Section: Orthopedics

Original Research Article

OUTCOME STUDY IN LONG BONE CHRONIC OSTEOMYELITIS IN ADULTS TREATED BY IMPLANTING ANTIBIOTIC IMPREGNATED BIODEGRADABLE BONE GRAFT SUBSTITUTE

Aditya Kumar[1], Anubhav Jain[2], Navneet Singh Saluja[1], Gunveen Kaur[3], Meeta Patel[4]

[1]Post Graduate Trainee, Department of Orthopedics, MGM Medical College & LSK Hospital Kishanganj, Bihar, India.
[2]Assistant Professor, Department of Orthopedics, MGM Medical College & LSK Hospital Kishanganj, Bihar.
[3]Post Graduate Trainee, Department of ORLHNS, MGM Medical College & LSK Hospital Kishanganj, Bihar, India.
[4]Assistant Professor, Department of Obstetrics and Gynaecology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri (Nalanda), Bihar, India.

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Corresponding Author:
Dr. Navneet Singh Saluja,
Email: navneet.dr97@gmail.com.

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Abstract

Background: To determine the efficacy of antibiotic impregnated biodegradable bone graft substitute in the treatment of osteomyelitis in long bones in terms of contribution to bone formation, controlling infection. **Materials and Methods:** It was Institution based descriptive case series study setting involving all patients attending in-patient department of Orthopaedic in M.G.M Medical College & L.S.K Hospital, Kishanganj, Bihar. A total 30 samples were considered for this study during the period from December 2020 to September 2022. Initial investigations were done by detailed history and clinical examination and subject is put for operation and followed by, to note control of infection, its duration, strengthening of bone by comparing it radiologically, duration of incorporation or any complication that are observable. Patients were evaluated in detail preoperatively, perioperatively and postoperatively both clinically and radiologically at 2weeks, 4weeks, 6weeks, 2months, 4 months, 6months or up to 1 year (in certain cases). **Results:** The study population consisted of 30 cases, with a mean age of 28.98 years, and predominantly male patients (73.3%). Post-operative infections were the most common mode of infection (80%). The mean duration of symptoms was 7.17 ±5.86 months, Staphylococcus aureus was identified in 30.0% of cases, Purulent discharge was observed in 70.0% of cases before surgery, while serous discharge was observed in 76.7% of cases after surgery. The mean time taken to control superficial infection was 14.03 ± 2.60 days, while the mean time taken for deep infection control was 37.56 ±4.68 days. Only 1 case (3.3%) had pain around the site, while 96.7% did not have pain around the site. The mean bone cement absorption time on x-ray was 5.86 ±0.41 weeks. Only 1 case (3.3%) had persistence of infection. **Conclusion:** Antibiotic impregnated biodegradable bone graft substitute is an effective treatment option for long bone chronic osteomyelitis, with 96.7% did not have persistence of infection and cement incorporation within 5.86±0.41 (weeks), which is considered reasonable. Femur and tibia are the most commonly affected due to post operative infection, associated with Staphylococcus aureus with elevated ESR and CRP levels and associated post operative serous discharge in 76.7% cases.

INTRODUCTION

In orthopaedic surgery and traumatology, bone infection is an underappreciated and difficult condition for both patients and doctors. Diagnosis can be challenging,[1] treatment is sometimes extensive and arduous, sometimes requiring numerous surgeries, and can place a considerable financial burden on the patient and the health care system as a whole. Despite significant advances in the treatment of musculoskeletal infection over the years, studies have shown that infection rates after elective surgery cannot be decreased below 1–2%, and revision surgery failure rates remain as high as

33%.[2,3] The expense of treating bone infection is high and will rise as the number of individuals with this condition continues to rise.[4]

There are two distinct types of orthopaedic infections: those that simply affecting bone (osteitis/osteomyelitis) and those that affect bone an accompanying implant, such as a joint replacement or osteosynthesis. The approaches of the two entities are distinct, notwithstanding some overlap. Biomaterials have been employed to aid in the eradication of infection, the repair of bone defects, and the support of remaining bone and/or implants in order to improve therapeutic outcomes. Some biomaterials, such as gentamicin loaded beads or spacers created by Wahlig and Dingeldein in the 1970s, serve as antibiotic delivery devices.[5]

For this reason, osteomyelitis often occurs in patients with predisposing factors such as diabetes, immunosuppression or peripheral arterial disease. In adults, osteomyelitis often occurs after traumatic infections or in combination with predisposing factors; in children, osteomyelitis usually follows after hematogenous spread of infection and without underlying diseases.

A side effect of chronic bone infections is the impairment of local vascularity. This leads to serious problems in ensuring effective local antibiotic doses after parenteral or oral drug replacement. Local implantation of an antimicrobial agent provides a simple method to achieve higher local antibiotic concentrations.[6] Polymethyl methacrylate (PMMA) has been used successfully as a local antibiotic carrier for the treatment of osteomyelitis over the past several decades. However, because PMMA must be removed during the treatment process, responsible for thermal necrosis, and potentially lead to the development of antibiotic resistance, researchers are looking for a substitute.

Coating technology and implant modification (e.g., biomaterials with empirical antimicrobial behavior) to combat biofilm formation and/or persistence, still address several concerns and require further research, but are becoming important future methods in managing implant-associated infections. For this reason, a separate working group was established at the International Consensus Meeting on Musculoskeletal Infection 2018 to provide insights into the issue of biomaterial surface.[7].

MATERIALS AND METHODS

It was Institution based descriptive case series study setting involving all patients attending in-patient department of Orthopaedic in M.G.M Medical College & L.S.K Hospital, Kishanganj, Bihar. A total 30 samples were considered for this study during the period December 2020 to September 2022. Initial investigations were done by detailed history and clinical examination and subject were put for operation and followed by, to note control of infection, its duration, strengthening of bone by comparing the serial radiologically, duration of incorporation or any complication that are observable. Patients were evaluated in detail preoperatively, perioperatively and postoperatively both clinically and radiologically at 2weeks, 4weeks, 6weeks, 2months, 4 months,6 months or up to 1 year (in certain cases).

Inclusion Criteria

1. Adults above the age of 18yrs
2. Pyogenic osteomyelitis with purulent discharge
3. Only pyogenic osteomyelitis
4. Affecting Long bone only
5. Chronic osteomyelitis for any reason.

Exclusion Criteria

1. Involving multiple areas
2. Healed pyogenic osteomyelitis with no discharge.
3. Associated joint involvement.
4. Systemic illness or immunocompromised state(HIV).

Therapeutic Procedure

Debridement with sequestrectomy and antibiotic impregnated biodegradable bone cement (Stimulan) application.

We included in our study, 30 adult patients above the age of 18yrs having chronic osteomyelitis of long bone only clinically and radiologically, without involving joint space at MGM medical college, Kishanganj, from a period of December 2020 to September 2022. We put the cases directly for definitive procedure, i.e., debridement and sequestrectomy with antibiotic impregnated biodegradable bone cement application after taking swabs for culture and sensitivity. We dealt all the cases as a single stage definitive procedure.

Anesthesia

Regional (Spinal) for lower limbs; In some cases, with associated upper limb osteomyelitis regional (Brachial plexus block) is used, on a standard radiolucent orthopaedic table ;1.5 gram of Cefuroxime given I.V. and continued for variable period of time (3 -5 days).

Assessment

Patients were evaluated in detail preoperatively, perioperatively and postoperatively both clinically and radiologically at 2weeks, 4weeks, 6weeks, 2months, 4 months,6 months or up to 1 year (in certain cases).

Statistical Analysis

This statement describes the statistical analysis conducted for the data using Microsoft Excel and SPSS software. Descriptive statistics were used to summarize the data, including the use of numbers and percentages to describe categorical variables and mean and standard deviation to describe continuous variables. The software used for the analysis was SPSS version 26.

RESULTS

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Table 1: Age distribution among study population (n=30)

Age Distribution(years)	No of Cases	Percentage (%)
18 – 20	13	43.4
21 – 40	07	23.3
41 – 60	09	30.0
>60	01	3.3
Total	30	100.0
Mean & SD	28.98±15.46	

Age distribution among study population most of the patients were belongs to 18 -20 years of age group i.e., 13(43.4%), followed by 41- 60 years age group patients consisted 9(30.0%), another 21 – 40 years of age group patients were 7(23.3%) and 1(3.3%) patients were > 60 years of age group respectively. The mean age was 28.98 years.

Table 2: Sex distribution among study population (n=30)

Sex Distribution	No of Cases	Percentage (%)
Male	22	73.3
Female	08	26.7
Total	30	100.0

The study population consisted predominantly of male patients, with 22 cases (73.3%), compared to only 8 female cases (26.7%).

Table 3: Site of injury(n=30)

Site of injury	No of Cases	Percentage
Femur	11	36.7
Tibia	10	33.4
Humerus	04	13.3
Ulna	03	10.0
Radius	01	3.3
Radius & Ulna	01	3.3
Total	30	100.0

The table no 3. Shows the distribution of injuries among 30 cases, classified by their site of injury. The most common site of injury was the femur, with 11 cases (36.7%), followed by the tibia with 10 cases (33.4%). The least common site of injury was the radius, with only 1 case (3.3%), while injuries to both the radius and ulna were also present in 1 case (3.3%).

Table 4: Side of injury (n=30)

Side of injury	No of Cases	Percentage (%)
Right	24	80.0
Left	06	20.0
Total	30	100.0

The table no 4. Shows the distribution of injuries among 30 cases, classified by the side of injury. The majority of injuries occurred on the right side, with 24 cases (80%), while only 6 cases (20%) were on the left side.

Table 5: Mode of infection (n=30)

Mode of infection	No of Cases	Percentage (%)
Post operative	20	80.0
Open fracture	05	10.0
Sequalae of acute osteomyelitis	05	10.0
Total	30	100.0

The table no 5. Shows the distribution of cases by the mode of infection in 30 cases. Post-operative infections were the most common mode, with 20 cases (80%), followed by 5 cases (10%) each for open fractures and sequelae of acute osteomyelitis.

Table 6: Duration of symptoms(n=30)

Duration of symptoms(Months)	No of Cases	Percentage (%)
1 – 5 months	10	33.3
>5 – 10 months	18	60.0
>10 months	2	6.7
Total	30	100.0
Mean & SD	7.17±5.86	

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The table no 6. Shows the distribution of duration of symptoms in months. 10 cases (33.3%) had symptoms for 1-5 months, 18 cases (60.0%) had symptoms for more than 5 to 10 months, and only 2 cases (6.7%) had symptoms for more than 10 months. The mean duration of symptoms was 7.17 ±5.86 months.

Table 7: Type of bacteria Isolates (n=30)

Type of bacteria	No of cases	Percentage (%)
Staphylococcus aureus	09	30.0
No growth	21	70.0
Total	30	100.0

The table no 7. Shows the type of bacterial isolates obtained from 30 cases. Among them, 9 cases (30.0%) were identified as Staphylococcus aureus, while 21 cases (70.0%) had no growth of bacteria.

Table 8: Pre-operative type of discharge (n=30)

Type of Discharge	No of cases	Percentage (%)
Purulent	21	70.0
purulent with white flakes	09	30.0
Total	30	100.0

The table no 8. Shows the type of discharge observed before surgery. Among 30 cases, 21 cases (70.0%) had purulent discharge, while 9(30.0%) cases had purulent discharge with white flakes.

Table 9: Type of post-operative discharge (n=30)

Type of Discharge	No of cases	Percentage (%)
Serous	23	76.7
purulent	01	3.3
No discharge	06	20.0
Total	30	100.0

The table no 9. Shows the type of post-operative discharge. Most of the cases 23 (76.7%) had serous discharge, while only 1 case (3.3%) had purulent discharge, and 6 cases (20.0%) had no discharge.

Table 10: Time taken for Superficial infection control (days) (n=30)

Time taken (Days)	No of cases	Percentage (%)
<15 days	24	80.0
>15 days	06	20.0
Total	30	100.0
Mean & SD	14.03±2.60 (days)	

The table no 10. Shows the time taken to control superficial infection. Among the cases, 24 cases (80.0%) had a time of less than 15 days to control infection, while 6 cases (20.0%) took more than 15 days. The mean time taken to control infection was 14.03 ± 2.60 days.

Table 11: Time taken for deep infection control (Days) (n=30)

Time taken for deep infection control (Days)	No of cases	Percentage (%)
<30 days	03	10.0
30 – 40 days	13	43.3
>40 days	14	46.7
Total	30	100.0
Mean & SD	37.56±4.68 (days)	

The table no 11. The data shows that out of 30 cases, 10% of cases took less than 30 days for deep infection control, 43.3% of cases took between 30-40 days, and 46.7% of cases took more than 40 days. The mean time taken for deep infection control was 37.56 ±4.68 days.

Table 12: Pain around site(n=30)

Pain around site	No of cases	Percentage (%)
Present	01	3.3
Absent	29	96.7
Total	30	100.0

The data shows that out of 30 cases, only 1 case (3.3%) had pain around the site, while the remaining 29 cases (96.7%) did not have pain around the site.

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Table 13: Bone cement absorption time on x-ray(weeks) (n=30)

Bone cement absorption time on Xray	No of cases	Percentage (%)
5 – 6 (weeks)	26	86.7
>6 (weeks)	04	13.3
Total	30	100.0
Mean & SD	5.86±0.41 (weeks)	

The data shows that out of 30 cases, 86.7% of cases had bone cement absorption time of 5-6 weeks on x-ray, while 13.3% of cases had absorption time of more than 6 weeks. The mean bone cement absorption time on x-ray was 5.86 ±0.41 weeks.

Table 14: Persistence of infection. (n=30)

Persistence of infection	No of cases	Percentage (%)
Yes	01	3.3
No	29	96.7
Total	30	100.0

The data shows that out of 30 cases, only 1 case (3.3%) had persistence of infection, while the remaining 29 cases (96.7%) did not have persistence of infection.

DISCUSSION

Local delivery of antibiotics from biodegradable cement for chronic osteomyelitis of long bones in adults is an advantage over standard intravenous therapy. It obliterates the dead space, delivers high doses of tissue antibiotics, aids in osseous repair, provides the parity with high concentration of the drug imbibed, systemic effects of the drug are evaded and does not need to be removed like methyl methacrylate. In the present study the patients showed evidence of excellent osseous repair. To date there have been only 1 out of 30 cases with relapses of infection. Most of the infections were due to Staphylococcus aureus. Only 30 patients were reviewed, but the performance of the local antibiotic implants was quite consistent. Full degradation occurred with bone repair in an orderly manner.

Klemm (1979) used gentamicin-impregnated beads for covering of dead space after taking out of infected and necrotic bone. He reported a cure of 91.4% of 128 cases.[8] McKee et al. [9] (2002) treated 25 patients (15 males and ten females) with a culture-positive, long bone infection using tobramycin impregnated calcium sulfate. They showed an effective eradication rate of 92% after posttraumatic osteomyelitis. Gauland.[10] (2011) reported on the use of Stimulan® in managing lower extremity osteomyelitis without oral and/or intravenous antibiotics. The results showed 279 of 323 patients (86.4%) healed with no recurrence of osteomyelitis to any specific anatomical location in follow- up of 5.5 years. Fleiteret al.[11] (2014) reported an 80% infection eradication rate in a series of 20 osteomyelitis patients treated with Herafill- G®. McNally et al. [12] (2016) in a prospective series of 100 patients, including 71 fracture related infections, showed eradication of infection in 96% cases. In our study, cure rate was 96.7% in 30 patients with minimum follow up of 6months, using vancomycin impregnated calcium sulphate.

Xiangwen et al. [13] (2022) showed tibia to be the most commonly affected part with 46.73% of patients (279/597), followed by femur (139/597, 23.28%). In our study femur showed more involved with 36.7% cases (11/30) followed by tibia 33.4% (10/30 cases). He also showed that Calcium sulfate pellets were completely absorbed at an average of 6 weeks (range, 30–60 days) in all patients, similar to our 5-6weeks (mean 5.86weeks) findings.

Over the past three decades, numerous advantages with antibiotic-impregnated beads over systemic therapy have been recognized. The use of antibiotic beads is simple, mostly is it done at the time of debridement for chronic osteomyelitis.

Calcium sulfate has been used since 1892 as an osteoconductive filler of bone defects.[14] It acts primarily as space filler, which restores morphological contour, prevents the ingrowth of soft tissue, and provides an osteoconductive matrix for the ingrowth of blood vessels. Surgical‐grade calcium sulfate has been optimized to resorb at a rate similar to that of new bone formation. When placed in contact with bone or periosteum, calcium sulfate will stimulate bone growth. Even when loaded with vancomycin, calcium sulfate is still osteoconductive and improves bone healing.

However, calcium sulfate has its own inherent shortcomings. The absorption of calcium sulfate can occur rapidly in vivo, and the mechanical strength of the material can quickly lose with degradation.[15] So, calcium sulfate is not intended to provide structural support. The degradation products of calcium sulfate carriers, generally resulted in persistent drainage from the wound which may aggravate deep infection.[16] Calcium sulfate absorbs plenty of water, subsequently promote seromas formation and increase the risk of secondary infection.[17] Additionally, calcium sulfate pellets cannot be expected to replace PMMA spacers in situations where mechanical support and integrity are important to the procedure (such as spacers in staged revision).

This study is relatively small, although promising. Only 30 patients were evaluated but performance of antibiotic coated biodegradable cement was persistent (96.7% showed no persistent of infection).

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CONCLUSION

Antibiotic impregnated biodegradable bone graft substitute is an effective treatment option for long bone chronic osteomyelitis, with 96.7% did not have persistence of infection and cement incorporation within 5.86±0.41 (weeks), which is considered reasonable. Femur and tibia are the most commonly affected due to post operative infection, associated with Staphylococcus aureus with elevated ESR and CRP levels and associated post operative serous discharge in 76.7% cases.

Overall, the study suggests that the use of antibiotic impregnated biodegradable bone graft substitute is a viable option for the treatment of long bone chronic osteomyelitis. However, the potential risk of complications and the cost of treatment should also be taken into consideration.

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