ISSN 2348-313X (Print)
International Journal of Life Sciences Research ISSN 2348-3148 (online)
Vol. 4, Issue 3, pp: (1-6), Month: July - September 2016, Available at: www.researchpublish.com

Therapeutic Considerations of Osteomyelitis: A review

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Abstract: **Osteomyelitis is inflammation of bone and bone marrow caused by the many pathogenic agents especially *S. aureus* originated by many etiologies e.g., trauma. Osteomyelitis is diagnosed by clinical signs and symptoms, laboratory tests, imaging analysis, histological studies, and microbiological studies and at the end identification of pathogen through blood culture. Treatment of osteomyelitis includes antimicrobial therapy and debridement of dead tissue. Combination of oral and parenteral antibiotics used in antimicrobial therapy to treat osteomyelitis. Surgical method involves when antibiotic therapy fails to treat the disease. Muscle flap and hyperbaric oxygen therapy is also used for the management of osteomyelitis. Recently maggot therapy is used to remove the dead tissue from the infected site; it is cost effective and rapid debridement method. Due to resistance to antibiotics, management of osteomyelitis is ultimate challenge for clinicians. Morbidity of osteomyelitis can be reduced through diagnosis and initiation of appropriate treatment at time.**

Keywords: **Bone-marrow, *S. aureus*, osteomyelitis, antibiotics, maggot-therapy.**

1. INTRODUCTION

Inflammation of bone and bone marrow is known as osteomyelitis. It includes the cancellous portion, bone marrow, cortex and periosteum (Giri *et al.,* 2014). It is the indication of infection and mainly caused by bacteria, also caused by fungi, parasites, and other microorganisms (Finland, 1972; Roy *et al.,* 2012; Gomes *et al.,* 2013). The relationship of trauma to osteomyelitis is speculative. When there is trauma to the bone it may causes local edema and responsible for change in blood flow, while bacterial proliferation best suitable when there is hematoma (Cierny *et al.,* 2003; De Boeck, 2005). Infection may be limited to certain areas of bone or may be spread throughout the bone (Glover, 1972; Lew and Waldvogel, 2004). There are several factors on which the clinical manifestation and the natural history of osteomyelitis depend; these factors include age of the patients, patient resistance, virulence of the infecting organism and site of infection (De Boeck, 2005; Nather *et al*., 2005). In acute osteomyelitis, suppurative inflammation bearing bacteria and microorganisms occur (Grayson *et al.,* 1995). Many inflammatory factors and leucocytes cause tissue necrosis and the demolition of bone trabeculae and bone matrix. (Lew and Waldvogel, 2004) In development of osteomyelitis, microbial and host factors are important. *Staphylococcus aureus* and *Staphylococcus epidermidi* are pathogenic microorganisms and causes 50% cases of osteomyelitis (von-Eiff *et al.,* 1997; Gomes *et al.,* 2013). Its virulence depends on many factors. Firs, bacterial adhesins proteins are important for attachment to extracellular matrix. Second, many factors promote avoidance from host defenses. Third, many factors promote entry into host tissue by specifically attacking host cells (Waldvogel *et al.,* 1970; Lew and Waldvogel, 2004). 35 osteomyelitis patients were selected randomly from the Jinnah Hospital, Lahore; Mayo Hospital, Lahore between the periods of 7th June 2010 to 28th June 2010. Performa was filled by both males and females: it was concluded from performa that males are more effective than females. Tibia (51.4%) and Femur (34.28%) were the most commonly affected bones by osteomyelitis. In 78.26% of patients, *S.aureus* was most common causative agent of osteomyelitis (Nadeema *et al.,* 2010).

2. SPECIAL FORMS OF OSTEOMYELITIS

ACUTE HAEMATOGENOUS OSTEOMYELITIS:

It is the infection of bone due to presence of bacteria in blood stream (Aynesworth, 1931; Roy *et al.*, 2012). This type of osteomyelitis mostly occurs in prepubertal children and in elderly patients by implementation of bacteria within slightly damaged bone (Lew and Waldvogel, 2004; Harik and Smeltzer, 2010). It may be converted into chronic form if not be treated (Roy *et al.*, 2012). Its prevalence is 1 case out of 5000 children (Blockey and Watson, 1970; De Boeck, 2005).

SUBACUTE AND CHRONIC OSTEOMYELITIS:

If the symptoms of infection exceeds more than 3 weeks then there is subacute or chronic osteomyelitis. It is less common and patients ranging from 2 to 16 years in age (De Boeck, 2005). Symptoms of subacute or chronic osteomyelitis include systemic illness, spasmodic pain over a period of 3 or 4 weeks. There is also local tenderness and limping if lower limp is involved (Simpson *et al.*, 2001; Spiegel and Penny, 2005; Mandíbula et al., 2010; Jardim-Júnior et al., 2010; Spellberg and Lipsky, 2011).

TUBERCULOSIS OSTEOMYELITIS:

Myobacterium tuberculosis is the main cause of this type of osteomyelitis. Symptoms are asymptomatic bone lesion and may be fever or not. Although any bone can be involved, 50% of the cases are in the spine (50% thoracic, 25% cervical, 25% lumbar), 12% in the pelvis, 10% in the hip and femur, 10% in the knee and tibia, 7% in the ribs, and 2% in the ankle, shoulder, elbow or wrist, and in 3% more than one region is involved. Diagnosis involves biopsy and tuberculin test. It mostly occurs in adults and rare in children (Feigin and Cherry, 1998).

NEWBORN OSTEOMYELITIS:

It is rare. Risk factors of newborn osteomyelitis are prematurity, low birth weight, another accompanying infection, blood transfusion, the presence of umbilical catheter. Its causes are *S. aureus*, group B streptococci, and enteric gram-negative bacilli, usually it is observed together in multiple bone and arthritis. Because of nonspecific symptoms, the diagnosis may be delayed. Leukocytosis; ESR and CRP not increased. There are lytic bone lesions in newborn osteomyelitis; it may disturb skeletal growth and causes permanent disorders in joints (Feigin and Cherry, 1998).

OSTEOMYELITIS IN SICKLE CELL ANEMIA:

There are increased bacterial infections when there is the sickle cell hemoglobinopathies. When there is sickling, intestinal microorganisms invade the blood. *S. aureus* causes this type of osteomyelitis. Symptoms include fever, bone ache and leukocytosis. Antibiotics are acquired for treatment (McLean *et al.*, 1996).

TRAUMATIC OSTEOMYELITIS:

Animal bites, needle sticking by newborns during blood take-up, bone marrow aspiration, rupture injuries and open fractures can lead to traumatic osteomyelitis (Wiley and Trueta, 1959; Roesgen *et al.*, 1989).

POSTOPERATIVE OSTEOMYELITIS:

Trimming of closed fractures, craniotomies, median sternotomies and other bone surgeries may lead to the postoperative osteomyelitis (Roesgen *et al.*, 1989).

MULTIFOCAL OSTEOMYELITIS:

Multifocal osteomyelitis occurs due to drug addiction. In this multiple tumors are present on bone (Feigin and Cherry, 1998).

CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS:

This type of osteomyelitis mostly observed in childhood, among young adults and most frequently present among girls. Antibiotics are not benefitted to this, than steroids and anti-inflammatory treatment is suggested (Feigin and Cherry, 1998).

VERTEBRAL OSTEOMYELITIS:

It is a type of osteomyelitis and rare bone infection of spinal region. Only 2-4% of all bone infections cases are related to this. It may be classified as acute or chronic depend on severity of disease (Kahn, 1982; Modic *et al.*, 1985; Newlands and Makielski, 1996; Roy *et al.*, 2012).

3. DIAGNOSIS OF OSTEOMYELITIS

Diagnosis of osteomyelitis include clinical signs and symptoms, laboratory tests, imaging analysis, histological studies, microbiological studies and at the end identification of pathogen through blood culture (Walter *et al.*, 2012; Lima *et al.*, 2014). There is variety of symptoms of osteomyelitis patient including an open wound exposing fractured bone, an indolent draining fistula, to no skin lesion, but local swelling and bone pain tendernes (Lew and Waldvogel, 2004). Laboratory test include leukocytosis and neutrophilia, laboratory findings are nonspecific in osteomyelitis. While histological studies include complete study of tissues of bone, in acute form polymorphonuclear leukocytes are dominant, while in chronic form lymphocytes, osteoblasts and osteoclasts are dominant (Lima *et al.*, 2014). In imaging analysis, plain radiography unable to reveal bone infections and abnormalities until the 2 weeks later of initial infection MRI better than plain radiography, as it detects the infection in 2-3 days of onset of infection (Newman *et al*, 1992; Nather *et al.*, 2005). The differential diagnosis should be performed, when there is high fever, pain and sensitivity in the extremities. Rheumatic fever, septicemia, septic arthritis, cellulitis, Ewing's sarcoma, metastatic neuroblastoma, leukemia, reflex neurovascular dystrophy, to thrombophlebitis hemoglobinopathies connected bone infarcts and toxic synovitis can be computed to be in these cases (Lew and Waldvogel, 2004).

4. MANAGEMENT OF OSTEOMYELITIS

There was 20% infection and 45% to 50% morbidity hematogenous osteomyelitis before the availability of antibiotics. Today in developed countries, acute osteomyelitis rarely causes death of children, but preventable morbidity remains. Morbidity can be reduced through diagnosis and initiation of appropriate treatment (Moule and Kahler, 1999; Moon and Jeong-Lim, 2000). Oral and parenteral antibiotics therapies are used for the treatment of osteomyelitis (Spellberg and Lipsky, 2011; Malhotra *et al.*, 2014). Surgical method is also used to remove dead and infected tissue. In acute osteomyelitis, shorter antibiotic therapy is needed while in chronic osteomyelitis longer antibiotic therapy is required (Bernard *et al.*, 2003; Nather et al., 2005). Intravenous antibiotic is used for the treatment of acute osteomyelitis. Chronic osteomyelitis treatment is complicated and requires 3 stages: debridement of dead tissue, systemic antibiotic therapy, and local antibiotic delivery system (Maurer *et al.*, 1981; Rubino *et al.*, 2009; Gomes *et al.*, 2013; Prasad *et al.*, 2014; Marais *et al.*, 2014). Chronic osteomyelitis is treated by rest and antibiotics (Evans and Davies, 1969; Asensi *et al.*, 2003). For the treatment of chronic osteomyelitis, the effectiveness and protection of three oral fluoroquinolones (lomefloxacin, levofloxacin, and ciprofloxacin) were studied and it was concluded that oral fluoroquinolones ia secure. Cephalosporins 57.14%, Fusidic acid and Linezolid 34.28%, Other Penicillins & Fluoroquinolones 20% are most commonly preferred antibiotics for osteomyelitis treatment. A combination of antibiotics, either given orally or parentally, is the best option for the treatment of osteomyelitis (Nadeema *et al.*, 2010). The erythrocyte sedimentation rate (ESR) is normally calculated in the range of 40-60 mm/hr; it reaches the highest rate within 3-5 days of the treatment, and it returns to normal within 3 weeks. As ESR slowly reduces with successful treatment, increased ESR indicates the response to the treatment. The rise of the C-reactive protein (CRP) level is the highest on 2nd day of the treatment increased level of C-reactive protein (CRP) is the highest (mean 83 mg/L) and it decreases to normal in 1 week. ESR and CRP, is used for examine response to the treatment (Lew and Waldvogel, 2004). Recently for the treatment of chronic osteomyelitis, non-muscle flaps are used. These flaps replaced the infected portion of the lower extremities to prevent further injury to bone (Mathes, 1982; Rubino *et al.*, 2009). Adjuvant therapy is used for the inflammatory tissues. In adjuvant therapy hyperbaric oxygen therapy is used in which patient is placed under pressure resistant hyperbaric chamber. 100% oxygen is supplied to the patient under hyperbaric condition (elevated oxygen above the atmospheric pressure). Due to pressure, oxygen given to blood than plasma and ultimately received by tissues Hyperoxygenation of tissues causes lysis of viruses and pathogens by leukocytes, elevated proliferation of fibroblasts and collagen, and vascularization of inflammatory tissues. This therapy is more effective, cost and wound healing time is reduced (Lima *et al.*, 2014). Recently blowfly maggots are used to treat osteomyelitis. As blowfly maggots eat only dead tissue, they are placed at infected site and treatment repeated foe 3-4 weeks, maggots eat most of the dead tissue. Maggot therapy is cost effective and rapidly removes the dead tissue (Baer, 2011).

5. CONCLUSION AND RECOMMENDATIONS

Osteomyelitis is serious bone infection with high rate of morbidity. Many pathogenic microorganisms contribute to this infection. Despite of development in antibiotics and surgical methods, osteomyelitis management is challenging due to the developing resistant of pathogens against antibiotics. Recently many therapies are used for its treatment included antimicrobial therapy, surgical method, muscle-flap method, hyperbaric oxygen therapy, and maggots therapy. Surgical method is used when antimicrobial therapy remains unresponsiveness. While hyperbaric oxygen and maggots therapy decreases the cost ant and wound healing time. There should be thorough study about patient health and disease status before the selection of appropriate treatment of osteomyelitis.

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