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Original Article

ROLE OF BIODEGRADABLE ANTIBIOTICS IMPREGNATED CALCIUM SULFATE BEADS IN ERADICATION OF INFECTION IN CASE OF OSTEOMYELITIS OF LONG AND SHORT BONES IN CHILDREN AND ADULTS

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Abstract

Background: *Despite recent advances, the difficulties involved in management of bone infections continue to plague the practice of orthopedics, this study reviews the clinical results using biodegradable antibiotics impregnated calcium sulfate (AICS) beads in 24 patients who suffered from osteomyelitis.* ***Aims of the work:*** *evaluation the role of antibiotics impregnated calcium sulfate in eradication of infection in case of osteomyelitis. all patient prepared for surgical debridement and calcium sulfate* ***Patient and methods*** *impregnated with vancomycin and gentamycin beads were inserted into the bone cavity and surrounding soft tissue.* ***Results****: this study include 24 patients, 17 (70.83%) patients were males while 7 (29.17%) patients were females, The mean follow-up was 9 months (range from 6-12 months), the mean age of the patients was 33.2 ± 19.5& tibia is the most common affected bone & Staphylococcus aureus was the organism that had been reported in 45.83% of all swabs, In the final results 21(87.5%) patients were completely healed while only3 (12.5%) patients still had infection.* ***Conclusion****: antibiotics impregnated calcium sulfate is safe and effective method in treatment of osteomyelitis and the results show high rate of eradication of infection.*

Keywords: *Osteomyelitis, Antibiotics impregnated calcium sulfate (AICS), Vancomycin, Biodegradable beads, PMMA, Cierny and Mader classification of osteomyelitis*

1. Introduction

Osteomyelitis is an inflammatory disorder of bone caused by infection leading to necrosis and destruction [1]. Hematogenous osteomyelitis (HO) is a type of osteomyelitis occurs when bacteria reach bone through hematogenous seeding. With a serious disease burden, and socioeconomic Impact osteomyelitis has become more common in recent years [2]. The challenge involved in the treatment of bone infections and non-unions continue to plague the practice of orthopedics Despite recent improvement Staphylococcus aureus and coagulase-negative staphylococci, streptococci, Gram-negative pathogens (e.g. enterobacteria, pseudomonads), and anaerobic bacteria are the causative pathogens in approximately 75 percent of cases of chronic osteomyelitis [3]. Since chronic osteomyelitis is challenging to manage and because it is difficult for the antibiotics to penetrate into localized area due to malformations that are secondary to chronic infection treating chronic osteomyelitis has become challenging issue in orthopedics [4]. Due to the availability

of new materials and methods, many new concepts and technologies have been developed for the treatment of chronic osteomyelitis on the basis of regular treatment. Following the regular use of antibiotic chains, the use of non absorbable antibiotics impregnated cement for bones and absorbable biological bone cement for treating infections has recently been described [5]. Local delivery systems have been explored to minimize systemic toxicity and eliminate concerns about antibiotic penetration, while also achieving high local doses of antibiotics. Although the reality that Polymethyl Methacrylate (PMMA) has emerged as the gold-standard form of antibiotic administration in both the management and prevention of orthopedic infections, bead removal requires a second surgical operation and does not contribute to the bone-healing processes. Calcium Sulfate has also been shown to exhibit osteoinductive properties another interesting property of Calcium sulfate delivery systems is its ability to combine with most antibiotics & as they slowly dissolve, there is a sustained release of antibiotics over a period. Calcium Sulfate beads do not require a second surgery for removal as they get absorbed overtime, this contrasts with the use of polymethylmethacrylate (PMMA) beads and Spacers which necessitates removal, On occasion the (PM MA) system may even serve as a nidus of infection once the antibiotic is completely eluted. Calcium sulfate provide bone graft substitute that resorb and is replaced with bone during the healing process& it is biodegradable and is absorbed by the body in approximately 30 to 60 days, The amount utilized, the patient's health, and the surgical site's vascularity are all contributing variables. This study aimed at evaluating the outcomes of using antibiotics impregnated calcium sulfate in treatment of bone infection (osteomyelitis), fig. (1)

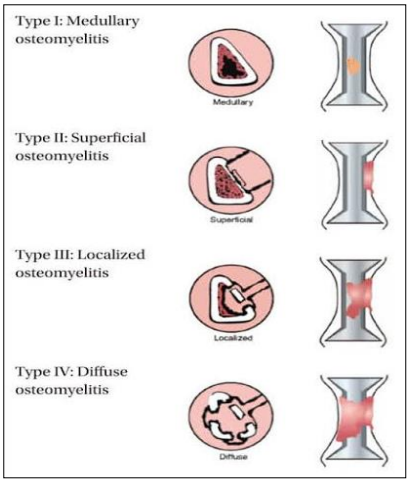

Figure (1) Cierny and Mader classification of osteomyelitis

2. Patients and Methods

In the period between April 2022 and April 2023, this study was carried out as a single-surgeon, single centered (Orthopaedic Surgery dept., Sohag Univ., Egypt) prospective cohort study. It was carried out on 24 patients presented to the Orthopedics and Trauma dept., Sohag Univ. Hospitals presented by osteomyelitis. All patients have written consents Following Departmental Research Committee approval and Research Ethics Committee approval.

2.1. *Inclusion criteria*

Patient with osteomyelitis of long or short bones at any age and of any sex. Patients who qualified for this study had **a)** intact vascular status, this was determined by either palpable pulses with evidence of intact local perfusion, **b)** confirmation of osteomyelitis and **c)** Patients with bone infections that were not responding to several trials of treatment.

2.2. *Exclusion criteria*

Patients with active peripheral vascular disease, pregnancy, with chronic kidney disease or allergy to vancomycin, patients refuse to participate

2.3. *Preoperative evaluation*

Radiological: plan x-ray & MRI. Laboratory: CBC &ESR &CRP& other preoperative tests as LFT, KFT and coagulation profile. Swab and culture &sensitivity

2.4. *Method (technique)*

1) Anesthesia general anesthesia; Children' general anesthesia. In adults (Upper limb' regional nerve block& Lower limb' spinal anesthesia). **2)** Position' Supine position. **3)** Incision with excision of the sinuses tracts. **4)** Local debridement' Removal of All unhe-althy granulation tissue and dead necrotic bone fragment, lavage with copious quant-ities of normal saline and hydrogen peroxide water. **5)** Preparation of Antibiotics imp-regnated calcium sulfate beads; Preparation of antibiotics impregnated calcium sulfate (AICS) beads, the antibiotic beads will be prepared by adding the liquid monomer to the calcium sulfate powder in an inert bowl, the choice of the antibiotic will be determined by the culture report when available, two antibiotics will be chosen in the presence of mixed infections, when preoperative culture reports unavailable broad-spectrum gram-positive and negative coverage will be combined, the antibiotic loaded cement will be made into spheres of 2-4 mm, the beads will be placed inside the bone cavity. preparation of AICS by Adding 2gm vancomycin powder to calium sulfate powder and mix together very well then, Adding 3 ampules of garamycin 80mg (6ml) to premixed calcium sulfate and van-comycin powder and mix for 30 seconds finally, Apply to the bead mat immediately & set in 3 to 5 minutes, fig. (2). **6)** App-lication of AICS beads after good deb-ridement of infected bone and soft tissue. Application of the AICS beads inside medulla or bone cavity and surrounding soft tissue. Closure of the wound in layers, sterile dressing is applied over the wounds.

Figure (2)

2.5. *After treatment*

Patient stay at hospital for 3-5 days & during this period neurovascular examina-tion & assessment of swelling & patients receive parenteral antibiotics till appearance of culture and sensitivity then shifted to the most sensitive antibiotics according to the results of culture and sensitivity.

2.6. *Discharge and follow up*

Patients Followed at regular intervals, 2 weeks postoperative and every month for 6-12 months. Patient examined clinically for signs of infection e.g. discharging sin-uses, redness, and swelling, radiological examination by means of plain radiograph and laboratory examination ESR &CRP & CBC

2.7. *Representing cases*

1) 33 years old female patient presented with chronic osteomyelitis proximal tibia (of 7 month duration) good debridement and local antibiotics impregnated calcium sulfate beads (AICS), fig. (3).

Figure (3) **Up** immediate post-operative x-ray, **Mid** & down 6 months follow up x-ray

2) 13 year male patient with osteomyelitis proximal tibia of 4 months duration' debridement and AICS beads, fig. (4).

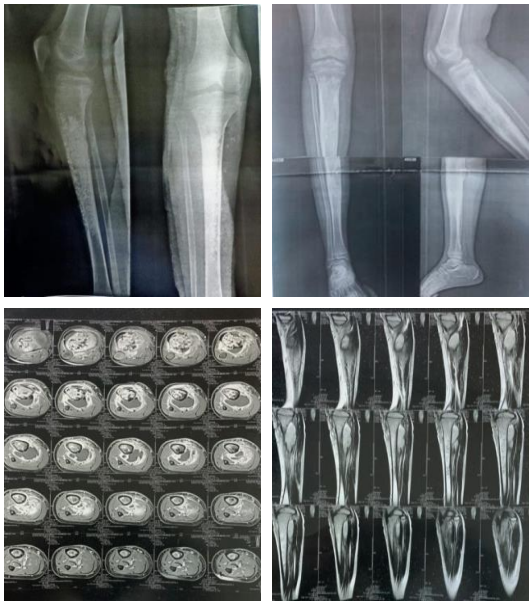

Figure (4) **Up** preoperative MRI, **down lift.** Immediate post-operative, **down right** 9 months follow up x-ray

3) 8 years male child with chronic osteomyelitis distal tibia (of 6 months duration), debridement & AICS beads, fig. (5).

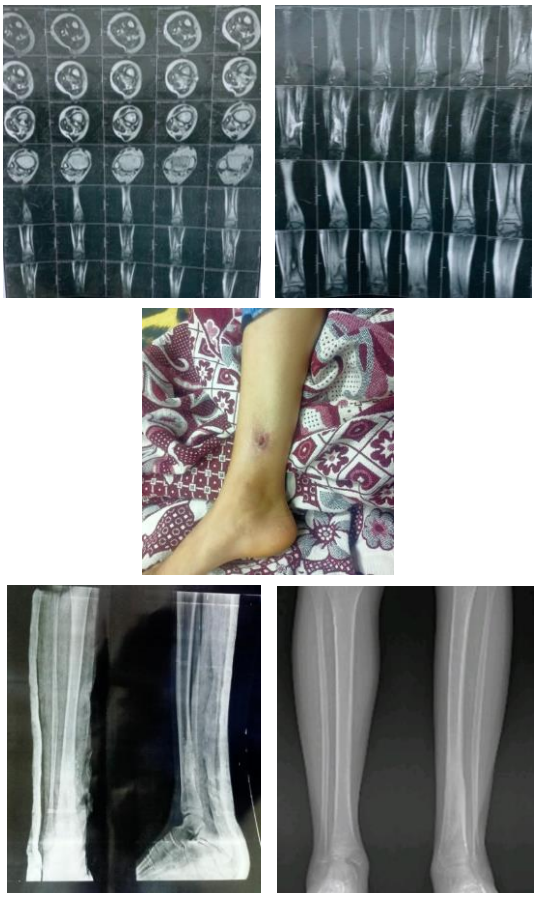

Figure (5) **Up L** preoperative clinical image, **up R** preoperative MRI, **down L** immediate postoperative x-ray, **down R** 9 months follow up x-ray

4) 55 years male patient with posttraumatic chronic osteomyelitis distal tibia (of 7 months duration), debridement & AICS beads, fig. (6).

Figure (6) **Up L** preoperative MRI, **up R** preoperative x-ray, **mid L** intraoperative, **mid R** immediate postoperative, **down L** 6 months follow up x-ray, **down R** 9 months follow up x-ray.

5) 4 years old male child with proximal femur osteomyelitis >>> debridement & AICS beads, fig. (7).

Figure (7) **Up** preoperative x-ray, **mid** postoperative x-ray, **down** 6 months follow up x-ray

6) 10 years female child with proximal tibia osteomyelitis with sinus discharging pus, debridement and AICS, fig. (8).

Figure (8) **Up L** preoperative x-ray, **up R** postoperative x-ray, **down R** 9 months follow up x-ray

3. Results

This study included 24 patients who had been suffering from long-bone infection (osteomyelitis). The mean age of the patients in this study was 33.2 ranging between 5 and 55 years, tab. (1) While the male to female ratio was 2,428. The average follow up was of 9 months (range. 6-12 months). According affected site tibia is the most common affected site (reported in 12 (50%) of cases), femur second common site (reported in 6 (25%) patients, while humerus affected in 3 (12, 5%) patients, radius affected in 2 (8,333%) patients, tab. (2). According Causative organism (intraoperative culture and sensitivity) results shown in tab. (3). Staphylococcus aureus is the most common isolated organism in 11(45, 83%) patients, tab. (4). According complete eradication or recurrence of infection, 21 (87, 5 %) patients show complete eradication of infection while 3 (12, 5%) patients show recurrence of infection, tab. (5).

Table (1) Age & sex distribution

		N=24
Age (years)	***Mean ± SD***	33.2 ± 19.5
	Range	6 – 55
		N (%)
Age groups	***-10***	8(33.33%)
	11-20	2(8.33%)
	21-30	7(29.17%)
	31-40	3(12.5%)
	41-50	2(8.33%)
	51-	2(8.33%)
Sex	***Male***	17 (70.83%)
	Female	7 (29.17%)

Table (2) Affected bones

		N=24
Affected bone	***Tibia***	12 (50%)
	Femur	6 (25%)
	Humerus	3 (12.5%)
	Radius	2 (8.33%)
	Short bones	1(4,166%)

Table (3) Side

		N=24
Side	***Right side***	15 (62.5%)
	Left side	9 (37.5%)

Table (4) Intraoperative culture of the studied patients

		N=24
Intraoperative culture	*Coagulase -ve staph aureus*	3 (12.5%)
	Gram negative bacilli	2 (8.33%)
	Pseudomonas aeruginosa	3 (12.5%)
	Staph aureus (MRSA)	9 (37.5%)
	Staph aureus (MSSA)	2 (8.33%)
	Streptococcus pyogenes	1 (4.17%)
	Mixed infection	2 (8.33%)
	No growths	2(8.33%)

Table (5) eradication or recurrence of infection

		N=24
Eradication or recurrence of infection	*Eradication*	21 (87.5%)
	Recurrence	3 (12.5%)

4. Discussion

Osteomyelitis therapy has become a challenging issue in orthopedics since it is hard to eliminate and because it is challenging for the medicines to penetrate into local areas because of deformities that are consequent to chronic infections [4]. Numerous

innovative ideas and technologies have recently been created to manage the symptoms of chronic osteomyelitis on base of regular therapy as a result of the accessibility of new materials and techniques. The ability to achieve greater and more effective concentrations in the local region of an infected bone by applying local antibiotics over an extended period of time is one benefit of local antibiotics. Another is the reduction in the possibility of systemic toxicity and the avoidance of side effects associated with systemic chemotherapy [5]. Following the regular use of antibiotic chains, the use of non-absorbable antibiotics impregnated bone cement and absorbable biological bone cement for treating infections has recently been described [6]. Researches have concentrated on the impact of employing a local drug carrier technique or giving vancomycin systemically [7]. The high rate of success that was attained is promising for the therapeutic use of vancomycin for MRSA-induced bone infections, since studies have shown that methicillin resistant staphylococcus aureus (MRSA) is responsive to high local dosages of vancomycin [5-8]. Although the application of antibiotic-impregnated PMMA has shown an excellent curative effect in the eradication of infection, its deficiencies have been obvious. Initially, owing to its non-biodegradable nature, PMMA has the ability to act as a nidus for recurrent infections if left in the void beyond the time when an efficient antibiotic has been eluted [9,10]. Second PMMA does not contribute to bone regrowth and requires an additional surgical procedure to be removed. This second procedure delays the healing process and increases the cost [11]. Other drawbacks of PMMA treatment include an increased probability of the development of antibiotic-resistant microorganisms and diminished immunity of the host. Calcium sulfate, an absorbable substance, has attracted therapeutic interest, calcium Sulfate that has been antibiotic-impregnated provides special benefits. Firstly, it is osteo-conductive, displays the typical steady and slow resorption, and may be removed without extra surgery [12]. Second, it has been discovered that calcium sulfate impregnated with antibiotics is osteo-inductive, which means it may be able to stimulate the differentiation of mesenchymal stem cells of the bone marrow into osteoblasts. Although any water-soluble antibiotic can be incorporated into Calcium Sulfate, the ideal antibiotic remains controversial. Vancomycin, gentamicin and tobramycin were the common choices for Calcium Sulfate loading. It has been determined that the antibiotic resistance of bacteria is one hundred to one thousand times greater than that of so-called planktonic microorganisms. Antibiotics may be used alone or in combination with surgical debridement. Infection eradication, prevention, and the majority of treatment options depend on concurrent local antibiotic therapy. Bioactive glass, calcium phosphate, and calcium sulfate ceramics are among the synthetic bone graft alternatives examined for local antibiotic administration. Calcium sulfate (CS) has been commonly used in orthopedics for a very long time as a production material for external fracture repair systems due to its antibacterial properties. Therefore, the aim of this work was the evaluation of the role of calcium sulfate loaded by antibiotics in eradication of infection in case of osteomyelitis. This prospective study included 24 patients at any age and of any sex with osteomyelitis of long or short bones. The patients underwent the clinical (general & local) evaluation, as well as radiological assessment in addition to the routine laboratory assessment. All patients underwent debridement, intra operative cultures and sensitivity was made. In our study mean age was 33.2 ranging between 5 and 55 years. In our study; **1)** male to female ratio was 2.428 (5-2). **2)** Tibia was the most common affected bone. **3)** Staph aureus is the most common organism. **4)** Recurrence of infection occurred in 3 (12.5%) patients. Vikas, et al. [13] retrospectively evaluated a consecutive series of 34 patients who presented with Chronic Hematogenous ost-

eomyelitis (CHOM) from 2011 to 2017. In each case, CHOM was classified according to the Beit CURE classification. Following thorough surgical debridement, the resulting dead space in the bone was filled with the antibiotic impregnated beads before primary closure. Results of the 31 patients available for follow up, effective regeneration of bone was confirmed in all cases, with radiographic bone healing typically observed at around 12 weeks. None of the children required reoperation for infection and none had recurrence of infection at the time of final review. The beads were completely absorbed within 3 months. No systemic adverse reactions to the local delivery of antibiotics were observed in this study. The authors found that single-stage debridement in conjunction with antibiotic impregnated calcium sulfate was an effective means of treating CHOM in children, with effective eradication of infection in every case. Qin, et al. [14] Aim of the study the present study is aimed at evaluating the effect of combined treatment on massive bone defect using radical debridement, antibiotic calcium sulfate, and monolateral external fixator. Method. 35 patients with tibial osteomyelitis received radical debridement, and during surgery antibiotics-impregnated calcium sulfate was used for filling the bone defect. Monolateral external fixator was used to manage the bone defect of average 9.5 (6.1-18.5) cm. Results. Bone union was achieved in 34 patients (97.1%) with no reinfection. One case was presented with reinfection and further debridement was conducted. The average time for the utility of external fixation was 17 (7-32) months, the mean follow-up duration after surgery was 33.7 (21-41) months. The most common complication was pain (100%) and superficial pin-tract infection (22.8%). Conclusion… our study reveals that radical debridement combined with antibiotics-impregnated calcium sulfate can suppress infection, and distraction osteogenesis using monolateral external fixators plays an effective role in managing osteomyelitis-induced massive tibial bone defect.

5. Conclusion

Antibiotics impregnated calcium sulfate is safe and effective method in treatment of osteomyelitis and the results show high rate of eradication of infection.

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