

Efficacy of Biodegradable Calcium Sulfate Impregnated Gentamycin Beads for the Management of Chronic Osteomyelitis

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Abstract

Introduction: Chronic orthopedic infections are always a nightmare not only in developing world but also in developed nations. They will always persist to be a continuing challenge for any orthopedic surgeon. Debridement is the answer and not to sit on any infection neglecting if any. Surgical aim and irrigation are to dilute the bug concentration for a viable vascularized base which helps healing. Local antibiotic delivery system always stood the test of time. The principle involved is achieving a germ-free environment locally, leading to better and faster union of fracture.

Objectives: The objectives of the study were to study the efficacy of biodegradable calcium sulfate impregnated antibiotic beads in treating chronic osteomyelitis and to study any adverse effect of biodegradable calcium sulfate impregnated antibiotic beads in the treatment of chronic osteomyelitis.

Materials and Methods: This is a prospective study conducted in Government T D Medical College Hospital from August 2017 to August 2019. Our sample size of 100 patients was included meeting consenting for the study and meeting inclusion and exclusion criteria. Efficacy of the biodegradable antibiotic beads was measured using the following parameters for all selected patients: (1) Clinical parameters (ASEPSIS scoring system), (2) radiological parameters (Cierny and Mader staging), (3) laboratory parameters (erythrocyte sedimentation rate and C-reactive protein), and (4) culture results (discharge/pus)

Results: There were 75 males and 25 females out of 100 selected patients.

Functional Outcome: While comparing clinical, radiological, and laboratory parameters, 80 patients had good results and 20 had bad outcome.

Complication: Product-related discharge in 5 patients, persistence of osteomyelitis in 10 patients, and persistence of non-union in 5 patients.

Conclusion: Local application of antibiotic-impregnated biodegradable calcium sulfate beads has better outcome in the treatment of chronic orthopedic infections.

Keywords: Chronic orthopedic infections, Antibiotic beads, Biodegradable antibiotic beads, Cierny-Mader staging.

Introduction

Chronic orthopedic infections are always a nightmare not only in developing world but also in developed nations. They will always persist to be a continuing challenge for any orthopedic surgeon.

There is no concrete evidence to show the efficacy of oral antibiotics in osteomyelitis. Oral antibiotics have no much bone penetration giving rise to the use of

intravenous antibiotics. Intravenous antibiotics have stood the test of time for all chronic osteomyelitis. Prolonged use of intravenous antibiotics when very high concentrations of the antibiotics are used it can lead to systemic toxicity. This has led to the use of antibiotics with local delivery system that has given better concentration by better tissue penetration and low serum concentration lowering systemic side effects of the drug, leading to better union of the fracture.

The means of using a local delivery system are that it is possible to achieve a very high concentration of the drug that is required in the tissue with the added advantage that there will be relatively very low about this drug in the serum of the patient.



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1. Clinical parameters (ASEPSIS scoringsystem)						
Wound characteristics	Proportion of wound affected					
	0	<20	20-39	40-59	60-79	>80
Serous exudate	0	1	2	3	4	5
Erythema	0	1	2	3	4	5
Purulent exudates	0	2	4	6	8	10
Separationofdeep tissues	0	2	4	6	8	10
Criteria		Points				
Proportion of wound affected antibiotics		10				
Drainage of pus under La		5				
Debridement of wound under Ga		10				
Serous discharge*		Daily 0-5				
Erythema*		Daily 0-5				
Purulent exudate*		Daily 0-10				
Separation of deep tissue*		Daily 0-10				
Isolation of bacteria		10				
Stay as Ipfor >14 days		5				



Graph 1: Distribution of the subjects in the study based on the erythrocyte sedimentation rate

It can also help to obliterate the dead space that is mostly present in the bone following a debridement.

Debridement and removal of avascular sequestrum leave a dead space which also gets filled by this antibiotic impregnated calcium sulfate compound.

Gentamycin is one of the most commonly used antibiotics that are prescribed in chronic infections with better musculoskeletal penetration.

The current concepts on treating chronic osteomyelitis have shown good result when used locally as an antibiotic bead.

2. Radiological parameters (Cierny and Maderstaging)		
Medullary	Endosteal disease	
Superficial	Cortical surface affected	
Localized	Cortical sequestrum with stability	
Diffuse	Cortical sequestrum without stability	
3. Laboratory parameters (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP])		
Laboratory parameters	Normal/(-)	Increased/(+)
C-reactive protein	<6 mg/dl	>6 mg/dl
Erythrocyte sedimentation rate	<15 mm/h	>15 mm/h
4. Culture results (discharge/pus)		
Culture	(+)	(-)

Therefore, these concepts made us think of this study to study the efficacy of biodegradable gentamycin-based calcium sulfate beads in the management of chronic orthopedic infections. We also intend to study the adverse effect of degradable gentamycin-based calcium sulfate beads.

Aims and objectives of the study

The aims and objectives of the study were as follows:

- To study the efficacy of biodegradable calcium sulfate impregnated antibiotic beads in treating chronic osteomyelitis.
- To study any adverse effect of biodegradable calcium sulfate impregnated antibiotic beads in the treatment of chronic osteomyelitis.

Materials and Methods

Source of data

This is a prospective study conducted in Government T D Medical College Hospital from August 2017 to August 2019.

Our sample size of 100 patients was included meeting consenting for the study and meeting inclusion and exclusion criteria. Efficacy of the biodegradable antibiotic beads was measured using the following parameters for all selected patients.

The predefined criteria

Inclusion criteria

The following criteria were included in the study:

1. Chronic osteomyelitis
2. Patients aged between 10 and 65 years of age.

Exclusion criteria

The following criteria were excluded from the study:

1. Infections associated with compartment syndrome
2. Infected fractures associated with neurovascular injuries.

Informed written consent was obtained from all patients recruited in the study and was given a detailed explanation regarding the objectives and method of this study.

A pre-tested semi-structured questionnaire was used for the collection of data.

Thorough history, clinical and functional examination, and hematological and radiological investigations were done.

Outcome of the biodegradable calcium sulfate-based

Table 1: Distribution of the subjects in the study based on the age

Age range in years	Frequency	Percentage
<20	0	0
21–30	4	4
31–40	12	12
41–50	24	24
51–60	32	32
61–70	20	20
>70	8	8
Total	100	100

Average age of the patient was 41.52±8.7 and majority were in the age group of 51–60 (32%)

Table 2: Distribution of the subjects in the study based on the gender

Gender	Frequency	Percentage
Males	75	75
Females	25	25
Total	100	100

There were 75 males, 75% and 25 females, 25%

gentamycin beads will be measured using the following parameters mentioned below:

Table 3: Distribution of the subjects in the study based on the CRP at various time intervals

CRP	CRP pre-operative	CRP 1 month	CRP 3 months	CRP 6 months	CRP 9 months
<6 mg/dl	8	52	60	96	100
>6 mg/dl	92	48	40	4	0
Total	100	100	100	100	100

CRP: C-reactive protein

Table 4: Distribution of the subjects in the study based on the ESR

Patients	ESR pre-operative	ESR 1 month	ESR 3 months	ESR 6 months	ESR 9 months
Mean	60.52	46.76	33.2	25.92	22.48
Standard deviation	15.85118	20.931	12.7	8.9	6
Sum	1513	1169	830	648	1458
Sum	1513	1169	830	648	1458

One-way ANOVAs $P < 0.001$, $t = 28$. ESR: Erythrocyte sedimentation rate

Table 5: Distribution of the subjects in the study based on the culture at various time intervals

Number	Culture pre-operative	Culture 1 month	Culture 3 months	Culture 6 months	Culture 9 months
Positive	48	16	12	12	64
Absent	52	84	88	88	36
Total	100	100	100	100	100
Positive (%)	48	16	12	12	64
Absent (%)	52	84	88	88	36
Total (%)	100	100	100	100	100

Preparation of beads

1. Mixing of the calcium sulphate powder with gentamycin in appropriate amount as per recommendation from the manufacturer.
2. Mix for adequate time.
3. Application of antibiotic paste over the mould of appropriate size for the appropriate setting time for the desired dimension.
4. Separation of beads from the mould.
5. Insertion of beads into the infected site.

Data processing and analysis:

Data processing and statistical analysis were done using the SPSS software Version 17.0.1.

Observation and Results

The pre pre-operative and post post-operative CRP values were compared with t-test. CRP comparison of t-value = -0.059 and P value < 0.05, mean CRP was 18.96 for pre pre-operative and 0.96 for post post-operative.

The pre-operative and post post-operative ESR values were compared with t-test. ESR comparison of t-value = -0.010 and P value < 0.05, mean ESR was 60.52 for pre-operative and 22.28 for post-operatively.

We had positive cultures in 48 cases (48%), 16 cases (16%), 12 cases (12%), and 64 cases (64%) at pre-operative period, 1, 3, 6, and 9 months, respectively.

We had positive cultures in 0 cases (0%), 24 cases (24%), 60 cases (60%), 60 cases (60%), and 60 cases (60%), at pre-operative period, 1, 3, 6, and 9 months, respectively.

We had clinical (ASEPSIS) disturbed in 0 cases (0%), 16 cases (16%), 8 cases (8%), 12 cases (12%), and 16 cases (16%), at pre-operative period 1, 3, 6, and 9 months, respectively.

We had clinical localized sepsis in 20 cases (20%), 28 cases (28%), 12 cases (12%), 8 cases (8%), and 4 cases (4%) at pre-operative period 1, 3, 6, and 9 months, respectively.

We had severe sepsis in 12 cases (12%), 4 cases (4%), 28 cases (28%), 8 cases (8%), 4 cases (4%), and 4 cases (4%) at pre-operative period 1, 3, 6, and 9 months, respectively.

Table 6: Distribution of the subjects in the study based on the clinical satisfactory sepsis

Clinical (ASEPSIS) satisfactory	Pre-operative	1 month	3 months	6 months	9 months
Satisfactory	0	24	60	60	60
Not satisfactory	100	76	40	40	40
Total	100	100	100	100	100
Positive (%)	0	24	60	60	60
Absent (%)	100	76	40	40	40
Total (%)	100	100	100	100	100

Table 7: Distribution of the subjects in the study based on the clinical (ASEPSIS) disturbed

Clinical (ASEPSIS) disturbed	Pre-operative	1 month	3 months	6 months	9 months
Positive	0	16	8	12	16
Absent	100	84	92	88	84
Total	100	100	100	100	100
Positive (%)	0	16	8	12	16
Absent (%)	100	84	92	88	84
Total (%)	100	100	100	100	100

Table 8: Distribution of the subjects in the study based on the radiological parameters (Cierny and Mader staging) at various time intervals

Degree of sepsis	1 month	3 months	6 months	9 months
Mild	12	8	4	4
Moderate	20	12	8	8
Severe	60	20	0	0
Nil	8	60	88	88
Total	100	100	100	100

Discussion

Gentamicin has always stood test of time in orthopedic infections due to its wide spectrum and better musculoskeletal penetration.

Acrylic cement would appear to allow the slow release of gentamicin (Wahlig and Buchholz, 1972; Wahlig et al., 1972). Klemm (1974, 1976) leading to the treatment of chronic osteomyelitis. We modified the system: The cement containing gentamicin was not introduced into the bone cavities while still in the plastic state, but in the form

of hardened beads unlike acrylic cement.

In this way, a novel treatment in chronic infection was possible (Wahlig and Bergmann, 1974; Dingeldein and Wahlig, 1976; Wahlig, Bergmann, and Dingeldein).

Average age of the participants was 41.52 ± 8.7 and majority were in the age group of 51–60 (32%); in the age group of 21–30 years, we had 4 cases (4%), least and at 31–40 years, we had 12 cases (12%); 41–50 years, we had 32 cases (32%); 61–70 years, we had 20 cases (20%); >70 years, we had 8 cases (8%).

There were 75 males, 75% and 25 females, 25%. The pre-operative and post-operative CRP values were compared with t-test. CRP comparison of $t = -0.059$ and $P < 0.05$, mean CRP was 18.96 for pre-operative and 0.96 for post-operative.

The pre-operative and post-operative ESR values were compared with t-test. ESR comparison of $t = -0.010$ and $P < 0.05$, mean ESR was 60.52 for pre-operative and 22.28 for post-operative. We had positive cultures in 48 cases (48%), 16 cases (16%), 12 cases (12%), 12 cases (12%), and 64 cases (64%) at pre-operative period 1, 3, 6, and 9 months, respectively.

The pre-operative and post-operative ESR values were compared with t-test. ESR comparison of $t = -0.010$ and $P < 0.05$, mean ESR was 60.52 for pre-operative and 22.28 for post-operative.

The pre-operative and post-operative CRP values were compared with t-test. CRP comparison of $t = -0.059$ and $P < 0.05$, mean CRP was 18.96 for pre-operative and 0.96 for post-operative.

We had positive cultures in 0 cases (0%), 24 cases (24%), 60 cases (60%), 60 cases (60%), and 15 cases (60%) at pre-operative period 1, 3, 6, and 9 months, respectively.

We had clinical localized sepsis in 20 cases (20%), 28 cases (28%), 12 cases (12%), 8 cases (8%), and 4 cases (4%) at pre-operative period 1, 3, 6, and 9 months, respectively.

While comparing clinical, radiological, and laboratory parameters, 80 patients had good results and 20 had bad outcome. Radiological comparison- Chi-square value-6.95 and $P < 0.001$.

We had severe sepsis in 12 cases (12%), 4 cases (4%), 28 cases (28%), 8 cases (8%), 4 cases (4%), and 4 cases (4%) at pre-operative period 1, 3, 6, and 9

Table 9: Distribution of the subjects in the study based on site of sepsis time intervals

Number	Localized pre-operative	Localized 1 month	Localized 3 months	Localized 6 months	Localized 9 months
Positive	20	28	12	8	4
Absent	80	72	88	92	96
Total	100	100	100	100	100
Positive (%)	20	28	12	8	4
Absent (%)	80	72	88	92	96
Total (%)	100	100	100	100	100

Table 10: Distribution of the subjects in the study based on severity of sepsis time intervals

Number	Superficial pre-operative	Superficial 1 month	Superficial 3 months	Superficial 6 months	Superficial 9 months
Positive	12	4	8	4	4
Absent	88	96	92	96	96
Total	100	100	100	100	100
Positive (%)	12	4	8	4	4
Absent (%)	88	96	92	96	96
Total (%)	100	100	100	100	100

months, respectively.

Radiological medullary involvement was seen in 4 cases (4%), 28 cases (28%), 24 cases (24%), 16 cases (16%), and 20 cases (20%) at pre-operative period 1, 3, 6, and 9 months, respectively.

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Conclusion

Local application of biodegradable antibiotic beads has better outcome for controlling chronic orthopedic infections than systemic antibiotics.

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