International Journal of Orthopaedics Sciences

E-ISSN: 2395-1958
P-ISSN: 2706-6630
IJOS 2022; 8(1): 123-126

www.orthopaper.com
Received: 20-11-2021
Accepted: 23-12-2021

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Are stimulan beads effective enough in managing chronic long-standing infections of bones?

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DOI: https://doi.org/10.22271/ortho.2022.v8.i1b.2998

Abstract
A long-standing infection of bone is called chronic osteomyelitis, which is a very debilitating condition for the patient. Management of which requires involvement from many medical specialities, including orthopaedics, plastic surgery, microbiology, etc. However, surgical debridement remains the most important mode of treatment, administration of proper anti-microbial therapy has utmost importance for the success of treatment. IV antibiotics have their own share of problems i.e., long hospital stay, Antibiotic's side effects, IV cannula related infection, thrombophlebitis, etc. Most times, surgical debridement creates dead space, which in itself is a problem to address. Stimulan works as an antibiotic carrier made up of calcium sulphate which is absorbable helps in battling issues like dead space & local antibiotic delivery. Here we aim to study the effect of Stimulan in the management of chronic long-standing infections of bones. Here we conducted a retrospective study on 24 patients operated with Stimulan beads at Civil Hospital Ahmedabad in the last 2 years with a minimum follow-up period of 1 year. This study aims to establish or nullify the efficacy of Stimulan bio-absorbable beads in patients operated on for chronic osteomyelitis.

Keywords: Antibiotics, chronic osteomyelitis, dead space, long bones, Stimulan

Introduction
Although the world has witnessed a decline in the incidence of chronic osteomyelitis nowadays but the number of people suffering complex trauma due to RTA, Machine injury etc. leading to subsequent bone and soft tissue infections is increasing day by day. Chronic infection presents a serious complication following such complex trauma. Conventional treatment for which included extensive saline wash, local and intravenous antibiotics, debridement etc. [1].

Calcium sulphate ($CaSO_4$) is inorganic and has three principal forms: anhydrous, known as anhydrite, with the formula $CaSO_4$; hemi-hydrated with the formula $CaSO_4 \cdot 0.5H_2O$ and di-hydrated with the formula $CaSO_4 \cdot 2H_2O$ [2]. Once water is added it converts to the dihydrate form, and this is the basis for the setting reaction. Stimulan is the synthetically pure hemi-hydrated form.

Data till date suggests superiority of calcium sulphate over PMMA for the purpose of filling void and delivering antibiotics. The implantation of antibiotic laden calcium sulphate into bone or soft tissue does not produce any foreign body reaction, infact itself is usually absorbed and removed from site of implantation and stimulates new bone formation when periosteum or bone is also present [2]. Today, calcium sulphate beads may be used as an alternative void filler to PMMA (poly methyl methacrylate) in the presence of infection, non-union or bone loss. Conventional antibiotic-loaded PMMA beads require subsequent removal and may develop biofilm on their surface if left in situ for long periods of time. It has also been found to have a relatively short period of antibiotic release with a decrease in local concentrations to 10% of the initial levels within 24 hours in contrast to calcium sulphate, which releases 100% of its antibiotic load as itself gets absorbed, resulting in superior drug-releasing profile and higher sustained antibiotic concentrations over a period of several weeks. This results in concentrations of antibiotic locally that can be many times higher than the MIC (Minimum Inhibitory concentration) for the relevant pathogen, while also ensuring that systemic levels and associated toxicity remain low as most commonly used drugs include gentamicin which has severe ototoxicity and nephrotoxicity [27].

Materials and Methods

For the purposes of this study, we chose Stimulan® [Bio composites, Keele Science Park, Staffordshire, UK] as the purified antibiotic carrier [3]. Since a broad-spectrum antibiotic preparation provides coverage against gram-positive and gram-negative species with few resistant bacterial strains, we selected vancomycin and gentamicin to treat gram-positive and gram-negative bacteria, respectively [3]. These antibiotics also act as an effective combination due to their synergistic bactericidal potential in treating serious infections involving Staphylococcus aureus and other pathogens. Data were collected retrospectively from operative records and demographic date such as age, sex, residence and also an indication for the patient were recorded.

24 patients with chronic osteomyelitis were selected at Civil Hospital Ahmedabad [tertiary care centre] based on the available Demographic data, including age and gender, and clinical data, including patient's general condition, indication for surgery, follow-up, mortality and complications. For retrospective review study of the effectiveness of antibiotic coated calcium sulphate beads who were followed up for a minimum period of 1 year. Patient at the time of primary surgery underwent sequestrectomy and radical debridement of infected bone and soft tissue till 'paprika sign' (punctate bleeding from margins of debrided bone suggestive of the reactive new bone surrounding an area of chronic infection is living and usually does not require debridement.) was achieved with a collection of histopathology and culture sensitivity samples intraoperatively. Inclusion criteria for using Stimulan were young active age, average built, no sepsis or other active infections in body, avail to follow up. Any previously implanted Orthopaedic hardware were removed followed by thorough irrigation of the local site with normal saline and then an external fixator was placed to hold the non-union site with appropriate reduction.

These antibiotic-laden Stimulan beads were placed in dead space created by debriding dead bone. After that, closure of the skin was performed. In case of inadequate soft tissue coverage, we did also use sterile porous polyethylene dressings. These beads become soft after hydration and demonstrated complete dissolution within a few weeks and can be seen in subsequent radiographs.

Outcome results were measured in terms of radiological and clinical recovery (Union and the presence of infection). Bone union was assessed as bridging of three out of four cortices and Infection was assessed by clinical signs (erythema, drainage, and wound problems), further need for systemic antibiotics and subsequent admission for the same. These parameters were assessed during the one-year follow-up period after discharge from the hospital.

Fig 1: Pre-Op Osteomyelitis

Fig 2: Post-Op Osteomyelitis

Fig 3: A string of antibiotic beads is placed into the wound for dead space management and to provide a high concentration of local antibiotic to the wound

Fig 4: In open fractures with significant soft tissue injuries, antibiotic beads can be placed in an open wound. The soft tissue defect can be covered with an adhesive, porous, polyethylene film

Fig 5: Stimulan used in upper tibia osteomyelitis

Fig 6: Stimulan used in calcaneal osteomyelitis

Discussion

Out of the 24 patients in whom beads were used 16 patients showed complete clinical (No discharging sinus, no local site erythema) and radiological (X-rays s/o Bone union) recovery after 1 year of extensive follow-up, 6 of them had shown partial recovery and a mean of 2.3 re-admissions during the follow-up period and 2 patients showed no response to the treatment and thus treatment failure.

Table 1: Definitions

Recovery	Clinical	Radiological Union
Complete	Present	Present
*Partial	Present/Absent	Present/Absent
No	Absent	Absent

(*Partial includes either clinical or radiological union, never both)

Most of the study patients achieved union during the follow-up period, as evidenced on radiographs. The average time to heal was 4 to 11 months. ESR was found to be normal in all 24 patients postoperatively with an average of 10.8 ± 3.6 mm/hr. All cases involving a draining sinus, or with local signs of infection such as erythema, warmth, swelling or pain over the treated segment are resolved in the post-operative follow-up period. No recurrences were noted in that time. Microbiological analyses of sample sent intra-operatively showed coagulase-negative Staphylococcus (10 cases) to be the most common. The other culture results were as follows: Staphylococcus aureus (4cases), Escherichia Coli (4 cases), Enterobacter cloacae (2 case), and 4 cases had mixed infections involving gram-negative bacilli and gram-positive cocci.

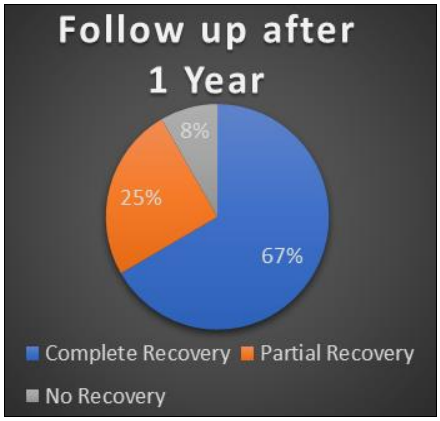

Fig 7: 1 year follow up

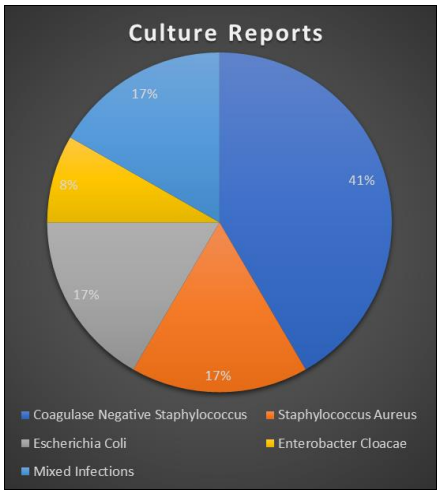

Fig 8: Common Microbes found

Conclusion

We can infer from the above-mentioned data that synthetically prepared sterile antibiotic-loaded dissolvable beads are an acceptable tool for local antibiotic delivery in limb salvage for chronic osteomyelitis of any variety of cause and is providing satisfactory results. It saves the patient from repeated admission and the need for long courses of intravenous antibiotics with toxicity associated with them.

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