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Original Research Article

Evaluating the Role of Antibiotic-Loaded Beads in Osteomyelitis Treatment in Patients with Diabetes

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Abstract:

Background and Aim: In light of the growing global awareness and advancements in socioeconomic and living conditions, there has been a concerning rise in the prevalence of diabetic osteomyelitis (DOM) and its associated complications. This research aimed to evaluate the efficacy of antibiotic-impregnated beads for the treatment of osteomyelitis in individuals with diabetic foot conditions within an Indian context. The research additionally examined the microbiological characteristics of the wounds.

Material and Methods: The study included all diabetic patients who had a chronic foot ulcer persisting for over three weeks, along with confirmed underlying osteomyelitis through culture results. The current main study involved a total sample size of 120 participants. The participants were assigned to the two groups in a random manner. Patients were divided into two distinct categories: the 'bead' group and the 'no bead' group. In the study, the 'bead' group received antibiotic beads, while the 'no bead' group was administered oral antibiotics, alongside empirical intravenous antibiotics for both groups. Patients underwent a comprehensive review over a six-month period, with ulcers that did not show signs of healing within this timeframe classified as instances of treatment failure.

Results: The findings of our study revealed a comparison of ulcer healing between two groups. Out of 120 patients involved, 102 experienced healing, while 18 did not achieve this outcome. Among the nine cases that did not heal, 14 were from the no bead group, while 4 were from the bead group. Among the 102 individuals who demonstrated healing, 46 were part of the group without beads, while 56 were in the bead group. The association regarding healing showed no statistically significant results. ($p>0.05$) The average healing time for the group without beads was 75.25±29.40 days, while the bead group recorded an average of 80.97±28.36 days, a difference that did not reach statistical significance.

Conclusion: The application of antibiotic beads enhances patient convenience by minimizing hospital visits and the necessity for daily dressing changes, all while maintaining an effective healing rate. The group without beads faced challenges in accessing hospitals on a daily basis, with some individuals even opting to forgo their daily dressings due to personal inconveniences.

Keywords: Antibiotic Bead, Diabetic Foot, Diabetic Osteomyelitis, Ulcer.

Introduction

In light of the growing global consciousness, advancements in socioeconomic conditions, and the evolution of wound care methodologies, the incidence of diabetes and its associated complications continues to surge at an alarming rate. [1-3] The consequences of an untreated diabetic foot ulcer can be severe, particularly when linked to advanced peripheral neuropathy. One of the most serious complications is osteomyelitis, which is associated with considerable morbidity, extended hospital stays, an increased likelihood of amputation, and escalating financial implications. [4] Diabetic osteomyelitis (DOM) frequently occurs alongside peripheral vascular disease, a lack of adherence to foot care guidelines, and various foot structural abnormalities. [5] The mechanisms behind this condition vary, encompassing both the autoimmune destruction of pancreatic β-cells and the phenomenon of insulin resistance. The microvascular complications associated with diabetes mellitus encompass retinopathy, nephropathy, and neuropathy, which can lead to

diabetic foot diseases. Myocardial infarction, transient ischemia, and stroke represent significant macrovascular complications. Diabetic foot disease remains a significant and preventable complication associated with diabetes mellitus. Foot ulceration and infections represent major contributors to elevated morbidity among patients. The lifetime risk for individuals with diabetic foot complications stands at 25%, marking it as a significant contributor to lower limb amputations and extended hospitalizations. [6,7] Epidemiological studies indicate that annually, 2.5% of the population is diagnosed with diabetes, while 15% experience complications related to diabetic foot diseases. [8]

Diabetic foot is a complication that arises from conditions such as peripheral neuropathy, peripheral vascular disease, and infections. [9] The diagnosis of diabetic foot infection involves a thorough clinical assessment, which is further supported by radiological investigations and bone culture analysis.

Diabetic foot infections often start with ulcers, necessitating a thorough treatment strategy to avert progression to osteomyelitis. In cases of diabetic foot osteomyelitis (DFO), it is essential to pursue aggressive treatment strategies to avert the potential necessity for amputations. In certain instances, amputations can be a crucial intervention to manage the infection effectively, all while preserving the foot's functionality. Amputations frequently present a range of complications, including difficulties with wound healing, a heightened risk of ulcerations, and the possibility of requiring further amputations. Consequently, there is an urgent demand for innovative therapies that can assist with sterilization, enhance wound healing, and avert the recurrence of infections. [10,11]

In the past, the primary approach to treatment involved the use of intravenous antibiotics in conjunction with debridement. Elevated concentrations are necessary to attain significant serum levels of antibiotics, potentially leading to a range of complications, such as nephrotoxicity and ototoxicity. Nonetheless, a significant number of patients are not in a suitable medical condition for extended intravenous antibiotic treatment or may experience multi-organ failure as a consequence of prolonged antibiotic use. Recent studies indicate that there is no statistically significant difference in the effectiveness of oral versus intravenous antibiotics for the treatment of diabetic foot osteomyelitis. [12] The localized delivery of antibiotics using bead technology provides an ideal concentration of selected antibiotics directly at the infection site. This represents a noteworthy advancement in the management of osteomyelitis among individuals with diabetes, enhancing convenience for those affected. [13] Beads are typically created using commercially available cement combined with a specific antibiotic. The beads undergo preparation in a sterile environment within the operating room before being applied directly to the ulcer. This method of administering antibiotics results in minimal systemic levels while achieving elevated concentrations in tissues, thereby minimizing systemic side effects. This approach is increasingly recognized as a viable strategy for managing dead space in cases of diabetic foot osteomyelitis.

This research aimed to evaluate the efficacy of antibiotic-impregnated beads for managing osteomyelitis in individuals with diabetic foot complications within an Indian context. The research further examined the microbiological characteristics of the wounds.

Material and Methods

A prospective comparative study was conducted at the Department of Surgery and Orthopedics in a Tertiary Care Teaching Institute in India over a period of one and a half years. The research adhered to the ethical guidelines established by the institutional review board, in accordance with the principles set forth in the 1964 Helsinki declaration and its subsequent amendments. The patient and caregiver provided informed consent for their participation in the study, as well as for the subsequent use of the data collected during the research.

The study included all diabetic patients who had a chronic foot ulcer persisting for over three weeks, along with confirmed underlying osteomyelitis through culture results.

Patients were divided into two distinct groups: the ‘bead’ group and the ‘no bead’ group. All chronic diabetic foot ulcers measuring 5 cm^2 or less were included in the study. Individuals who are immunocompromised were not included in the study.

To achieve a 95% confidence interval and an 80% statistical power in a two-sided test, a sample size of 59 participants per group was necessary. The target sample size for each group was set at 60 participants. The total sample size in our current main study was 120 participants. The participants were allocated randomly into the two groups.

A comprehensive history was gathered, and an extensive clinical examination was conducted for the patients visiting the outpatient departments of general surgery and orthopedics. Following the achievement of satisfactory glycemic control, the patients were scheduled for debridement in the operating room, with systemic antibiotics administered for coverage, and bone cultures collected for analysis. The initiation of culture-specific antibiotics occurred at a later stage. In the

study, the group receiving antibiotic beads was designated as the 'bead' group, while the 'no bead' group was administered oral antibiotics. Both groups received intravenous antibiotics as a precautionary measure. Amoxicillin clavulanic acid and cefoperazone-sulbactam emerged as the most frequently utilized options. Patients in both groups experienced a hospitalization period of approximately one week, following which they were discharged. Patients underwent evaluation according to the duration of their healing process. The wound is deemed healed once there is full epithelialization of the ulcer.

In the 'bead' group, following the debridement of the wound, antibiotic beads were formulated according to the culture and sensitivity report and subsequently positioned over the ulcer associated with underlying osteomyelitis. The beads were created by combining the necessary antibiotic concentration with synthetic implant-grade calcium sulfate dihydrate, which serves as a stimulant for rapid curing, ensuring both biodegradability and biocompatibility. Following thorough mixing, a consistent paste was achieved, which was then evenly applied using the paste applicator onto the bead mat. The mixture was allowed to remain undisturbed to facilitate proper setting. The bead mat was subsequently flexed to facilitate the release of the beads. The treatment involved applying these to the ulcer, followed by the placement of sterile gauzes on top. These dressings were to be changed every three days by the patient or their caregiver.

Patients underwent evaluations in our outpatient department every three weeks, during which their wounds were re-assessed. In instances of slough or lingering infection within the tissue, debridement was performed, after which the antibiotic beads were reloaded until the wound achieved healing. Patients in the 'no bead' group received discharge instructions that included a course of oral antibiotics, tailored according to the results of their culture and sensitivity reports.

Individuals in this cohort necessitated daily wound care from either the outpatient department or nearby hospitals. It was essential to conduct a review and reassessment of the wound every three weeks. Patients underwent a comprehensive review over a six-month period, with ulcers that did not show signs of healing within this timeframe classified as instances of failed therapy.

Statistical analysis

The collected data was systematically organized and input into a spreadsheet application (Microsoft Excel 2019) before being transferred to the data editor interface of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). The quantitative variables were characterized using means and standard deviations or medians and interquartile ranges, depending on their distribution patterns. Qualitative variables were reported in terms of counts and percentages. The confidence level for all tests was established at 95%, while the level of significance was determined to be 5%.

Results

The study involved 120 participants, evenly divided into two groups of 60. The ages of the participants ranged from 35 to 80 years, with an average age of 59 years in the 'bead' group and 60 years in the 'no bead' group. The study revealed that out of the total participants, 18 were female and 102 were male, indicating a notable male predominance in cases of diabetic foot osteomyelitis. The analysis revealed no statistically significant differences in mean age, body mass index, random blood sugar, and HbA1c values between the two groups, as illustrated in Table 1.

Our research examined the healing outcomes of ulcers across two distinct groups. Among the 120 patients involved in the study, 102 demonstrated healing, while 18 did not achieve healing. Among the nine cases that did not heal, 14 were from the no bead group, while 4 were from the bead group. Among the 102 individuals who demonstrated healing, 46 were part of the group without beads, while 56 were in the bead group.

The findings regarding the healing association did not reach statistical significance. ($p>0.05$) The average healing time in the group without beads was 75.25±29.40 days, while it was 80.97±28.36 days in the bead group, a difference that did not reach statistical significance (Table 1). The healing duration for the no bead group (n=46) was 22 individuals within 60 days, 18 within the 60-120 day range, and 6 within 120-180 days. In contrast, the bead group (n=56) showed 14 individuals healing within 60 days, 40 within the 60-120 day period, and 2 within 120-180 days.

Our study identified staphylococcus aureus as the most prevalent organism across both groups. Following this, the focus shifted to Enterococcus, Klebsiella, and Pseudomonas.

Table 1: Demographics, laboratory and wound characteristics of the study population

Variables	No bead group (n=80)	Bead group (n=80)	P value
Mean age (years)	58.15±8.14	60.47±09.36	0.22
Gender			
Male	52	50	0.68
female	8	10	
Random blood sugar (mg/dl)	185.41±14.23	196.14±16.78	0.09
BMI (kg/m2)	38.03±3.14	39.35±3.14	0.48
HbA1c	8.50±0.45	7.37±1.06	0.68
Wound size at presentation (cm2)	3.26±1.48	4.59±1.02	0.36
Duration of wound at presentation (days)	**22.77±4.32**	**24.97±4.06**	**0.58**
Wound healing			
Yes	49	56	0.10
no	11	4	
Mean duration of wound healing (days)	75.25±28.31	81.57±29.36	0.62

Statistically significance at p≤0.05

Discussion

Addressing diabetic foot infections presents significant challenges, particularly when complicated by underlying osteomyelitis. Foot ulcerations and infections represent major contributors to elevated morbidity among patients. The lifetime risk for individuals with diabetic foot complications stands at 25%, marking it as a significant contributor to lower limb amputations and extended hospitalizations. [6]

The study comprised 120 patients, evenly divided into two groups of 60. Participants' ages spanned from 35 to 80 years, with an average age of 58 in the first group and 60 in the second. Among the subjects, 18 were female and 102 were male, indicating a notable male predominance in cases of diabetic foot osteomyelitis. A comprehensive study conducted at a multi-disciplinary foot clinic at Royal Darwin Hospital in Northern Territory, Australia, between 2003 and 2017, involved 513 patients suffering from diabetic foot ulcers. The average age of participants was 59.9 years, with a standard deviation of 12.3 years, and a notable 62.8% of the cohort were male. [14] The findings of our study indicated a notable predominance of diabetic foot osteomyelitis among males.

Our research examined the healing outcomes of ulcers across two distinct groups. Among the 120 patients involved in the study, 102 demonstrated signs of healing, while 18 did not achieve healing. Among the nine cases that did not heal, 14 were from the no bead group, while 4 were from the bead group. Among the 102 individuals who demonstrated healing, 46 were part of the group without beads, while 56 were in the bead group.

The findings regarding the healing association did not reach statistical significance. ($p>0.05$) The average healing time for the no bead group was 75.25±29.40 days, while the bead group recorded an average of 80.97±28.36 days. This difference was not statistically significant, as shown in Table 1. The healing duration for the no bead group (n=46) showed that 22 participants healed within 60 days, 18 within 60-120 days, and 6 within 120-180 days. In contrast, the bead group (n=56) had 14 individuals heal within 60 days, 40 within 60-120 days, and 2 within 120-180 days. The highest number of wounds healed in the 'no bead' group occurred within 60 days, while the 'bead' group saw healing take place between 60 and 120 days. The antibiotic beads most frequently utilized in our study comprise colistin, with meropenem and gentamycin following closely behind. In a study involving 60 patients treated with antibiotic beads, colistin beads were specifically utilized for 18 of those individuals. A recent study from the Department of Diabetes at the University Hospitals of Leicester, NHS Trust, UK, conducted by Kong and Jogia, involved 20 patients suffering from diabetes-related nonhealing foot ulcers and forefoot osteomyelitis. These patients were treated with a combination of debridement and antibiotic beads, specifically vancomycin and gentamycin, utilizing HPS calcium sulfate as part of their care regimen. The observation period lasted for 18 months.

In these patients, osteomyelitis was diagnosed through bone culture and foot X-ray examinations. A combination of calcium sulfate, 1 gram of vancomycin, and 80 milligrams of gentamicin was prepared. All patients experienced healing within a median duration of 5 weeks, with no reported recurrences over a 12-month period. All patients exhibited no adverse reactions during the study. [15] A study conducted in Toronto by Israeli surgeons from Rambam Medical Center revealed that 15 patients were diagnosed with diabetic foot osteomyelitis. All of these patients received treatment through localized antibiotic therapy. In an 11-month follow-up study, it was observed that one out of 15 patients underwent amputations, while the remaining individuals showed healing

through local antibiotic treatment. [16] The study lacked a comparison group.

The duration of hospital stays was analyzed between the groups receiving the 'bead' intervention and those without it. The duration of hospital stay was longer for the 'bead' group, which necessitated a week of empirical antibiotics and debridement, followed by the application of culture-based local antibiotic beads in the operating theatre. After a two-day observation period, the patients were discharged. The procedure was performed on an outpatient basis for several individuals. The other group received similar management, with the distinction that they were discharged with oral antibiotics and required daily dressings. The procedure was performed on an outpatient basis for several individuals. The other group received similar management, but they were discharged with oral antibiotics and instructed to perform daily dressings. Antibiotic bead treatment presents a practical alternative for patients who cannot tolerate oral or intravenous antibiotics because of their overall health status. Recent observations indicate that antibiotic beads significantly contribute to decreasing the frequency of hospital visits and the necessity for daily dressings.

Conclusion

In our study, we have found a male predominance of diabetic foot infections with a mean age of 59. The usage of antibiotic beads improves patient convenience by reducing hospital visits and the need for daily dressing without compromising the healing rate.

The 'no bead' group had difficulties accessing hospitals daily, and few even skipped their daily dressings due to personal inconveniences. Local delivery of antibiotic beads increases the local tissue concentration of the antibiotic with low serum levels, thus reducing the systemic side effects. Intravenous use of antibiotics for osteomyelitis, which was used earlier, is being replaced by oral antibiotics with the highest bioavailability and antibiotic beads, increasing the tissue concentration without systemic toxicity.

This has significantly improved patients' quality of life and reduced the duration of hospital stays.

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