Custom-made cemented antibiotic nail for the treatment of infected non-union Tibia fracture

Abdirizak Moalin Hussein, Gianfranco Tarsitani, Stefano D' Amelia

Abstract

Objective: The objective of study was to summarize our experience with the use of custom-made antibiotic cement intramedullary nail to treat the infected and non-union of tibia fracture

Methods: the prospective study of 52 patients with infected nonunion of tibia was made from 2014 to 2018, treated with custom-made antibiotic cemented coated nail. Evaluation of functional outcome was made in reference with controlling of infection and bony union.

Result: Eradication of the infection and bony union was achieved in 51 patients treated with custom-made antibiotic cemented nail. One patient was persisted with infected non union.

Conclusion: custom-made antibiotic cement nailing is a simple technique procedure, effective, less expensive and suitable to the poor countries where treatments infected non union of the long bones are very challenging.

Keyword: Custom-made antibiotic cement nail, infected non-union Tibia

INTRADUCTION

The management of an ununited tibial fracture with infection of intramedullary canal presents a challenging situation to the treating surgeon and infection disease specialist,even with recent advances in antibiotic delivery.Infected nonunion of long bones is a chronic and debilitating disorder.

The epidemiologic studies demonstrate that population fragmented aging and increased urbanization, and motorization across the globe increase the prevalence of the trauma the number of the fracture treated with implantation of hardware was increased. The prevalence of posttraumatic deep infection is projected to increase at faster rate as a result of tendency of operate more on high risk patients, at greater age, with diabetes, other comorbidities and immunosuppression. This is further increasing the severity of septic complications and other adverse outcome, which can often lead to functional impairment, long lasting disability, and permanent handicap or even life threatening conditions with an inevitable social and economic burden.

Musculoskeletal infections place and additional cost burden on the health care especially poor country where health service is not well invested
The course of the treatment is long and often requires multiple surgeries and prolonged hospital stay [1, 3]. This has significant implications for the patient morbidity and major socio-economic impact especially in a low and middle income country.

Despite improvement in preventive, diagnostic and treatment strategies there has been a steady increase in the incidence of osteomyelitis in the adult population [1,]. Over the last few decades the predisposing factor and causative microorganisms of osteomyelitis have changed dramatically. In the past, bone infections were mostly due to acute haematogenous spread of Gram-positive cocci, such as staphylococcus aureus. In contrast, today, osteomyelitis is commonly post-traumatic, implant-related, and affects patients with chronic diabetic mellitus. By definition posttraumatic osteomyelitis (PTO) is a microbial infection of bone and may lead to bone destruction, resulting from any type of trauma or nosocomial infection from the surgical treatment of trauma that allows organisms to enter bone and proliferate in traumatized tissue [5,6]. Osteomyelitis associated with fractures can cause delayed union or non-union and complicate the treatment [2].The causative organisms are typically methicillin resistant staphylococcus aureus (MRSA), biofilm-forming coagulase-negative staphylococcus, or multidrug resistant (MDR) gram negative bacilli including Pseudomonas aeruginosa, Acinetobacter baumannii among others [3, 4, 5, and 6].
A Chinese cohort study addressing the epidemiology of chronic osteomyelitis (COM) confirmed its rising frequency, especially among previously healthy young adults involved in road traffic accidents and interpersonal violence. [8].

The combination of prompt diagnosis, aggressive surgical debridement, and targeted administration of antibiotics may help reduce the growing frequency of Posttraumatic Osteomyelitis (PTO), especially among populations in the developing world [9, 10]. In contrast to data showing the rising incidence of PTO, research focusing on outcomes and predictors of recurrent bone infection following PTO treatment is scarce [11]. Recurrences following treatment of lower extremity bone infection are between 20% and 30% [12].
In a retrospective study of patients with contiguous osteomyelitis, bone infected by pseudomonas aeruginosa and inappropriate antibiotic therapy for S. aureus were independent risk factor for recurrent [13]. Furthermore, in a recent Colombian cohort study of recurrent chronic osteomyelitis, lower rate of treatment failure were observed in the patients on appropriate antibiotic therapy who had been treated by infectious disease specialist in a multidisciplinary team alongside orthopedic surgeons [14]. What we can understand for all these studies regarding recurrence of PTO, the importance of two stage procedure and its cornerstone to be done a radical debridement of the soft tissue, intramedullary canal should be ream in order to eradicate biofilm formed in the canal, to treat local antibiotic as well as intravenous antibiotic and to stabilize the fracture.

It is more difficult to deal with when the implant used for internal fixation itself becomes a potential media for infection because of bacterial adhesion and biofilm formation. The bacteria is capable to form a biofilm on the orthopeadic implants which protects the microbe from the immune system by forming a protein and ploysaccharide matrix, which is a immunopriviledged site causing systemic antibiotics to be unsuccessful in providing a definitive solution.This biofilm is resistsnt to systemic antibiotic alone.Once formed, it protects the microorganism from antimicrobials, opsonization, and phagocytosis, thus contruting to the chronicity of infections.

Materials and Methods:
This is a prospective study of 52 patients with infected nonunion of tibia aged from 19 to 59years (mean, 38 years), during 2014 till 2018 were treated using custom-made antibiotic cement coated nailing. Of these 52 patients, 36 were sustained open fractures, which were subdivided by (Gustelo open fractu
re classifications), type I (n = 6), type II (n = 7), type IIIA (n = 9), type IIIB (n = 14) and 16 were close fracture, primarily all the patients with open fractures was treated debridement of the wound, IV antibiotics and intramedullary tibia nailing was fixed where other patients with close fracture fixed with intramedullary tibia nailing. Twenty three patients having draining sinus and swab taken, staphylococcus aureus was positive. However preoperative investigation CBC, ESR, CRP, was high in all the patients.

Operative procedure:
The first step we take was removal of the infected implant, followed by radical debridement of the infected bone and soft tissues. After that, intramedullary canal was adequately reamed till the fresh bleeding bone was reached and, it was thoroughly washed and irrigated by antiseptic solution and norm saline. Specimens of the bone, soft tissues and any purulent material in a separate matter were sent for culture and sensitivity test. An appropriate size custom-

Made antibiotic cement coated nailing was prepared on a separate sterile table.
Nancy nail (elastic nail for the pediatric fracture fixation) of 4 mm diameter, 80g gentamicin PMMA powder, 2g vancomycin powder, sterile mineral oil, and a chest tube was chosen an inner diameter similar to the outer diameter of the last reamer, to make our custom-made cemented nail. The nail was measured to the length of the medullary canal and a chest tube of the approximate size of the nail was selected.
The chest tube is cut to the measured medullary length, pretreated with mineral oil and the elastic nail is cut 5mm longer than measured and bent into a loop for the proximal portion of the nail. We used 2 gm of vancomycin and 80 gm gentamicin mixed with 40gm PMMA bone cement and injected into the chest tube. The precut nail is then inserted into the chest tube and once the cement begins to harden the chest tube is cut longitudinally with surgical knife and peeled from the cemented nail. Then we wait for the nail to cool and for the monomer to evaporate. Care must be taken at this point not to peel the chest tube away too quickly as the uncured cement can peel away from the nail and remain attached to the plastic. Once the cement nail is fully cured and cooled in room air, which usually takes around 15 to 20 minutes.
The cleaned and cured Nail is then inserted into the medullary canal with the nail loop left protruding from the proximal Tibia medullary canal.

The wound was closed and if necessary soft tissue flaps were created to cover any identified defects preoperatively. All patients were placed into splints/cast postoperatively for a minimum of 6 weeks to minimize motion at the fracture sites to maximize osseous healing.
Intravenous antibiotic were given according sensitivity of the their culture, and weekly infection markers was checked, after 6 weeks custom-made antibiotic nail was removed and replaced fixed with definitive normal tibia nail.

Result.
The intraoperative specimen reported positive culture for all 52 cases.
Third seven samples were positive for *Staphylococcus aureus*,
11 samples were positive for *Staphylococcus aureus*
and Pseudomonas aeruginosa and 4 samples were positive for *klebsiella.*
Post-operatively, the wound was inspected at 48-72 hours intervals.
A complete blood count (CBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels were performed initially and then at regular weekly intervals to record rising or falling trends.
All patients were administered 6 weeks of intravenous antibiotics according to the culture reports. Infection control was judged on the basis of discharge from the wound, clinical signs of inflammation, and laboratory parameters like CBC, ESR, and CRP.

After 4 to 6 weeks all the infection markers were normal and wound was heeled, the custom-made cement nail was removed and was inserted normal intramedullary tibia nail,7 patient was needed flap coverage and bone graft

Patients was discharged and followed up every 2 weeks for the first two months after discharge, then once a month for 6 months and then once every 2 months till the final follow-up. The average period of follow-up was 25 months. Patients were evaluated in terms of infection control and bony union. Infection markers was controlled every follow up and check x ray was taken. In 51(98%) patients there follow up x ray showed bone healing and all infection markers was negative, with average of 18 months, one patient in 6 months post-operative was seen infection markers get high and no bone union, he had high energy trauma open fracture Grade III B with soft tissue loss from the trauma after wash and debridement temporarily external fixators was fixed to stabilize the fracture and free flap coverage of the tibia was used. He was readmitted and removed nail, reamed ,washed the modularly canal and the specimen sent to the lab a *Staphylococcus aureus* was positive, gain same above mention procedure was done at the second surgery. Period of 12 months bone union was achieved and no recurrent infection.

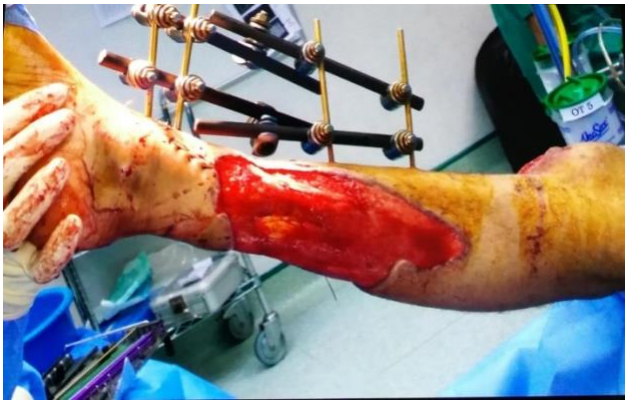

Fig.6 temporary external fixation was fixed to treat soft tissue

Fig.7 after healed soft tissue coverage

All the patients showed bone union an average of 18 months while the infection control was showed an average of duration 3.4 weeks

Fig.8 post op x ray with custom-made antibiotic cemented nail

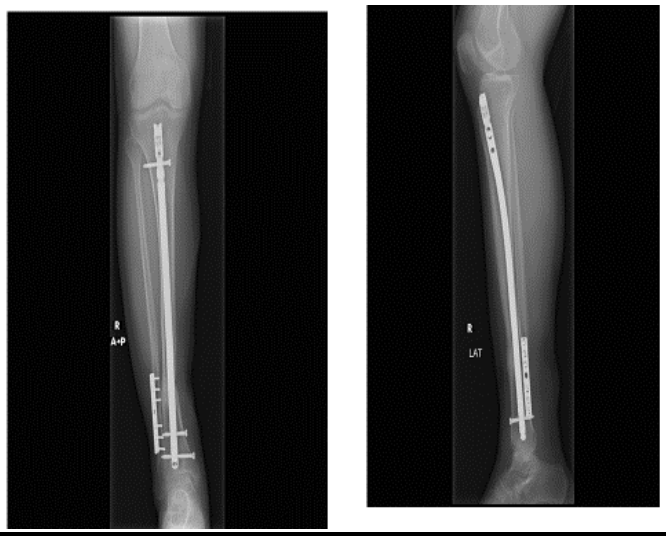

Fig.9 after 12 months healed fracture

Fig.10 after 2 years healed fracture and removed nail

Discussion:

The treatment of infected nonunion of the tibia requires two stage procedures to control the infection and to provide stability in order to achieve union 14. Through the debridement intramedullary canal by reaming in order to remove biofilm, local delivery antibiotic and prolonged parenteral antibiotic is the mainstay in treatment of infected non-union of the tibia.

There is no single universally accepted modality of treatment presently available for the management of infected nonunion fractures.

The use of Antibiotic coated nail available in the commercial market can give local delivery of antibiotics without any systemic toxicity and some studies has been documented for the management of osteomyelitis and open fractures [82, 83].However, it's not cost-effective, since the price of such kind of nail is very expensive, especially into the low- and middle-income countries. There is also the use of antibiotic cement beads treated intramedullary canal infected nonunion. However, they do not provide any stability across fracture site and cannot be placed in the intramedullary canal as it entails difficult removal due to fibrous ingrowths.

The use antibiotic impregnated cement was first noted by Buchholz and Engelbrecht.[84, 85]. A high local concentration of antibiotic and low systemic side effects were the major advantage [86, 87]
Gentamicin and Vancomycin has been the most widely used antibiotic, which we used in our custom made antibiotic cement nail [88, 89]. Use of the two antibiotics, "Gentamycin and Vancomycin" with bone cement widens the spectrum of activity and also enhances the elution properties of the two antibiotics [90, 91]
Ashok *et al.*2009 studied 25 cases of infection nonunion used debridement and

reaming medullary canal and same setting fixed custom made nail for definitive fixation and parenteral antibiotic they achieved 80% infection control and bone healing the remaining cases 20% (n=7) not controlled the infection and was necessitated for second procedures.
In our study after debridement reaming and washed the intramedullary canal of the tibia we inserted custom-made nail and kept for 4-8 weeks with parenteral antibiotic till clinically and infection markers come normal.
Second stage the custom made antibiotic nail we remove and fixed with normal tibia interlocking nailing. We believe that it's important to eradicate the biofilm in intramedullary canal of the tibia with antibiotic cemented nail. For the most popular antibiotics, bactericidal concentrations were found for up to 6 weeks after the insertion of the antibiotic cemented nail [93].
We believe also, after long period of time (36 weeks) the elution of the antibiotic cemented nail will decrease and cement will become foreign body in the medullary canal and may bacteria colonialize and form biofilm again [94]. For that reason after when we make sure that clinically and all infection markers become negative we remove the custom- made nail and replace definitive tibia interlocking nail.
Geurt *et al. 2017,* performed a systemic review of the treatment strategies for chronic osteomyelitis in low-and middle – income countries including Africa

(Kenya, Malawi, Nigeria, Congo, Uganda, and Ethiopia) and Asia (Nepal, India). In all the studies, patients received local surgical innervations at the infected bone sites, including debridement through sequestrectomy,saucerisation or curettage, bone grafting ,amputation and application of local antibiotic delivery systems (antibiotic cemented beads). Additional antibiotic therapy was administered systemically in all the studies. They concluded that there no evidence sufficiently robust to identify the most effective treatment, or to even allow a recommendation of the best suitable treatment of chronic osteomyelitis in low-income countries.
In our study of 52 patients treated custom-made antibiotic nail of the tibia infected nonunion. All the patients showed bone union an average of 18 months while the infection control were showed an average of duration 3.4weeks, only one patient in 6 months post-operative follow up was not controlled the infection and second surgery was underwent, at 12 months no recurrent of infection and bone was united

Conclusion:

Since the introduction of antibiotic loaded bone cement by Buchholz and Engelbrecht, it remains a golden standard in local antibiotic delivery. This is also very useful in case long bone medullary infections, where antibiotic cement nails remain an important treatment option. The major advantage of custom-made antibiotic nail is the local release of high antibiotic concentrations, which vastly exceed those after systemic administration with no or low systemic toxicity. In addition to that, they are able to provide stability to the fracture site, which promotes infection healing.

The custom-made antibiotic cement nailing is a simple, economical and effective procedure for the management of infected non-union of tibia. It is advantageous, less expensive and avoidable material. The method utilizes existing, easily available instrumentation, materials and its technically less demanding, and therefore can be performed at any general orthopedic/Trauma center and also suitable in low-income countries.

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