

## Use of Antibiotic Beading Technique in Treatment of Osteomyelitis in a Local Hospital of Islamabad, Pakistan

Zahra Hassan Kiani <sup>a</sup>

Iter Un Nisha <sup>b</sup>

Maria Amjad <sup>c</sup>

Sadia Bibi <sup>d</sup>

**Abstract:** *Despite the advancement in prevention and treatment against infection, osteomyelitis has always remained a challenge for an orthopedic surgeon. Although this problem is more prevalent in developing countries rather than developed countries, still it cannot be overlooked. That's why we have aimed this case study to consider the therapeutic plan and techniques used for the treatment of osteomyelitis. A 67 years old male was presented in a local public hospital of Islamabad, Pakistan with severe pain in right lateral thigh unable to move hip and knee joint and swelling. Emergency treatment included diclofenac. X-rays result showed fracture of right femur. Cultures DHS fixation (Dynamic Hip Screw fixation) was done, pus was drained and culture reports indicated Staphylococcus areas that was sensitive to Cefotaxime. The therapy plan included antibiotics along with pain killers, but the infection was not treated. Beside x-ray. Finally this infection was treated using antibiotics beading technique.*

**Key Words:** Beading Technique, Antibiotic Cementing, Cefotaxime, Cefoperazone, Osteomyelitis

### Introduction

Osteomyelitis is one of the most common diseases which has diverse clinical and microbiological subdivisions. (Hake et al., 2015) Osteomyelitis is actually inflammation of bone due to infection which may be due to bacteria (mostly Staphylococcus aureus) (Beck-Broichsitter, 2015). This disease can involve any bone and can affect all ages. Osteomyelitis can affect only a portion of bone or it can affect various regions, like periosteum, bone marrow, bone cortex or soft tissue that surrounds the respective bone (Lew, 2004). It can occur if the infection enters bone tissue via blood stream which may infect both the bone as well as bone marrow. It can also occur due

to any complication of surgery or an injury (Jaspaul S. Gogia, 2009). Osteomyelitis is being divided into three categories; first being hematogenous osteomyelitis which is bone infection that spreads through blood. Second category includes osteomyelitis which result from contiguous infection with no involvement of vascular insufficiency; occurring probably after trauma and surgery. Lastly, third category is the osteomyelitis involving vascular insufficiency from a contiguous infection. This category primarily occurs in lower extremities for example diabetic foot infection. The occurrence of any of these categories of osteomyelitis can be in any bone, either in acute

<sup>a</sup> MBBS Candidate, Rawalpindi Medical University, Rawalpindi, Punjab, Pakistan.

Email: [zahrahassankianigmail.com](mailto:zahrahassankianigmail.com)

<sup>b</sup> Lecturer, Department of Pharmacy, Iqra University Islamabad Campus, Islamabad, Pakistan.

<sup>c</sup> Riphah Institute of Pharmaceutical Sciences, Riphah International University, Islamabad, Pakistan.

<sup>d</sup> Riphah Institute of Pharmaceutical Sciences, Riphah International University, Islamabad, Pakistan.

or chronic phase, with causative agent mostly being bacteria and seldom being fungi. (Fritz & McDonald, 2008) Currently, no standard multidisciplinary classification for osteomyelitis is available, though there are different ways to differentiate the disease in clinical practice based on type of bacteria, duration of disease or on the bases of the affected area (Schmidt HG, 2011) (Diémé, 2014).

Not every case of osteomyelitis is the same. The causative agent and the pathological changes are associated with the disease progression, its anatomical location, as well as changes in structure of bone due to the patients age (Urish, 2020). Swelling is often observed in the bone marrow which is the soft inner part of the infected bone. The respective swollen tissue inside applies force to on the rigid and tough outer wall of the bone, which may compress or cut off the blood supply (M. Fantoni, 2019). Such areas are regarded as difficult locations of infection, because it is not easy for the bodys natural immune cells and antibodies to reach these areas. There is also a chance of infection to spread outside the bone, which will cause the pus to collect in nearby tissues as well like muscles (Bucher, 2019).

In majority of the cases of osteomyelitis, treatment involves a long term parenteral antibiotic therapy followed by removal of infected bone and soft tissue surgically. Despite various breakthroughs in the knowledge of osteomyelitis and its deteriorating effect on bone, there has been lack of advancement in level of treatment management (Masters, E.A., 2019). Although the data available suggests that in more than 70% of the instances, surgery paired with anti-infective treatment results in long term infection management (Walter, 2012). In cases of osteomyelitis which are of acute and uncomplicated nature, treatment involves antibiotic alone upon meeting the preconditions. The antibiotic is administered for a period of 4 to 6 weeks and known to show 80% success rate approximately. On the other hand, if the patient of osteomyelitis is chronic or has implant-associated osteomyelitis, then using the antibiotic alone does

not prove to be successful and needs debridement. The debridement itself becomes quite a challenge as judging the extent of debridement of bone is difficult. Additionally, perplex interventions and lengthy healing time may be needed for managing dead space. The failure chances in such cases still revolves around a percentage of 20 in spite of efficient treatment. (Hofstee et al., 2020)

The literature review establishes the fact that local antibiotics can help prevent occurrence of infection in the case of open fractures. The treatment recently adopted involves several steps; first step being irrigation and debridement. In the second step stabilization of skeleton followed by providing soft tissue coverage at the wound site. Therefore, the therapy revolves around the fixation of external skeleton and covering the wound along with co administration of antibiotics parenterally. (Henry & Seligson, 1990) However, to ensure therapeutic levels of antibiotic at the target site there must be high levels of antibiotic in the serum which is both toxic and least cost effective. Therefore, to overcome this problem concept of antibiotic beading technique raised back in World War II where the local antibiotic crystals were applied to control microorganism. Today this technique has been modified and the delivery of antibiotic is ensured via polymethylmethacrylate(PMMA) first explained in hip arthroplasty. For treating the chronic osteomyelitis, Klemm produced gentamicin-PMMA bead chains through extension indicated for the antibiotic laden bone cement. This ensures the efficient removal of the implant. (Henry & Seligson, 1990) To treat such an infection sometimes local application of antibiotics in the form of beads and rod seems to be a very creative and useful substitute. These beads may be placed at the site of infection by surgery and then are enclosed and, after the infection subsides, they may be removed. Biodegradable implants are also available for such treatment options (Wassifa, 2021).

The antibiotic beading technique has several advantages in comparison to the conventional treatment. In this technique the chance of

systemic complications is low because of the reduced systemic levels whereas the concentration at the target site is high increasing its efficiency. It can also help to manage the dead space. Furthermore, these are inexpensive and easy to handle and well tolerated by the patient. There is variation in the beads depending upon the size, type of bone cement and type and quantity of antibiotic. These can be simply prepared by molding or by rolling. (DeCoster & Bozorgnia, 2008) The most commonly used carrier is PMMA cement which is considered nonbiodegradable. For incorporation of the antibiotic, mixture of antibiotic and cement polymer in powdered form is made prior to the addition of liquid methylmethacrylate. Before using the antibiotic, several criteria are to be met for example its heat stability, water solubility and powdered form of the antibiotic, broad spectrum activity and hypo allergenicity. The release of antibiotic in the initial four days after implantation is highest which keeps on eluting at a persistent rate for weeks to months. This is considered sustained release in which diffusion of the antibiotic from the PMMA occurs after the body fluids gets penetrated into it. PMMA is being hydrophilic helps to attract the water molecules into the bead followed by antibiotic release into body fluids. (DeCoster & Bozorgnia, 2008)

Bead molds come in sizes with diameter ranging from 2-8mm. In case of wounds which are smaller in size, small beads with diameter of 2mm are preferred so that the surface area and elution of antibiotic is increased. To make sure easy passage of bead into tight spaces, the size and shape of the beads should be constant. For applying the beads, first step should be its production followed by its placement in the debrided wound. After the bead is being placed, soft tissue is closed. Through the antibiotic beads, the wound gets washed by the antibiotic at a high concentration which helps in combating infection. The risk of hematoma accumulation is reduced along with the prevention of scar tissue formation through dead space management. Upon failure and persistence of infection, the procedure is repeated after several days or weeks whereas on achieving

successful results the surgical removal of beads is ensured. Once the infection is well controlled, the beads are surgically removed. (DeCoster & Bozorgnia, 2008)

### Case Report

A 67 years old man, suffered from a road accident. He is a known patient of smoking, Diabetes type 1 and asthma. He was presented to a local hospital, Islamabad, Pakistan with severe pain in right lateral thigh, unable to move hip and knee joint, moderate swelling right lateral thigh, right leg was externally rotated, dorsalis pedis was palpable, sensory motor was intact. In emergency Diclofenac sodium was administered.

After thorough examination he was given Tramadol 50mg 1\*TDS, Gravinate 50 mg 1\*TDS, Paracetamol 500mg 1\*TDS, Paracodine 500mg 1\*TDS, Cap. Celbex 1\*TDS, Brufen topical cream for local application, along with application of non adhesive skin traction with 4kg weight. X-rays AP pelvis was performed and x-ray result showed intra trochanteric fracture of right femur. After 3 days DHS fixation of right femur was done post operatively Augmentin 1.2BP\*IV was administered and medicated gauze was placed and no drain was observed that's why on 3<sup>rd</sup> day drain was taken out.

On 7<sup>th</sup> post-operative day patient complained of pain, swelling and fever at night. Dressing was examined, swelling was there and gauze was soaked. Gauze was removed and the wound was pressed which resulted in oozing of pus. Sample was taken and sent for culture while pus was drained, wound was regressed and dressing was done. Blood CP was performed which showed CRB and TLC.

Augmentin was continued, Amikacin, Grasil 500mg, along with Cefotaxime 1g IV\*BD. The culture report indicated that organism was fully sensitive to Cefotaxime. Cefotaxime was continued along with Cipro 200mg IV\*BD. After 2 months of therapy, there was still no substitute of puss. Local infiltration of antibiotics into the injury was tried, using Antibiotics Beading Technique. For this 4g of Cefoperazone in combination with

Salbactam was incorporated into bone cement, as organism was sensitive to Cefoperazone, beads were prepared, which were placed at the site of infection and was enclosed. Novidat and pain management was continued. Again, drain was passed to remove the pus. In 3-4 days 8ml drain was evacuated.

Beads remained inside for 36 days. After that, beads were removed and specimen was sent for culture. Culture report indicated no bacterial growth. During the therapy very mild drug associated side effects were observed like tramadol caused vertigo, Celbex caused epigastric pain. To relieve the epigastric pain Famotidine was given.

During the whole course of therapy patient also developed UTI (calcified prostate) that later on subsided. As the patient was a smoker as well as suffered from diabetes that's why healing was slow, but the most interesting fact was that during the stay in hospital, patient's fasting BGL remained within 100 to 140 without the use of Insulin.

## Discussion

This case study demonstrated the efficacy and effectiveness of regional application of antibiotics in the management of osteomyelitis infection. Antibiotic used locally to treat osteomyelitis has been in use for years and have proven to be very effective. Various medicine delivery methods have been established for both the prophylaxis of disease as well as for infection treatment.

With the introduction of joint arthroplasty in 1970s in Europe, the localized usage of certain antibiotics to avoid bone infections was adopted in to general practice. Gentamicin, erythromycin as well as penicillin mixed with the cement used to affixed prostheses to the bone were observed to deliver high amount of antibiotics for long durations, enabling the use of antibiotics in infection prophylactic treatment for joint arthroplasty, according to Buchholz and Engelbrecht in a sentinel paper (C. Berberich, 2022) (RA Elson, 1977).

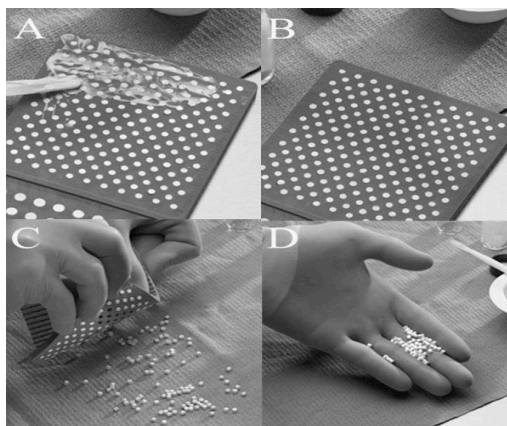
Apart from this, use of localized antibiotic therapy can be observed in the treatment of

prophylaxis especially for open fractures, treatment of arthroplasty infections as well as in treatment of chronic osteomyelitis. Klemm developed gentamicin-impregnated beads in 1979. He used these gentamicin beads to fill up the empty space after removal of infected bone. A cure rate of 91.4 percent out of more than 100 cases was achieved (Klemm K., 1979).

Non-biodegradable poly-methyl-methacrylate has been the majority of treatment in this sort of application for more than last 20 years. This material has outstanding elution properties as well as structural support features. More recently, biodegradable materials like bone grafts and calcium sulfate have been used. Alternative biodegradable implants, such as synthetic polymers, have not yet been approved by authorities for usage on, however these alternatives have shown promising outcomes in laboratory demonstrations. A recent development of antibiotic-impregnated metal holds great potential to be used for the treatment and/or prophylaxis of complicated diseases such as osteomyelitis in future (Pantus, 2020).

## Image 1

Also in the given case, patient's first culture report indicated the presence of staphylococcus aureus



but due to negligence of nursing staff timely administration of drugs was not observed. Due to the presence of antibiotic-resistant organism, MRSA, the antibiotic treatment became

complicated (Gimza, 2021). Antimicrobial therapy ought to be extended (four to six weeks) if the infected bone is not surgically resected. Improvement in surgical techniques have raised the chances of saving bones (as well as limb in certain cases) and preventing reoccurrence of infection.

The infection was finally healed by local application of antibiotics as IV drug was unable to reach in sufficient amounts at the site of infection as bone had very less blood supply. Doses were according to those given in BNF and no drug interactions were found. Overall the therapy protocols followed were found to be rational (Anon., 2021).

### **Conclusion**

Osteomyelitis being a very serious medical condition must be addressed with great care. A diverse team is the most effective way to manage

the condition. It involves precise diagnosis along with host defense optimization (strengthening of the immune system) as well as proper anti-infective therapy and, in some cases, bone reconstructive surgery and debridement. For the prevention and treatment of osteomyelitis, local antibiotics are not only effective but are also considered safe. Low risk of toxicity, less cost and significantly higher concentration of antibiotic at its required site of action are some of the major advantages of localized drug delivery system compared to the systemic therapy.

A second course of action to take out the drug delivery device is required in majority of the current treatment techniques, although biodegradable devices are under development that have potential to provide modified antibiotic therapy depending on the organism and patient characteristics.

## References

- Beck-Broichsitter B. E., Smeets, R., Heiland, M. (2015). Current concepts in pathogenesis of acute and chronic osteomyelitis. *Curr Opin Infect Dis*. Jun; 28(3), 240-5.
- Berberich, C., (2022). Does Antibiotic-Loaded Bone Cement Trigger Widespread Antibiotic Resistance Affecting Prosthetic Joint Infection Treatment?. In: E. Hansen, ed. *Essentials of Cemented Knee Arthroplasty*. Berlin: Springer Verlag, 701-706.
- Buchholz, H. W., & Engelbrecht, H. (1970). Depot effects of various antibiotics mixed with Palacos resins. *Chirurg* 41, 511-515.
- DeCoster, T., & Bozorgnia, S. (2008). Antibiotic Beads. *Journal of The American Academy of Orthopaedic Surgeons*, 16(11), 674-678.
- Diémé, C. (2014). Therapeutic Aspects of Chronic Bone Infections and Management Challenges. *Open Journal of Orthopedics*, 4(2).
- Fritz, J., & McDonald, J. (2008). Osteomyelitis: Approach to Diagnosis and Treatment. *The Physician And Sportsmedicine*, 36(1), 50-54.
- Gimza, B. D., & Cassat, J. E. (2021). Mechanisms of Antibiotic Failure during Staphylococcus aureus Osteomyelitis. *Frontiers in immunology*, 12, 638085.
- Hake, M., Young, H., Hak, D., Stahel, P., Hammerberg, E., & Mauffrey, C. (2015). Local antibiotic therapy strategies in orthopaedic trauma: *Practical tips and tricks and review of the literature*. *Injury*, 46(8), 1447-1456.
- Henry, S., & Seligson, D. (1990). Management of Open Fractures and Osteomyelitis with the Antibiotic Bead Pouch Technique. *Southern Medical Journal*, 83(Supplement), 2S-98.
- HG, S. (2011). Definition of the Diagnosis Osteomyelitis-Osteomyelitis Diagnosis Score (ODS). *Z Orthop Unfall*, 149(4), 449-460.
- Hofstee, M., Muthukrishnan, G., Atkins, G., Riool, M., Thompson, K., & Morgenstern, M. et al. (2020). Current Concepts of Osteomyelitis. *The American Journal of Pathology*, 196(6), 1151-1163.
- Jaspaul, S., Gogia, M. D., John, P., Meehan, M. D., Paul, E., Di Cesare, M. D., & Amir, A., Jamali, M. D. (nd). Local Antibiotic Therapy in Osteomyelitis. *Seminars in Plastic Surgery*, 23(2), 100-107.
- Klemm K. Gentamicin-PMMA-beads in treating bone and soft tissue infections (author's transl) *Zentralbl Chir*. 1979; 104:934-942.
- Lew, D. P., Waldvogel, F. A. (2004). Osteomyelitis. *Lancet* 364, 369-379.
- Masters, E. A., Trombetta, R. P., de Mesy Bentley, K. L. et al. (2019). Evolving concepts in bone infection: redefining biofilm, acute vs. chronic osteomyelitis, the immune proteome and local antibiotic therapy. *Bone Res* 7, 20
- Pantus, A. V. (2020). Antimicrobial Activity of Impregnated Antibiotic. *Balkan Medical Union*, 55(1), 22-30.
- RA Elson, A. J. (1977). Antibiotic-loaded acrylic cement. *The Journal of Bone and Joint Surgery*. 59-B (2).
- Ramanujam, C. L, Zgonis, T. (2010). Antibiotic-loaded cement beads for Charcot ankle osteomyelitis. *Foot Ankle Spec*. 2010 Oct; 3(5), 274-7.
- Rao, N., Ziran, B. H., Lipsky, B. A. (2011). Treating osteomyelitis: antibiotics and surgery. *Plast Reconstr Surg*. 2011 Jan; 127 Suppl 1:177S-187S.
- Urish, K. L. (2020). Staphylococcus aureus Osteomyelitis: Bone, Bugs, and Surgery. *Infection and Immunity*.
- Walter, G., Kemmerer, M., Kappler, C., & Hoffmann, R. (2012). Treatment algorithms for chronic osteomyelitis. *Deutsches Arzteblatt international*, 109(14), 257-264.
- Wassifa, R. K. (2021). Recent advances in the local antibiotics delivery systems for management of osteomyelitis. *Drug Delivery*, 28(1), 2392-2414.