



End-capping of amputation stumps with a local antibiotic containing hydroxyapatite bio-composite - A report of 13 cases with chronic lower limb osteomyelitis



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ABSTRACT

We present our novel technique of end capping of amputation stumps with absorbable antibiotic containing hydroxyapatite bone cement as a marrow plug controlling bleeding and achieving high local concentration of antibiotics in cases complicated by chronic osteomyelitis. Our case series consisted of 13 patients who underwent lower limb amputations for chronic medullary osteomyelitis. Of 13 patients 12 had below knee and 1 had above knee amputation. All wounds healed uneventfully without any surgical site infection. There were no stump hematomas/seromas or instances of recurrent stump osteomyelitis or need for revision surgery.

1. Introduction

Major limb amputations can be complicated by bone and soft tissue infection and prolonged wound healing times which can delay recovery and return to function. Amputation may be preceded by attempts at limb salvage in cases with medullary long bone osteomyelitis due to canal instrumentation, open fractures and implant-related infection. Such patients often have multiple comorbidities and a poor physiologic reserve for additional surgery. Stump infections have been reported in up to 50% of cases in some series¹ and hence it is the responsibility of surgeon to ensure every step is taken to prevent infections and related complications in amputations stumps. Retention of adequate residual bone length is important for prosthesis fitting, rehabilitation and long term mobility. Deep bone and joint infections are less responsive to IV antibiotics due to poor blood supply, large dead spaces in bone and biofilms resisting systemic antibiotics and hence new techniques are required to prevent and treat infections in bone² We believe that local antibiotics at the site of amputation reduce the risk of early wound complications and local infection.

2. Study design and methods

We present a series of 13 patients with lower limb amputations for chronic medullary osteomyelitis in whom, at the time of primary

amputation, local antibiotic eluting absorbable bio-composite was used as an end cap. Cerament G is a gentamicin eluting synthetic bone graft substitute, that consists of hydroxyapatite and calcium sulphate, which has shown incorporation into bone radiologically.^{2,3} Cerament G contains 17.5 mg/ml of gentamicin as a paste which been designed to have a neutral pH (7.0–7.2). Mixing and injection devices ensure a homogenous distribution of antibiotic, whilst the material properties of Cerament G mean that all of this antibiotic is made available for elution and delivered in a controlled fashion.

At the time of the amputation procedure, Cerament G was used a medullary plug/end cap by injecting the bio-composite into the medullary canal of the stump (Figs. 1 and 2). On average 10 cc of Cerament G was used for the end-capping procedure. Amputations were carried out adhering to general precautions of adequate haemostasis, careful soft tissue handling and coverage. All patients received a single dose of intravenous Teicoplanin and Gentamycin at time of induction (age and GFR appropriate). The end cap plugs the medullary canal controlling bleeding, and also delivers high local doses of antibiotic treating any residual infection and providing continued local antibiotic prophylaxis.

Data we collected included patient demographics, level of amputation, indication for amputation, time to healing of amputations stump, incidence of wound complications like infection, fluid collection, seroma formation, hematoma formation, leaking of

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Fig. 1. ceramnet inside amputation stump AP view.



Fig. 2. ceramnet inside amputation stump lateral view.

cerament, microbiological data and incidence of return to theatre.

3. Results

Our case series consisted of 13 patients. 12 cases underwent a below-knee amputation and one an above knee amputation. The indication for amputation in all cases was chronic osteomyelitis with the failure of limb salvage surgery. In all cases, the infection was present in excess of 6 months and diagnosis established by microbiological cultures. Pre-operative investigations included blood tests, plain radiographs, MRI scans, CT scans, and WBC bone scans. In all cases, there was previous multiple attempts at debridement and systemic antibiotic therapy with a failure to control bone and soft tissue infection. Amputation was carried out through the area of medullary signal changes on MR Scan, to preserve length in 6 patients although deep tissue cultures were negative in all.

The primary cause of infection in 8 patients was an open fracture, diabetic osteomyelitis in 2 patients and implant-related osteomyelitis in the remaining 3 patients. The mean age was 59 (range 27–84) with 9 males and 4 females. In all cases, there had been prior instrumentation of the medullary canal. Mean time to stump healing was 21 days (18–28 days). All wounds healed uneventfully without any surgical site



Fig. 3. clinical photograph showing dry wound.

infection. (Fig. 3). None of the patients required a post-operative blood transfusion. There were no stump hematomas/seromas encountered. All patients were followed up for a minimum of 12 months. Most infections were poly microbial. The most common organism identified was coagulase negative staphylococci. Isolates also included streptococci, enterococci, Serratia, pseudomonas, klebsiella and diphtheroids. There were no cases where fungal involvement of bone was identified. There were no instances of recurrent stump osteomyelitis or need for revision surgery. All the wounds remained dry without any leaking and led to satisfactory healing and successful prosthetic fitting.

4. Discussion

Short term complications after major limb amputations include superficial and deep infection and hematoma formation with wound dehiscence leading to revision surgery. Harris et al.⁴ in a series of 149 patients reported a wound infection rate of 34.2% and a wound dehiscence rate of 13.4% after major limb amputations. Study done by Wadhvani et al. showed 43% of stump problems in lower limb amputees.¹³ Similarly, Polfer et al.⁵ reported on 300 cases of major lower limb amputation as having a return to surgery rate of 23% due to early hematoma formation. All these complications prolong hospitalisation and delay functional recovery.⁵

Several methods have been described to reduce infections and related complications in amputation surgeries, including prophylactic antibiotics, local antibiotics, PMMA impregnated beads, gentamicin impregnated collagen sponges, synthetic bone graft substitutes impregnated with antibiotics etc. There are published reports of antibiotic-impregnated PMMA (Polymethyl methacrylate/bone cement) beads having been previously used in extremity amputations for local antibiotic prophylaxis. Animal studies by Seligson et al.⁷ have demonstrated the efficacy of antibiotic-impregnated PMMA beads in amputation stumps to prevent the evolution of a localised infection. However, PMMA beads are bulky, can interfere with wound closure and as they are not bioabsorbable and require removal. Retained PMMA beads and plugs can lead to secondary infection.⁸ The rate of antibiotic release from PMMA bone cement relies on surface area and concentration gradient between its surface and surrounding tissue. The antibiotic release with PMMA is high during the first 2–3 days but quickly falls to sub therapeutic levels thus promoting multidrug resistant organisms and biofilm formation.

Chronic osteomyelitis may recur if dead-space management after excision of infected bone is inadequate. McNally et al. in his prospective study of 100 patients showed eradication of infection in 96 patients by a single stage protocol of debridement, multiple sampling, culture specific antibiotics and dead space management with antibiotic loaded bio

composite, Cerament.¹⁴ Application of cerament immediately leads to closure of dead space left in amputation stumps effectively preventing anterograde and retrograde spread of infection.

Diaphyseal bone in its natural state does not exist as a cavity without a cortical covering. Stump capping by various techniques has been previously attempted. Marquardt et al., in 1974 introduced cap-plasty of amputation stumps using an autologous cartilage bone graft to allow weight bearing and prevent ulceration of skin.^{9,10} Several other techniques have been used to cap bone ends including bone wax, osteoperiosteal flaps, silicone implants, autologous/allograft bone, cartilage transplants and plugs fashioned out of cortical bone.¹¹ These marrow plugs are not without its share of complications. Bone wax is mainly composed of beeswax. It can cause chronic inflammation, wax granulomas, and infection. Wax interferes with bone healing, does not integrate with the bone and remains there indefinitely as a foreign body.¹² Many cases have been associated with intense foreign body reactions with giant cells, plasma cells, and fibrous tissue and it can be a source of postoperative pain.¹²

Therefore, an absorbable bone graft substitute which can be applied easily, can carry and deliver local antibiotics predictably, and can remodel and integrate with bone would be ideal in such circumstances. Cerament G is a bio-ceramic of hydroxyapatite particles embedded in an injectable synthetic calcium sulphate carrier. The compressive strength provided by this injectable bio-ceramic is like that of cancellous bone to ensure at least the same mechanical stability as with autografts. It provides a flowable delivery system and once mixed it forms a paste that can be injected into bone defects, completely filling the cavity without any dead space. In vitro studies have shown gentamicin elution from Cerament G has a high initial peak (> 1000g/mL) and remains above the minimum inhibitory concentration (MIC) for at least 28 days. It has been proven that serum antibiotic levels remain in safe range despite high local tissue concentration.¹⁵ These levels of gentamicin can be effective in biofilm prevention and eradication. In addition, the dissolution of calcium sulphate allows high early release of antibiotics leaving a more porous hydroxyapatite scaffold to support the ingrowth of blood vessels and subsequent new bone formation.

Stump revision to a more proximal level increases the energy expenditure¹⁶ and hence every effort should be made to maintain the optimum stump length. The clinical decision to retain the optimum stump length for an energy efficient prosthesis often conflicts with the need for completely eradicating infection from bone and multiple debridements leave bony defects. Versatility of cerament to function as a bone graft substitute and antibiotic carrier gives surgeon more confidence in retaining adequate stump length.

Our case series demonstrates that end capping of amputation stumps with a resorbable antibiotic laden bio-composite is safe, effective and reproducible. The endcap occludes the medullary canal preventing excessive bleeding and reducing the risk of hematoma formation and transfusion requirements. Application of local antibiotic provides both bone and soft tissue prophylaxis minimising the risk of infection. We feel the application of local antibiotic is of particular importance, in cases where there has been previous instrumentation of the medullary cavity with a high risk of residual marrow infection or reactivation of infection. The high local levels of gentamicin achieved can be effective in both biofilm prevention and eradication. The antibiotic laden end cap also is effective against any residual planktonic organisms remaining after debridement. The advantage of using Cerament G as an end cap over PMMA is that an effective one-stage treatment can be performed and additional surgery for removal is not required. Unlike bone wax, Cerament G integrates with the host bone with no long term complications. We feel that the technique enhances wound healing, reduces complication rates and allows a more rapid return to function.

The drawbacks of our observational report include the limited

number of cases, lack of any comparative controls and a short term follow up. We feel that the technique reported merits additional research and review of long-term results. The cost involved in cerament application of offset by its effect in avoiding multiple surgeries.

5. Conclusions

Absorbable Gentamycin loaded calcium sulphate -HydroxyApatite bio composite as a marrow plug in amputation stumps is a novel technique which has shown promising results in lower extremity amputations and is a step towards reducing wound complications to get an early functional amputation stump. Our study has shown that Cerament is a better marrow filler with multiple desirable effects, and should be routinely used in those patients with multiple comorbidities were return to theatre should be avoided at all costs.

Author contributions

Anoop Anugraha: Concept; AcademicWriting; Literaturesearch; Statistics; Editing. Noman Jehangir: Literaturesearch; Statistics; Editing. Mohammed Alqubaisi: Literaturesearch. Asan Rafee: Concept; Editing. Nasser Kurdy: Concept; Editing. Anand Pillai: Concept; AcademicWriting; Literaturesearch; Statistics; Editing.

Declaration of competing interest

There are no conflicts of interest among authors.

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