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ORIGINAL RESEARCH

The Role of Antibiotic Impregnated Bone Cement in Management of Infected Implant in SITU

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ABSTRACT

Background: Infection in orthopedic surgeries is a serious complication mostly resulting in removal of infected implant. But recently, with use of antibiotic loaded polymethylmethacrylate, attempts have been made to prevent and cure orthopedic implant infections in primary and revision surgeries. In this study, the role of antibiotic impregnated bone cement in management of infection in infected implant (nailing or plating used for internal fixation of fractures) with implant retained in situ is studied and compared with other modalities of treatment where antibiotic bone cement was not used. This study aims to assess the role of antibiotic impregnated bone cement to control infection in postoperative patients with implant in situ (Nailing and Plating).

Materials and Methods: Forty (40) postoperative patients with fractures treated by internal fixation who presented our department from March 2017 to February 2021 and showing signs of infection, were included in study based on inclusion and exclusion criteria. Five patients were lost to follow up so the results were based on study of thirty-five (35) patients. All the patients were managed by debridement, intra operative sample collection of infected tissue for cultures and antibiotics sensitivity testing, thorough lavage with 3 liters of normal saline, placement of antibiotic impregnated bone cement beads, and post operative antibiotics according to culture and sensitivity. Patients were followed-up with two weekly investigations of Total leucocyte count, Differential leucocyte count, Erythrocyte sedimentation rate, C-reactive protein and examination of pulse rate, body temperature, discharge from wound and any sign of inflammation in overlying skin. Subsidence of infection was considered as normalization of all above mentioned parameters.

Results: Out of 35 patients, 30 patients (85.71%) experienced subsidence of infection with 3 patients (8.57%) (2 cases of plating and 1 intramedullary nailing) continued to have draining wounds and 2 patients (5.71%) (2 cases of intramedullary nailing) experienced recurrence of infection. There was early and significant improvement in Total leucocyte count, Differential leucocyte count, Erythrocyte sedimentation rate, C-reactive protein, pulse rate, body temperature and absence of discharge from wound and no sign of inflammation in overlying skin in these patients.

Conclusion: Use of antibiotic impregnated bone cement along with intravenous antibiotics in management of infected implant in situ is advocated as there was a significant and early reduction in laboratory parameters and improvement in clinical condition was observed without the need for removal of implants used for internal fixation.

Keywords: Polymethylmethacrylate, Bone cement, Bone cement beads, Antibiotic impregnated bone cement, Infected implant in-situ.

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INTRODUCTION

Infection in orthopedic surgeries is a serious complication, which often becomes a cause for removal of infected implant, as there is a formation of biofilm consisting bacteria on the implant surface which protects the organisms from the host immune system and antibiotic therapy.[1,2] In recent scenario, with use of polymethylmethacrylate with antibiotics, attempts have been made to prevent and cure orthopedic implant infections in primary and revision surgeries. In 1970, Buchholz and Engelbrecht used antibiotic impregnated bone cement beads to reduce the infection rates in orthopedic surgery,[3] with thought that the antibiotic will gradually be released locally to give higher concentrations which is way more than minimum inhibitory concentration level, that cannot be achieved by systemic therapy. Polymerization of monomeric, liquid methyl methacrylate (MMA) is an exothermic reaction initiated by the decomposition of a catalyst (benzoyl peroxide) result in production of free radicals that set off additional polymerization of the methyl methacrylate.[4,5]

Antibiotics for use with bone cements should have broad antibacterial spectrum, including both gram-positive and Gram-negative pathogens, sufficient bactericidal activity, high specific antibacterial potency, low rate of primary resistant pathogens, minimal development of resistance during therapy, low protein binding, low sensitizing potential, marked water solubility facilitating its release from the bone cement, and chemical and thermal stability.[6] Now days common antibiotics used are Gentamicin, Tobramycin, Erythromycin, Cefuroxime, Vancomycin, Colistin etc.[7,8]

MATERIALS & METHODS

This study was conducted between March 2017 to February 2021 in department of Orthopedics, SRN hospital, Prayagraj. In this study, 40 postoperative cases of fracture fixation complicated by infection were selected based on inclusion and exclusion criteria to assess role of antibiotic impregnated bone cement to control infection. Five patients were lost to follow up, so the results were based on study of 35 patients. The study design was Prospective Observational study

Inclusion criteria

- Post-operative case of fractures managed by internal fixation either plating, or intramedullary nailing showing signs of infection.
- Diagnosis of infection, based on bacterial identification in cultures of samples collected, when first seen.

Exclusion criteria

- Known history of allergy from antibiotics or other conditions with contraindication to use of long-term antibiotics intended to be used with bone cement (e.g. Chronic kidney disease).
- Patient unfit for surgery due to co-morbid conditions.

- Patient showing evidence of osteomyelitis.
- Patient lost their follow up.
- Patients not sensitive for heat stable antibiotics.

Method of Collection of Data:

Detailed history and physical examination was done. Patients were managed by debridement, intra operation sampling for culture and sensitivity, thorough lavage with 3 liters of normal saline, placement of antibiotic impregnated bone cement beads, and post operation antibiotics according to culture and sensitivity.

All patients were followed with two weekly investigations. Subsidence of infection was considered as normalization of Total leucocyte count, Differential leucocyte count, Erythrocyte sedimentation rate, C-reactive protein, pulse rate, Body temperature and absence of discharge from wound with no sign of inflammation in overlying skin.

Age, Sex, Total leucocyte count, Differential leucocyte count, Erythrocyte sedimentation rate, C-reactive protein, pulse rate, Body temperature status and skin condition were recorded using a pilot tested proforma.

For culture, all antibiotics were stopped 72 hours prior to sample collection and sample from each site of infection was collected and sent for culture and antibiotic sensitivity.

Antibiotic loaded bone cement beads preparation:

Maximum 4 grams of antibiotics for each 40 grams of simplex bone cement was used. Antibiotics were taken in powder form for better integration with cement. Antibiotics in various combinations were mixed with 40 grams of powdered bone cement before the 20 ml liquid monomer component was added. All components were then hand mixed in a container till it attained doughy status and then manually molded in to small rounded beads through which stainless steel wire was passed.[8] [Figure 1(a,b)]

After thorough debridement and lavage of wound beads were placed in zone of infection retaining the implant in situ. Soft tissue coverage and skin closure was done. [Figure 2(a-c), 4(a-c), 5(a-e) and 6(a-d)].The patients with infected intra-medullary nails were assessed for site of infection. The infection was lodged either at nail entry site, bolt insertion site, fracture site or combination of above-mentioned sites. Excluding the infection at fracture site, the other three possibilities were managed by thorough lavage of cavity of nail using a tube inserted from proximal end of nail after removal of bolts with 3 liters of normal saline. After lavage, antibiotic loaded bone cement beads were placed at the infection site with proper skin closure [Figure 3(a-d)]. The fracture site was examined for any evidence of instability, if found new bolts were reinserted in their original position. If infection was found at the fracture site, it was managed by placing antibiotic loaded bone cement beads at the fracture site after thorough debridement.

Wound inspection and dressing were done on 2nd, 4th and 6th post operative day and when found satisfactory patients were discharged on 7th post operative day. Suture was removed on 12th to 15th post operative day.Outcome of study was determined by subsidence of infection as assessed normalization of clinical and laboratory parameters as mentioned earlier.

Removal of antibiotic loaded bone cement was done after 6th week of bone cement placement irrespective of wound condition and patients were evaluated weekly till stitch line healed then further follow-up was done at monthly interval for next 6 months for any complications.

Table 1: Age Distribution

Age(years)	No of patient	Percentage%
18-40	12	34.29%
40-60	15	42.85%

>60	8	22.86%
Total	35	100.00%

Table 2: Sex Distribution

	Total	**Antibiotic loaded bone cement used**
No. of patient having infected implant in situ	35	35
Male	22	22
Female	13	13

Table no-3: Infected implant distribution

Infected Implant	Number of patients
Plate	24
Nail	11

Table 4: Different Parameters Used for Monitoring of Infection

	Mean±SD				
	Pre op	**POST OP**			
		2nd day	**2nd week**	**4th week**	**6th week**
TLC	13606±1366	11543 ± 956	10646 ± 1409	9411 ± 1461	85489 ± 1684
DLC	N-81±2.5 L-17±2.4	N-77 ± 3 L-19 ± 3	N-75 ± 4 L-22 ± 4.2	N-70 ± 5 L-26 ± 4.6	N-68 ± 4.5 L-28 ± 4.6
ESR	52±8.4	39 ± 5	34.5 ± 5.4	30 ± 5.8	25 ± 5.5
CRP	19±3.3	11.2 ± 3.5	8.9 ± 4	4.8 ± 3.7	3.3 ± 3.6
Pulse Rate	104±7.3	86 ± 7.8	82 ± 8	78 ± 6.4	77 ± 6

Table 5: Temperature Monitoring

Temperature (febrile/afebrile)	**Pre op (number of patients)**			
		2nd week	**4th week**	**6th week**
Febrile	28	6	3	0
Afebrile	7	29	32	35

Table 6: Patients with Discharge When Bone Antibiotic Bone Cement Used

Discharge		**2weeks**	**4weeks**	**6week**
Present	35	6	4	5
Absent	0	29	31	30

Table 7: Inflammation of Overlying Skin

Antibiotic loaded bone cement	**Pre-Treatment**	**2weeks**	**4weeks**	**6week**
Used	35	6	3	3

Table 8: Complications

	Antibiotic bone cement used	
	Infected nail (11)	**Infected plate (24)**
Persistent infection	1	2
Recurrence of infection	2	-
Wound dehiscence	-	1

Figure 1: (a) Anibiotic bone cement beads (b) Bone Cement Preparation

Figure 2: (a) Infected distal femur plate; (b) Antibiotic loaded bone cementbeads placement after debridement; (c) Antibiotic bone cement beads removal after subsidence of infection

Figure 3: (a) Infected femur nail with discharge from fracture site; (b) Anibiotic bone cement beads placement after thorough irrigation of nail canal (c& d) Antibiotic bone cement beads removal after subsidence of infection

Figure 4: (a) Infected upper end tibia plate; (b) Anibiotic bone cement beads placement after debridement and thorough wash (c) After 4 week of Anibiotic bone cement beads placement.

Figure 5: (a & b) Infected philos plate; (c & d) Anbitiotic bone cement beads placement (e) After six weeks of antibiotic bone cement beads placement

Figure 6: (a) Infected humerus plate; (b) Antibiotic bone cement beads placement; (c & d) Antibiotic bone cement bead removal after subsidence of infection

OBSERVATIONS AND RESULT

The Observations and Results were based on the 35 patients out of which 22 (62.86%) were male and 13 (37.14%) were female. The mean age of patients was 46.5 years, ranging from 18 to 75 years. (Table 1) Out of 35 patients, 11 patients with infected nail(tibia interlock nail, femur interlock nail, proximal femoral nail) and 24 patients with infected plate(distal femur plate, proximal tibia plate, humerus plate, forearm plate). [Table 2] Number of patients with infected implants in situ presenting within 1 month of index surgery were 21(60%), between 1 to 3 months of index surgery were 9(25.71%) and after 3 months of index surgery were 5(14.29%).

Most common organisms cultured from discharge were methicillin sensitive staphylococcus aureus (26%) and methicillin resistant staphylococcus aureus (23%). Other were coagulase negative staphylococcus (14%), E.Coli (11.43%), pseudomonas aeruginosa (11%),klebsiella pneumonae(6%), streptococcus pneumonae (2.86%),streptococcus pyogenes (2.86%),Acinetobacter (1.43%) and proteus mirabilis (1%).

Antibiotic sensitivity test revealed maximum number of cases being sensitive to amikacin (94.28%) followed by chloramphenicol (91.4%), vancomycin (91.4%) and teicoplanin (88.57%), while amoxycillin + clavulanic acid (48.57%) was found to be sensitive in least number of cases. In all cases, the patients were found to be sensitive to more than one antibiotic.With limited spectrum of antibiotics to be used along with bone cement (according to criteria mentioned earlier); vancomycin, tobramycin, gentamycin and cefazolin in different combinations were antibiotics of choice in this study. So, according to culture and sensitivity vancomycin plus gentamycin was used in 21 patients; vancomycin plus tobramycin was used in 10 patients whereas in 4 patients gentamycin plus cefazolin was used. Monitoring was done by measuring TLC, DLC, ESR, CRP, and pulse rate two weekly.

This study showed that out of 35, 30 patients (85.71%) of antibiotic impregnated bone cement group experienced no recurrence of infection. 3 patients (8.57%) which included two cases of plating (8%) and one intramedullary nailing (9%) continued to have persistent discharge. 2 patients (5.71%) (2 cases of intramedullary nailing) experienced recurrence of infection. However, in 1 patient (distal femur plate) in whom antibiotic impregnated bone cement bead was used, wound dehiscence was seen as complication which was further managed by re-suturing [Table 4-8].

DISCUSSION

In this study, only one type of bone cement, simplex bone cement(polymethylmethacrylate) was used in all patients as local drug delivery system in order to nullify the effect of variable antibiotic elution from different type of bone cements.[9,10]

Antibiotic impregnated bone cement used in form of chain of small beads as it allowed maximum elution of antibiotics.[8,11]According to microbiological data of our institution, the antibiotic combinations commonly used were vancomycin plus gentamycin, vancomycin plus tobramycin and tobramycin plus cefazolin.[9]

The disadvantages of implant removal and failure rate of treatment with implant retention were also considered, hence a waiting period of 6 weeks was considered after placement of antibiotic impregnated bone cement before implant removal.Age, sex distribution, and delay in presentation of surgical site infection did not play any role in outcome of this study.Inflammatory markers were used in diagnosing the infection of orthopaedic implants as well as their serial values also helped in monitoring treatment progress.[12,13]Pulse rate is considered as an indicator of presence of infection in the body although it is a vague parameter. As inflammatory markers settle down to normal, pulse rate also normalizes. As mentioned above, no supporting or contradicting study was found in literature.

A significant number of patients turned afebrile early after the placement of antibiotic bone cement.Significant improvement in the skin conditions along with decline in the amount of purulent discharge was observed in patients in 1st week post operation.However, even with such stringent methods persistence of infection was found in 3 patients.This study showed there was 85.71% success rate and only 8.57% patients continued to have persistent discharge, but the discharge was significantly reduced. 2 patients (5.71%) (2 cases of intramedullary nailing) experienced recurrence of infection.
Buchholz et al. in 1984,[7] first used antibiotic-loaded bone cement in revision surgery and reported an increase in the rate of success to 77% with a single exchange and to 90% with multi-stage revision.Emamiet alin 1995,[14] treated 37 cases of infected tibia nonunion by debridement and bone grafting. 21 patients required repeat debridement. No recurrence of infection was noted in any cases for 2 years of follow-up.Qiu XS et al in 2018,[15] studied retention of infected implant (plate) and the use of antibiotic impregnated bone cement in the management of early infection after fracture fixation. Ten patients were studied. Only in 1 case, recurrence of infection was observed.Wound dehiscence as a complication was found in 1 patient (distal femur plating) which was managed by secondary suturing.No allergic manifestations to the antibiotic combinations used were observed in this study.

CONCLUSION

Based on the findings of our study, use of antibiotic impregnated bone cement along with debridement and intravenous antibiotics in management of infected implant in situ is advocated This statement is further strengthened by the fact that significant reduction in laboratory parameters and significant and early improvement in clinical condition was observed.

Only 3 cases of persistent infection in spite of appropriate treatment was found though there was decrease in the amount of discharge. This finally resulted in implant removal with application of an external fixator in cases of fracture instability after implant(nail and plate) removal.

This method is suboptimal for infected intramedullary nail since it is difficult to remove all infected foci from infected intramedullary nail as evident from higher incidence of failure using this method of treatment. Hence, alternative methods have to be adopted to achieve better results in such cases.

However,limited choice of availability of antibiotics to be used along with necessity of the second surgery for bone cement removal, lack of osteoconductive and development of resistance against these antibiotics are the major concerns associated with this modality of treatment and which needs to be addressed.

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