Efficacy of Fixation Technique Using Antibiotic Cement-coated Intramedullary Nail in Infected Pseudarthrosis

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ABSTRACT:
Efficacy of fixation technique using antibiotic cement-coated intramedullary nail in infected pseudarthrosis

Objective: Non-union accompanied by infection requires both the treatment of infection and stabilization of the fracture. This study examined the efficacy of a fixation technique using antibiotic impregnated polymethylmethacrylate (PMMA) cement-coated intramedullary nail in patients with infected pseudarthrosis of the femur oribia.

Material and Methods: Fourteen patients with Cierny-Mader stage 4 infected non-union of the femur oribia were included. Patients were treated with local debridement, antibiotic containing PMMA cement-coated intramedullary nail application and systemic antibiotics. They were followed-up for union and recovery of infection.

Results: Femoral and tibial pseudarthrosis were present in 3 and 11 patients, respectively. Eleven patients had hypertrophic and three patients had atrophic infected non-union. The mean duration of follow-up was 24.7 months (range: 8-37 months). During follow-up, infection improved in 85.7% of the cases (12 patients). Union was achieved in 10 (71.4%) patients during follow-up. Ten over 11 patients (90.9%) with hypertrophic pseudarthrosis achieved union. On the other hand, none of the patients with atrophic pseudarthrosis achieved union.

Conclusion: Considering the high-dose local antibiotic effect and the advantage of stabilization with intramedullary nail, antibiotic impregnated PMMA cement-coated locked intramedullary nail application may be recommended in the treatment of hypertrophic pseudarthrosis. However, regarding the treatment of atrophic pseudarthrosis, it seems to be effective for the treatment of infection but ineffective for bone union. Larger trials are warranted.

Keywords: Antibiotic impregnated polymethylmethacrylate, chronic osteomyelitis, intramedullary nail, non-union, pseudarthrosis

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INTRODUCTION

In the presence of chronic infection with nonunion, stabilization of the fracture is required for both treatment of infection and effective healing. Treatment of infection requires proper debridement and use of local and/or systemic antibiotics.

When trauma occurs, the bone circulation deteriorates, but if there is no infection, revascularization develops over time and remodelizes. In the presence of infection, the regional defense and repair mechanisms are redirected to try to clothe and terminate the infection, but the discharge accumulated under pressure leaves the intact surrounding tissue avascularized by periosteal elevation and spreading to endosteal intramedullary spaces (1-3). For the treatment of osteomyelitis in this clinical form, all infected bone or foreign material must be removed (1,3,4).

Antibiotic impregnated polymethylmethacrylate (PMMA) was used to provide local antibiotic effect in the treatment of bone and soft tissue infections (5-9). Antibiotic impregnated PMMA is applied with manually prepared or prefabricated cements, antibiotic spacers or antibiotic coated rods. High and systemic toxicity risk is low in antibiotic release from bone cement. The release is high in the first 48 hours (10,11), while the dose required for local sterilization of the antibiotic is up to 28 days (12).

While these methods solve the infection problem, they have little impact on fracture stability and require additional methods of fixation, such as an external fixator. However, there is risk of complications of external fixator such as pin site infection and limitation of motion of the joint. The use of antibiotic coated intramedullary nails removes the need for external stabilizing materials.

In this study, we aimed to evaluate the effectiveness of fixation technique using debridement and antibiotic impregnated polymethylmethacrylate (PMMA) cement coated intramedullary nail in femur and tibia patients who developed Ciernyl-Mader stage 4 infected nonunion.

MATERIAL AND METHODS

Patients

A total of 14 patients with Cierney Mader stage 4 tibia and femur infected nonunion who applied to our hospital between 2009 and 2012 were enrolled in the study. The patients were treated with local debridement and antibiotic impregnated PMMA-coated intramedullary nail application.

Diagnosis

Clinical and radiological evaluation criteria were used together for the diagnosis of pseudoarthrosis. In the clinical evaluation, the presence of pain with load applied to the affected extremity, pain with palpation and the presence of pathological movement and the presence of discharge of fistula were checked. In addition, in the direct conventional radiograph, whether there was cortical continuity, whether there was any difference in healing in the fracture line within 3 months and whether cortical bridging occurred or not were checked. Cases with stage 4 according to Cierny-Mader anatomical classification were included in the study (patients with diffuse infection that may cause instability). Culture samples were taken from preoperative fistula discharge.

Surgical Technique

All patients underwent combined spinal epidural anesthesia. Tibia-infected nonunion patients were placed on the operation table at knee flexion in the supine position, and patients with femur-infected nonunion in the lateral decubit position. No tourniquet was used in patients. No antibiotic prophylaxis prior to surgery was done to avoid deep culture samples to be affected. Immediately after culture samples were taken, prophylactic 1 g cephazoline sodium prophylaxis was performed.

First, fistula excision, and if present, extraction of the current implant and local debridement were performed. Pseudoarthrosis area was removed and sclerotic bone excision was performed until the haversian hemorrhagic bone tissue was observed.
Irrigation with saline was performed by ensuring continuity of the medulla. Deep tissue culture samples were taken.

Then, an entrance for intramedullary nail was prepared for tibia from the anterior part of tibia eminensia, and for femur from piriformis fossa. The length of the nail to be used was determined by intraoperative fluoroscopy and a nail with a diameter 2 mm smaller than the diameter of the engraver was selected. The silicone tube was selected to be 2 mm thicker than the nail diameter. 3.6 gr teicoplanin was added to the bone cement of 40 gr and this mixture was filled into the silicone tube with the aid of a 50cc syringe while the cementum was in liquid form, and the nail was placed into the silicone tube. The nail was cemented so as not to include the proximal screw level. After the completion of the polymerization of the cement, the silicone tube was cut with lancet and the cement was observed to completely cover the silicone tube’s wall. Before the intramedullary nail was applied, the distal screw locking hole was opened with the aid of a drill. Intramedullary nail covered with antibiotic impregnated cement was advanced from the proximal screw hole to distally and the nail was locked as the proximal and distal screw were applied with the aid of external guide. After the bleeding control and the folds were closed, the elastic bandage was wrapped and the operation was terminated.

Parenteral NSAID and empirical antibiotherapy (cefazolin 1 gr 3x1) were started postoperatively, following the elevation of the extremity. Appropriate antibiotherapy was applied according to the result of deep tissue culture.

**Follow-up**

The patients were followed up for the discharge to discontinue and bone healing in the early
RESULTS

The mean age of the patients during surgery was 51.2 years (range, 30-84 years), 4 were female and 10 were male. Three of the patients were treated with the diagnosis of femur, and 11 were with tibia infected pseudoarthrosis. Three of the patients had atrophic and 11 had hypertrophic infected nonunion. All patients had pain associated with weight loading and local palpation at the associated extremity. There were pathological movements in 5 patients without internal or external implants. All patients had low flow discharge of fistula. The mean follow-up period of patients was 24.7 months (range: 8-37 months).

Preoperative cultures taken from the sinus opening showed MRSA growth in 3 patients, MRSE in 1 patient, E. Coli in 1 patient, staphylococcus capitis in 1 patient, staphylococcus auricularisin 1 patient, and enterobacter in 1 patient; no growth was seen in 6 patients. Postoperative deep tissue cultures showed MRSA growth in 6 patients, MRSE in 1 patient, proteus in 1 patient, pseudomonas in 2 patients, E. coli in 1 patient; 3 patients showed no growth. In the preoperative and postoperative cultures, the same culture results were obtained in the bone cultures taken during surgery in 3 patients who had S. Aureus growth, in 3 patients who showed no growth, in 1 patient who had S. epidermidis and in 1 patient who had E. coli.

Figure-2: The preoperative and postoperative anteroposterior graphies of three patients with hypertrophic pseudoarthrosis. Patient no. 2, preoperative (A) and postoperative (B). Patient no. 4, preoperative (C) and postoperative (D). Patient no. 1, preoperative (E) and postoperative (F).
After the follow-up, infection showed regression in 85.7% of the patients (12 patients). In 2 patients, the discharge continues after debridement, nonunion was observed in the same patients. In 1 patient with hypertrophic pseudoarthrosis, who had union and improved infection, late term recurrence of infection was seen after 1 year.

Union was seen in a total of 10 patients (71.4%). Ten of 11 hypertrophic infected pseudoarthrosis patients (90.9%) showed union. None of 3 patients with atrophic infected pseudoarthrosis showed union (0%). Patient characteristics and treatment results are presented in Table-1.

**CONCLUSION**

In the treatment of infected nonunion, union can be achieved with infection control and stabilization. Debridement, local high döše antibiotic and systemic antibiotics are used for infection control. In this study, particularly in infected hypertrophic pseudoarthrosis, we have seen that the intramedullary nail applied with PMMA is effective in achieving stabilization, in regression of infection and in fracture healing.

S. aureus is one of the leading causes of chronic osteomyelitis. The infection may be due to a single or mixed agent. Malkowiack et al. (13) in their study reported that S. aureus showed growth in 60%, enterococci in 23%, pseudomonas in 9% and streptococci in 9%. In our study, 35.7% of the cases showed S. aureus growth, 14% showed pseudomonas growth. In five patients (35.7%), no growth could be obtained. The most reproducing microorganism was found to be similar with the literature; however the rate was lower. The reason for this was explained as the cultures of 3 patients were taken under antibiotic use continuity, and no microorganism growth in these patients, even though there was osteomyelitis clinic present.

In the literature, significant incompetence has been shown between the cultures taken from the non-bony tissues and the bone tissue during surgery (13-17). For S. aureus, this incompetence was found to be relatively low (13,17). In our study, the predictive values of the preoperative sinus opening and peroperative bone cultures were found to be low. However, the same microorganism was also obtained in the bone culture taken during surgery in patients who had S. aureus growth preoperatively (3 patients). As a result, it is very important that the cultures are taken from deep tissue and the culture material taken is the bone tissue.

First, Klemm et al. (8) used antibiotic impregnated PMMA in the treatment of chronic osteomyelitis. Subsequently, gentamicin impregnated PMMA chains have been used in the treatment of osteomyelitis by many investigators, and they reported good results.

Evans et al. (18) in their experimental study on rabbits showed beneficial effects of gentamicin impregnated PMMA treatment on chronic

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age/Gender</th>
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<th>Infection healing</th>
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*Recurrence of infection developed 1 year later
osteomyelitis, and they obtained the best result in animals that they applied gentamicin impregnated PMMA with systemic antibiotic.

Mohanty et al. (6) treated 49 patients with chronic osteomyelitis with gentamicin impregnated PMMA after surgical debridement and removed PMMA at 3 weeks postoperatively. In this series, low-level infection was seen in 6 of 10 patients who developed recurrence. In addition, the patients were followed for approximately 3.7 years and 39 patients showed no recurrence of infection in their last follow-up. Similarly, Wallenkamp et al. (9) treated 100 patients with chronic osteomyelitis diagnosis with surgical debridement and gentamicin impregnated PMMA, and published their results of a mean follow-up period of 5 years, reporting successful results in 92 out of 100 patients. Foldyna et al. (5) applied gentamicin impregnated PMMA in 29 patients with bone infection and reported a success rate of 69%.

Lyons et al. (19) have investigated the antibiotic impregnated PMMA chains with non-antibiotic impregnated PMMA chains used in the treatment of prophylaxis and treatment of bone infections, comparatively. They detected that the bacteria adhere to the non-antibiotic-containing PMMA chains in the experimental osteomyelitis by electron microscopic examinations. On the other hand, when tobramycin-impregnated PMMA chains were used, they observed that the bacteria didn’t adhere to the beads. These bacteria were found to be sensitive to tobramycin in the antibiograms. Therefore, if the bacteria are susceptible to the antibiotic used, the bacteria cannot adhere to the PMMA beads. In this regard, antibiotics can provide both prophylactic and therapeutic benefits.

Studies on the use of PMMA in patients with infected pseudoarthrosis are rare. Reichert P et al. (7) used debridement+antibiotic-containing PMMA and unlike our study, external fixator combination in 16 patients with Cierny Mader stage 3 and 4 infected tibia pseudoarthrosis. They reported that they achieved eradication of infection in 13 patients and union in 12 patients, and the Stage was 4b in 7 patients which the treatment was unsuccessful. In our study, antibiotic-containing PMMA+debridement +intramedullary fixation+systemic antibiotic treatment was used and the eradication of infection was calculated as 85.7%.

Teicoplanin was used as antibiotic in our study. The advantages of this antibiotic are its effectiveness, particularly in MRSA infections, its thermostability, its lesser effect on the mechanical stability of PMMA than gentamicin and vancomycin, and its better systemic and local side effect profile (20).

Since our patients had pseudoarthrosis along with infection and the implant which provided stabilization we applied for treatment was coated with antibiotic-impregnated PMMA, the spacer extraction could not be done without the adequate bone union, which can be evaluated as the disadvantage of our technique. This increases the likelihood of a potential bacterial glycocalyx layer formation in the case of a late osteomyelitis recurrence. As a matter of fact, late recurrence of osteomyelitis which couldn’t be eradicated by systemic antibiotic therapy occured in 1 patient. Tüzüner et al. (21) in their study wanted to avoid implant-associated osteomyelitis by adding calcium sulfate to teicoplanin-containing PMMA and achieved successful results in their histopathological experiment. In addition, use of biodegradable materials such as calcium phosphate cement instead of PMMA can be used as a solution of glycocalyx layer formation on PMMA, but its cost is high (22).

In our study, reamed locked intramedullary nail which is recommended for the treatment of tibia and femur pseudoarthrosis (23) was used. The 2 mm of the total diameter of the nail used in our cases is formed by antibiotic-containing PMMA. This can be considered to lead a decreased rigidity and implant stability. The small diameter is a disadvantage of the technique in reducing rigidity, however we think that the high elastic modulus of the surrounding PMMA increases the rigidity. As a matter of fact, we didn’t find any implant failure in our cases. We think that biomechanical studies are needed in this regard.

Because of the bacterial adhesions and microorganism colonization of the internal implants, external fixator use is recommended in infected pseudoarthrosis. However, this disadvantage dissapears when the internal implant is coated with antibiotic-containing PMMA, allowing the use of intramedullary nail which is the best biomechanical
treatment for long bone diaphysis pseudoarthrosis and removes the risk of complications of external fixator such as pin site infection and limitation of joint motion.

We recommend the use of antibiotic-impregnated PMMA coated reamed locked intramedullary nail use in the treatment of hypertrophic pseudoarthrosis without segmental defect, due to the advantages of high dose local antibiotic effect and intramedullary nail stabilization. In atrophic pseudoarthrosis, although the number of cases is low, it can be said to be effective in the treatment of infection, but inadequate in terms of bone remodeling. Further studies are needed in this regard.

REFERENCES