LOCAL APPLICATION OF CALCIUM SULPHATE IMPREGNATED WITH VANCOMYCIN AND TOBRAMYCIN IN THE TREATMENT OF CHRONIC OSTEOMYELITIS

Ibrahim E. Abdellatif

Abstract

Background: *Despite the variety of available treatment options, including surgical procedures and antimicrobial therapy, bone infections are still a medical challenge as they are difficult to treat and cure.* ***Aim of the work:*** *The goals of this treatment protocol are to eradicate infection, heal the ulceration/abscess/wound, and reduce or eliminate the need for intravenous antibiotics in the treatment of osteomyelitis and complex infections of the skin and soft tissue structures.* ***Patients and methods****: From January 2011 to October 2013 a series of 14 chronic osteomyelitis procedures were performed. All patients underwent surgical debridement followed by application of synthetic pure dissolvable calcium sulphate beads impregnated with antibiotics were employed.* ***Results and conclusion:*** *The clinical outcome after six months amounted to successful treatment assessed as eradication of infection in 14 patients over the time of observation.*

Key words: *calcium sulphate, vancomycin, obramycin and chronic osteomyelitis*

INTRODUCTION

Chronic osteomyelitis represents a major health problem due to its significant morbidity and low mortality rate[1]. Despite the variety of available treatment options, including surgical procedures and antimicrobial therapy, bone infections are still a medical challenge as they are difficult to treat and cure[2]. Systemic antibiotics are part of the standard therapy after debridement of infected bone, but their efficacy may be limited due to impaired blood supply

and a low penetration rate at the site of infection[3]. Furthermore, long-term treatment and high doses are associated with severe side effects. The main problem associated with chronic bone infection is the capacity of the microorganisms to remain in necrotic bone tissue for long periods, especially in tissues that has not undergone adequate surgical debridement[4].

Traditionally, the management of chronic osteomyelitis emphasizes the excision of necrotic and infected material (sequestrectomy/debridement) followed by prolonged administration of antibiotics. The steps in the treatment of chronic osteomyelitis consist of correct microbiological diagnosis; improvement of the host's defenses; stabilization of underlying diseases; correct anatomical localization of bone involvement; adequate antimicrobial therapy; surgical debridement of all devitalized tissue; repair of soft tissues; and bone reconstruction and rehabilitation[5].

The most important factor for a successful treatment of patients with bone infection is the quality of debridement. The debridement must achieve a clean and viable wound through anon-traumatic exposure. All devitalized tissues need to be removed, and the surgical technique used will depend on the extent of the bone lesion[6&7].

Autogenous bone grafting in a second stage procedure has been the gold standard for this type of treatment, but its quantity is limited. In addition the autogenous bone graft will be absorbed or become sequestrum if the inflammation control is not sufficient[8&9]. Allogeneic bone, although solving the problem of limited supply, is likely to cause or increase the immune response and infection[10&11]. In situations in which there is a dead space after the removal of devitalized tissues, the use of polymethyl-methacrylate cement impregnated with an antibiotic for local. Antibiotic-impregnated bone void fillers or cements can act as local anti-infective drug release systems, which not only fill up the dead space after surgical debridement but also deliver high antibiotic

concentrations at the site of potential infection, without increasing serum antibiotic levels[12-16]. Disadvantage of polymethyl-methacrylate (PMMA) is that the material is non-biodegradable, making subsequent invasive procedures necessary to remove the implant in many cases[17]. Additionally, PMMA has a poor elution profile, characterized by an initial bolus release of relatively high concentrations followed by a rapid decline to sub-inhibitory concentrations[18]. However, antibiotic impregnated bone cements are non-absorbing, can support a biofilm and become a foreign body and nidus for infection at the implant site. They must be removed in a further surgical procedure if bone graft implantation is required. Stimulan is a synthetic hemihydrate form of Calcium Sulfate. It is produced using a synthetic process resulting in 100% purity with no traces of potentially toxic impurities which has been associated with naturally occurring mineral sources of Calcium Sulfate. Stimulan also has the advantage of delivering a wider spectrum of antibiotic combinations into the joint. It cures at a low temperature, thus allowing heat-sensitive antibiotics to be mixed with Stimulan. This is in contrast to PMMA in which only heat-stable antibiotics can be used. Even with these advantages, there has been concern with using dissolvable antibiotic-loaded Calcium Sulfate[19&20].

Calcium sulfate has several advantages over other local antibiotic delivery systems: it is biodegradable; it has predicable elution characteristics; it is osteoconductive; and it can fill dead space[21&22]. Synthetic calcium sulfate is a pure, biocompatible bone graft material with the absence of any traces of organic impurities. Such impurities have been associated with the complications of mined and refined calcium sulfate[23]. The carrier was calcium sulphate (Stimulan) commonly used as a bone graft to fill bone cavities resulting from disease, trauma or surgery. Its main characteristics are 100% purity and its ability for biodegradation[24].

MATERIAL AND METHOD

This study was a retrospective analysis of cases of chronic osteomyelitis over a 2-year period. From January 2011 to October 2013 a series of 14 chronic osteomylitis procedures were performed in Al-Azhar University hospital Assuit and Alhelal insurance hospital. Patients referred for treatment of osteomyelitis were pre-operatively imaged. The mean of the age is 28 (10-48), the eight of 14 patients were males and the six of 14 patients were females. The most common bones affected were the tibia (8 patients, 66%) and radius (4 patients, 33%) and femur (2 patients, 16%) (Fig. 1-7) & (table,1). All patients underwent surgical debridement includes resection of soft tissue focus, removal of sequestrum, fenestration drainage of bone lesions, lavaging and multiple drilling the surface of sclerotic bone with a drill followed by application of synthetic pure dissolvable calcium sulphate beads impregnated with antibiotics were employed. The calcium sulfate powder was mixed with 1g of vancomycin powder with 240 mg of tobramycin in all cases. Calcium sulfate bone graft substitute impregnated with antibiotics (1 gram of vancomycin and 240 mg of gentamycin) to fill in the residual gap.

Resorption of implanted beads and bony reconstruction were evaluated by means of radiographs obtained at immediately postoperative, two weeks, one, three and six months after implantation.

The aim of this treatment protocol are to eradicate infection, heal the ulceration/abscess/wound, and reduce or eliminate the need for intravenous antibiotics in the treatment of osteomyelitis and complex infections of the skin and soft tissue structures.

Table 1: Cases of Chronic Osteomyelitis

Case no.	Age	Sex	Site of infection	Previous treatment
1	10	Male	Right distal tibia	Multiple drainage and curettage
2	13	Female	Left lower third radius	Multiple drainage and curettage
3	19	Female	Right mid shaft femur	Multiple drainage and curettage
4	16	Male	Right tibia lower third	Multiple drainage and curettage
5	22	Male	Left upper third of tibia	Multiple drainage and curettage
6	27	Female	Left mid shaft of tibia	Multiple drainage and curettage
7	30	Male	Left lower third radius	Multiple drainage and curettage
8	33	Female	Right mid shaft femur	Multiple drainage and curettage
9	23	Male	Left upper third of tibia	Multiple drainage and curettage
10	40	Female	Left upper third of tibia	Multiple drainage and curettage
11	37	Male	Left mid shaft of tibia	Multiple drainage and curettage
12	42	Male	Right upper third of tibia	Multiple drainage and curettage
13	48	Female	Left mid shaft of tibia	Multiple drainage and curettage
14	19	Male	Right lower third radius	Multiple drainage and curettage

(Table, 1)

Ethical approval

Approval to conduct this research has been provided by the University hospital of Al-Azhar, Assuit and Alhelal insurance hospital, Sohag , in accordance with its ethics review and approval procedures. Any person considering participation in this research project, or agreeing to participate, may raise any questions or issues with the researcher at any time.

RESULT

A radiological implant evaluation after approximately six months showed that bony integration of the beads. Most of the calcium sulphate had completely absorbed within 3 months post surgery. No foreign body reactions or infection were found in all 14 patients. Primary wound healing occurred in 9 patients and secondary wound healing in 4 patients. The clinical outcome after six months (or at the time of early termination) amounted to successful treatment assessed as eradication of infection in 14 patients over the time of observation.

DISCUSSION

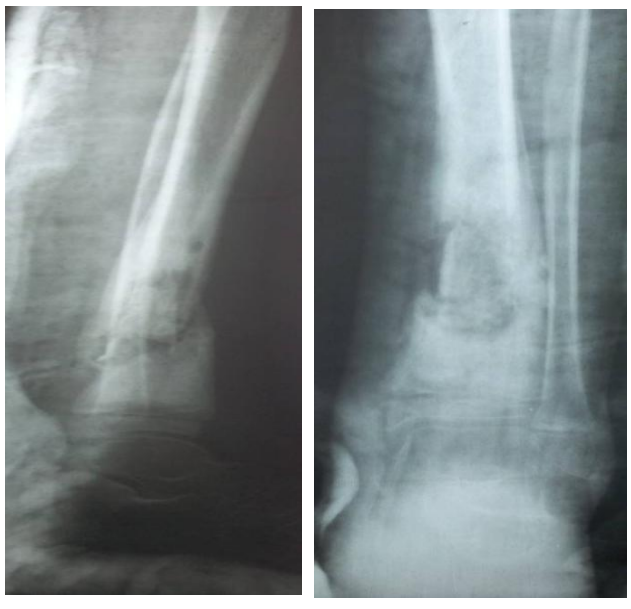
Chronic osteomyelitis is an infection difficult to treat due both to multidrug resistance of common pathogens and to poor penetration of antibiotics into bone[25]. Insufficient release of the antibacterial agent to the site of infected bone is a frequent problem associated with systemic antibiotic therapy and sometimes even with local drug delivery systems[26]**.**

Disadvantage of PMMA is that the material is non-biodegradable, making subsequent invasive procedures necessary to remove the implant[17]. Additionally, PMMA has a poor elution profile, characterized by an initial bolus release of relatively high concentrations followed by a rapid decline to sub-inhibitory concentrations[18]. They must be removed in a further surgical procedure if bone graft implantation is required. Stimulan is a synthetic hemihydrate form of Calcium Sulfate. It is produced using a synthetic process resulting in 100% purity with no traces of potentially toxic impurities which has

been associated with naturally occurring mineral sources of Calcium Sulfate[19&20]. Stimulan also has the advantage of delivering a wider spectrum of antibiotic combinations into the joint. It cures at a low temperature, thus allowing heat-sensitive antibiotics to be mixed with Stimulan.

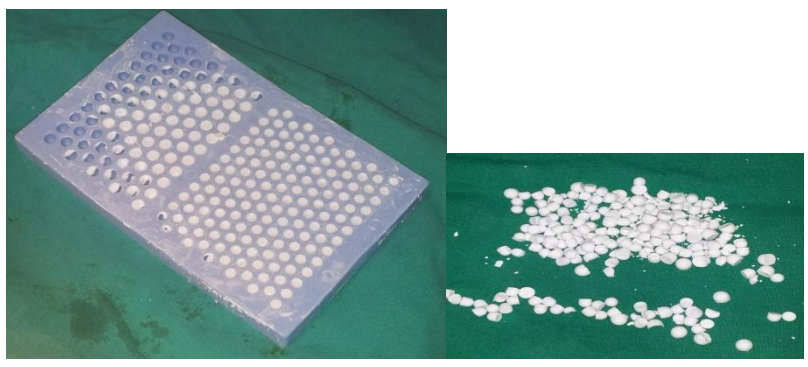
Synthetic calcium sulfate offers the advantages of predictability in the elution of antibiotic agents over a three to four-week period, buffering the local wound pH (towards physiologic), elimination/reduction of dead-space and compatibility with a number of antimicrobial agents. Subsequent procedures to remove implanted material and the recreation of dead space are avoided due to the ability of the beads to resorb.

Surgical debridement, obliteration of dead space resulting from debridement and a long course of antibiotics remain the mainstay in the management of osteomyelitis. Many studies have demonstrated that combining debridement with the use of antibiotic impregnated material achieve better eradication of infection and possibly decrease the duration of systemic antibiotics needed[27&28].



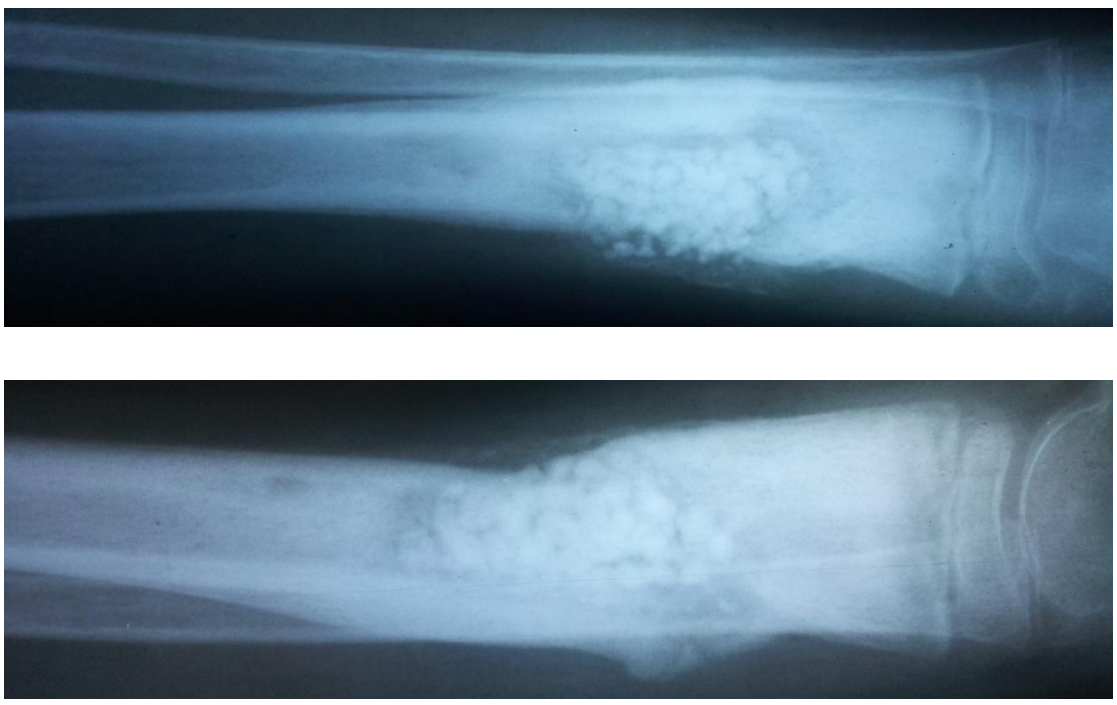
(Fig. 1): Plain x-ray of male child 11 years old has severe chronic osteomyelits distal third of tibia.

(Fig.2): Intra operative photo showed that sequestrectomy and debridement.

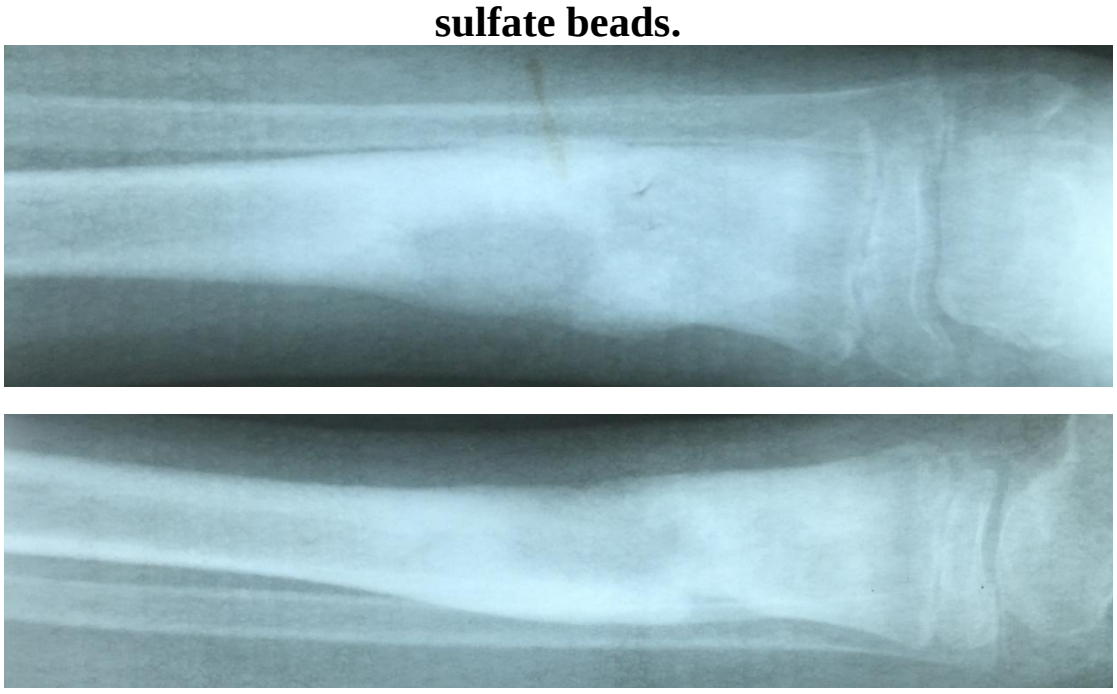


(Fig. 3): Intra operative photo showed that preparation of calcium sulfate with antibiotic.

(Fig. 4): Intra operative x-ray showed that calcium sulfate beads.



(Fig. 5): Plain x-ray two weeks postoperative showed that partially absorbed calcium sulfate beads.



(Fig. 6): Plain x-ray evaluation after six months showed that bony integration of the beads and the calcium sulphate had completely absorbed post surgery.

(Fig. 7): Photo evaluation after showed that completely skin healing with no sinus post surgery.

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الملخص العربي

استخدام كبريتات الكلسيوم مع المضاد الحيوى فى علاج تنكرز العظام

البحث تم إجراؤه لتقييم استخدام كبريتات الكلسيوم مع المضاد الحيوى فى علاج تنكراز العظام. في هذا البحث تم علاج ١٤ حاله ممن يعانون من تنكراز العظام وتم أيضاً استعراض الطرق المتبعة تنكراز العظام بداية من دراسة خطة العلاج قبل العملية والطرق الجراحية المتبعة وخطة العلاج فيما بعد العملية وكان متوسط العمر ٢٨ سنة وتمت متابعتهم لمدة متوسطها ٢٤ شهر والغرض من البحث هو استئصال المكروب والتئام العظام والجلد

تم تقييم النتائج الإكلينيكية والوظ يفية لمختلف الحالات مع عرض المضاعفات التي حدثت لبعض الحالات في أثناء مرحلة العلاج . كما تم أيضاً مناقشة نتائج البحث ومقارنتها بالأبحاث المشابهة أو المنشورة بالدوريات العلمية مع إلقاء الضوء على الإمكانات الكبيرة