was calculated using following formula $N = (Z_{\alpha/2})^2 * (PQ) / E^2$, where N = Sample size, $Z_{\alpha/2}$ = Z value at 5% error (1.96), P = taken as 90%, Q = 1-P and E = allowable error (taken as 10% of P) $N = [(1.96)^2 * (0.9*0.1)] / (0.09)^2 = 42.68$. So, we included 50 consecutive eligible patients in the present study.

Operative details

Preoperative care was provided to each patient in the form of a preoperative check-up and fitness for surgery. Prior to incision, the expected nail length was established. If a sinus was present, a sinogram with Methylene blue was done to help with sinus tract excision. Tissue and fluid from the non-union site were cultured aerobically and anaerobically, and a biopsy was conducted. The intramedullary canal must be prepared carefully. A sufficient amount of reaming was done to accommodate a larger diameter nail, guaranteeing greater stability. The medullary canal and incision were completely lavaged with saline prior to the insertion of an antibiotic-impregnated cement nail. The most essential step is the fabrication of the antibiotic cement coated nail. This was done on a separate sterile table. Preoperatively, a guide wire assessed nail length, and intraoperatively, the reaming diameter approached nail diameter. Femur antibiotic-impregnated cement rod manufactured using K-nail. Vancomycin and gentamycin were utilised because they are thermostable. In order to reduce cement setting time, 2 g vancomycin and 2 g gentamycin were added to every 40 g bone cement. We used palacos bone cement to make cement rods. An intramedullary nail two millimetres smaller than the largest reamer was utilised, with an 8–9 mm nail being the most often used. Manual cement mixing was performed, and the cement was applied on the nail in a consistent manner. The nail's eye was left uncemented to facilitate removal. A smooth and equal surface was achieved by manual rolling and occasional width-by-width measuring scale inspections. To achieve similar thickness, the nail was passed through a width measuring scale many times. For 15 minutes, the nail was exposed to air to allow the monomer to dissipate. The nail is retrogradely introduced through the fracture location once the cement has set. When there is a lack of bone, the bone ends are approached. The closure was done once the wash was delivered.

From the first post-operative day, all patients were encouraged to do static quadriceps and straight leg raising activities, followed by dynamic and passive hip and knee exercises within 48 hours, as tolerated by the patient. In all cases, partial weight bearing was introduced using crutches or a walker frame, depending on the patient's pain, compliance, local soft tissue condition, and bone quality. We began IV or oral antibiotics for 4–6 weeks depending on the culture findings. The bone was considered healed when three of the four cortices were linked and the patient was pain-free while bearing full weight and had normal ESR and CRP. Infection control and osseous union were assessed using clinical, radiographic, and haematological indicators.

Data Collection and Data Analysis

A pre-designed semi-structured research proforma was used to gather data. The medical records were used to acquire demographic information about the patients, such as their age and gender. Throughout the visits, infection control was defined as the absence of both clinical symptoms and normalisation of test inflammatory markers. All instances had problems such as re-infection, nail failure, deformity, cement debonding, and hypersensitivity responses. The investigation includes patient profile based on several demographic, laboratory, and clinical characteristics. Means and standard deviations were used to describe quantitative parameters. Ordinal data were represented in absolute numbers and percentages. All analyses were performed using SPSS 24.0.

Results

In the present study, 50 patients were included. Mean age of the patients was 37.3 ± 6.2 years, ranging from 18 to 70 years. It was observed that 36% of the patients were in the age group of 21 to 40 years and 24% were aged 41 to 60 years (Table 1). In addition, 72% of the patients were males (n=36) and rest being females (28%, n=14). Based on the past medical history of the patients, we found that 32% were hypertensive and 16% had a history of diabetes mellitus. There were two patients who had a history of coronary artery disease, one had hyperthyroidism and one patient had a history of migraine. Tibia was involved in 60% of the cases and rest had their femur involved. Wound culture revealed staphylococcus aureus in 60% of the patients and Enterobacter in 20% of the patients. No organism could be isolated from wound culture in 20% of the cases. It was observed the pre-operatively, 90% of the patients had pain, 78% had site swelling, 50% had site tenderness and 46% had discharging sinus. Post-operatively we observed a significant decrease in all the symptoms (Table 2). Post-operative at 6 months, pain was experienced by only 26% of the patients, site swelling by 30%, site tenderness by 22% and discharging sinus by 2% only. At 6 months, bone union was achieved by 92% of the patients and infection control was achieved in 94% of the cases. At 6 months, 90% of the patients had no complications. Reinfection was observed UN four cases (4%). Apart from this, nail break, nail migration and malunion was observed in one patient each.

Table 1: Baseline variables of the patients included in the study

Age groups	Frequency	Percent
Less than 20	10	20%
21 to 40	18	36%
41 to 60	12	24%
More than 60	10	20%
Gender		

Male	36	72%
Female	14	28%
Comorbidities		
Hypertension	16	32%
Diabetes mellitus	8	16%
Others	4	8%
None	28	56%
Bone involvement		
Femur	20	40%
Tibia	30	60%
Organism isolated		
Staph aureus	30	60%
Enterobacter	10	20%
None	10	20%
Total	50	100%

Table 2: Change in clinical symptoms of the patients

	Pre-operative		Post-operative at 6 months		p value*
Clinical symptom	**Frequency**	**Percent**	**Frequency**	**Percent**	
Pain	45	90%	13	26%	< 0.01
Site swelling	39	78%	15	30%	< 0.01
Site tenderness	25	50%	11	22%	< 0.05
Discharging sinus	23	46%	1	2%	< 0.01

*analyzed using chi-square test

Table 3: Clinical outcomes of the patients included in the study

Bone union at 6 months	Frequency	Percent
Yes	46	92%
No	4	8%
Infection control at 6 months		
Yes	47	94%
No	3	6%
Complications		
Reinfection	2	4%
Nail break	1	2%
Nail migration	1	2%
Malunion	1	2%
None	45	90%
Total	50	100%

Discussion

This prospective observational research was carried out at Janki Medical College's Department of Orthopedics in Janakpur, Nepal. In this research, we included patients who had antibiotic cement coated nailing for infected non-union post-operative tibia or femur fractures. For every 40 g of bone cement, we added 2 g of vancomycin and 2 g of gentamycin. We evaluated infection control and bone union 6 months after surgery.

Habib and colleagues looked at the use of antibiotic cement impregnated nailing for the treatment of infected femoral non-union [6]. They examined 19 cases of diaphyseal infected femoral nonunion. The research population was exclusively made up of male patients with an average age of 34 + 5.4 years. All of these patients had previously had surgery on the affected femur, which had been exacerbated by infection and non-union. Bhatia *et al*. performed a prospective study on 20 patients with infected tibial nonunion aged 22 to 61 years who were treated with antibiotic cement coated nailing [7]. Pradhan *et al*.'s study comprised 20 males and 1 woman with a mean age of 34.42 13.76 years (range 20–63 years), with the majority of patients aged 20 to 30 years [8]. Pisal *et al*. studied the function of an antibiotic-impregnated bone cement rod in the treatment of bone infection as well as its involvement in long bone union in cases of infective nonunion in another study [9]. Thirty people with infective nonunion of the long bones were included in the study. Out of a total of 30, we had 22 male patients and 8 female patients. The patients' ages varied from 18 to 45 years, with a mean of 34.5 years.

In the present study, wound culture revealed staphylococcus aureus in 60% of patients, Enterobacter in 20%, and no organism could be identified from wound culture in 20% of cases. Bhatia and colleagues observed that thirteen of the twenty patients had open fractures and seventeen had had one or more surgeries [7]. Seventeen patients reported positive preoperative cultures for Staphylococcus aureus, 10 of whom were resistant to gentamicin. Despite clinical symptoms of illness, eight people had negative cultures. Pradhan *et al*. observed that methicillin susceptible Staphylococcus aureus was the most often isolated bacteria from 9 patients, followed by methicillin resistant Staphylococcus from 5 patients in a comparable study [8]. According to Pisal *et al*., twenty patients were cultured for Staphylococcus aureus from a preoperative or intraoperative sample, and six patients had a positive Enterobacter culture [9]. Despite obvious signs of disease, the remainder of the patient had a sterile culture.

Desouza and colleagues discovered that 12 of 20 patients had positive pre-operative cultures for Staphylococcus aureus, 10 of which were resistant to gentamicin [10]. Despite clinical symptoms of illness, eight people had negative cultures. Staph aureus was isolated from 17 people, 10 of whom had MRSA, according to Pruthi *et al*. [5] Five patients were infected with Klebsiella, three with pseudomonas aeruginosa, and four with symptoms but no organism was collected. Numerous microbes were found in the remaining patients.

In most cases, infection eradication, soft tissue care, and bone union treatment are used to treat infected non-union [11]. The pillars of infection control include adequate surgical debridement of diseased and necrotic tissue, as well as a combination of systemic and locally delivered antibacterial drugs [12]. Local antibiotic administration resulted in higher local antibiotic concentrations than IV administration. Because it fills empty space, provides high antibiotic concentration locally, and provides mechanical stability, the function of the antibiotic cement impregnated nail has received greater attention. Its administration results in lower serum concentrations and, as a result, less toxicity than

systemic dosage. Aminoglycosides and vancomycin are preferred local delivery options because to their broad spectrum of activity, thermal stability, and low allergenicity [13]. Palacos bone cement has been shown to be more effective in eluting antibiotics (Zimmer). Sterling *et al*. revealed that gentamicin and vancomycin are antibiotics that keep their activity even after being exposed to high temperatures induced by poly (methyl methacrylate) hardening [14]. Klekamp *et al*. proposed combining vancomycin with an aminoglycoside in bone cement to see whether there was a synergistic effect in the treatment of severe infections caused by resistant S. aureus [15]. This was confirmed by González Della Valle *et al*. [16] Miller *et al*. verified that when infection is combined with fractures, stability is critical in infection management [17].

At 6 months, 92 percent of patients in the present experiment had reached bone union, and 94 percent had achieved infection control. In one case, the infection was treated, but bone union was not achieved. Furthermore, there were three cases where neither bone union nor infection could be treated. In the study by Habib *et al*., 14 (73.68 percent) of the 19 patients were cured of infection and had fracture site union at 24 weeks and 1 year later [6]. Three (15.78%) patients experienced sterile non-union, requiring a second procedure to achieve union. One patient (5.26 percent) was still afflicted but was able to unionise. According to Bhatia *et al*., bone union was achieved in 90% of the patients, with or without further procedures [7]. Eight people required further procedures to be cured of infection or to establish bone union. Six out of the eight patients were able to achieve union after later procedures. One patient with a chronic disease and one with a managed infection refused to have any further procedures done. In a similar study, Pisal and colleagues discovered that 26 of 30 patients had complete union at 6 months or sooner [9]. In two other instances, there was considerable callus development. In two cases, no callus developed at the fracture site until 6 months.

After 6 months, we noticed that 86 percent of the patients had no difficulties. Reinfection was seen in four cases (8 percent). Aside from that, one patient had a nail break, another had a nail migration, and yet another had a malunion. Bhatia *et al*. observed that three people had trouble getting their nails removed, two people had their nails broken, one person had their nails bend, and one person had their nails move into their ankle joints [7]. In another study, Desouza and his coworkers found that nail removal was difficult for three patients, two nails broke, one bent, and one moved into the ankle joint in one person [10].

There are various limitations to this study. The operating surgeons' surgical competency, post-operative technique, and experience would all have an influence on the clinical results of the patients in terms of bone union and infection treatment. As a result, the present study's results may not be applicable in other surgical centres. The clinical and functional results of the patients were not tracked over time.

Fig 1: Broken nail and nail migration into the ankle joint

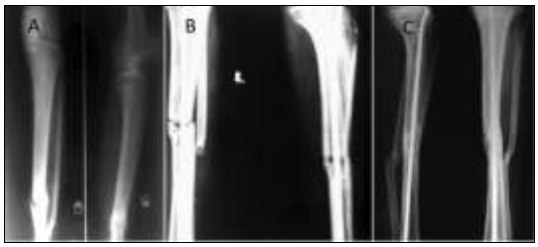

Fig 2: Radiographs of a tibial nonunion before surgery, after surgery, and after 28 weeks: (A) Pre-operative radiograph of a patient with an infected nonunion, (B) post-operative radiograph after surgery, and (C) radiograph showing bone union at 28 weeks

Fig 3: Infection of femur treated with antibiotic cemented nail with beads

Conclusion

Based on the study's results, we can conclude that infection control was achieved in 94 percent of the cases and bone union was achieved in 92 percent of the patients at 6 months post-operatively. Furthermore, at 6 months post-operatively, the patients' discomfort, edoema, soreness, and discharging sinus were all significantly decreased. So, we think that using antibiotic cement-coated nails to treat infected long bone nonunions is a good way to get rid of the bacteria, keep the bone in place, and get the bone to heal in a single procedure. We think it's best to use antibiotic cement-coated nails to keep bones from getting infected and to help with the healing of infected nonunions of long bones. A larger, more controlled study will be needed to back up the findings of this study.

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