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RESEARCH ARTICLE

MOXIFLOXACIN AND ITS USE IN ODONTOGENIC INFECTIONS. AN ALTERNATIVE FOR PATIENTS WITH PENICILLIN ALLERGIES? LITERATURE REVIEW

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Abstract

Maxillofacial infections of odontogenic origin are a frequent cause of dental emergencies, primarily caused by caries, periodontal disease, and dentoalveolar abscesses. These infections, which can vary in severity and spread throughout facial spaces, sometimes require surgical management and intravenous drug treatment in hospitals. The oral bacterial flora is predominantly polymicrobial, with a majority of streptococci and the presence of staphylococci and anaerobic bacteria. Regarding antimicrobial treatment, penicillins (PEN) continue to be accepted as the first-line option, growing resistance has prompted the search for alternatives such as clindamycin and quinolones, with moxifloxacin being particularly notable for its broad spectrum and effectiveness against oral pathogens. This study evaluates the in vitro and in vivo efficacy of moxifloxacin in the treatment of maxillofacial infections, including maxillary sinusitis, abscesses, and cellulitis of odontogenic origin.

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Introduction:-

Odontogenic infections of the maxillofacial region are one of the main causes of emergency in dental practice. Their etiologies are primarily caries, periodontal disease, and dentoalveolar abscesses (1). These infections can range in severity because they can spread throughout facial spaces Some cases can be highly complex, requiring hospital care and timely surgical and intravenous pharmacological management. (2)The oral bacterial flora is characterized by being polymicrobial, with a predominance of streptococci, representing approximately 90%, and staphylococci, 5%. Anaerobic bacteria have a greater abundance of species; Among the most common are gram-positive cocci and gram-negative bacilli.(3)

Regarding antimicrobial treatment, penicillins (PEN remain widely accepted as a first-line therapy and are commonly recommended as the antibiotic of choice. However, their high rates of antibacterial resistance require ongoing monitoring and consideration. The use of clindamycin (CLI) for the treatment of odontogenic abscesses is supported in the dental literature; nonetheless, a significant increase in resistance rates to this antimicrobial has been

reported. Quinolones have emerged as an alternative due to their broad spectrum of activity against oral microbial flora, particularly moxifloxacin (MXF), a fourth-generation quinolone that has demonstrated good results with high sensitivity to oral pathogens.The objective of this article is to present the efficacy of MXF in vitro and in vivo studies for the treatment of maxillofacial infections such as maxillary sinusitis, abscesses, and cellulitis of odontogenic origin.

Materials and Methods:-

A comprehensive literature search was conducted using the PubMed and Scopus databases between August and September 2024. The keywords used included moxifloxacin, clindamycin, amoxicillin, dental infections, maxillofacial infections, and abscesses, combined using Boolean operators AND and OR.

Inclusion criteria:

1) Studies reporting the use of moxifloxacin in vitro or in vivo in dental and maxillofacial infections, including clinical, observational, and randomized trials relevant to the central topic.
2) Articles published in English and indexed in PubMed or Scopus.
3) Studies after 2000.

Exclusion criteria:

1) Reviews, meta-analyses, and book chapters.
2) Studies published in languages other than English.
3) Studies that do not mention or compare the use of moxifloxacin with other antibiotics
4) Studies before 2000

Results:-

The initial search yielded a total of 182 primary studies, 147 from PubMed and 35 from Scopus. Fourteen studies relevant to the initial search topic were selected. The remaining studies were excluded for not meeting the inclusion criteria or lacking relevance.

For better understanding, the included studies were categorized as follows: maxillary sinusitis (4-7), odontogenic abscesses (8-15), and post-extraction bacteremia (16-17).

Use of Moxifloxacin in Odontogenic Infections:

Moxifloxacin is a broad-spectrum, fourth-generation fluoroquinolone. It belongs to a group of quinolones known as 8-methoxy fluoroquinolones and is effective against both gram-positive and gram-negative bacteria. Compared to other fluoroquinolones, Moxifloxacin has a broader spectrum of action.(18)Due to its broad spectrum of action, good tissue penetration, and high oral bioavailability, it is being used successfully in the treatment of respiratory infections, such as sinusitis and bronchitis, mixed abdominal infections, and soft tissue infections.(19) It has also demonstrated good results in the treatment of odontogenic infections, with an efficacy profile comparable to that of amoxicillin/clavulanic acid (AMX-AC).(11) The dosing regimen for MXF is 400 mg every 24 hours, typically for 5 days. This treatment guideline could ensure better adherence to prescriptions.

Moxifloxacin in Maxillary Sinusitis:

In a clinical trial, Rakkar's group (Rakkar et al., 2001) of 475 adult patients with acute sinusitis received a 10-day oral regimen of moxifloxacin (400 mg once daily) or amoxicillin-clavulanic acid (875 mg twice daily). The primary outcome was clinical resolution. Secondary outcome measures included clinical relapse during follow-up and assessment of patient-reported outcomes. The study concluded that once-daily moxifloxacin was as effective and safe as twice-daily AMX-AC in the treatment of acute sinusitis.

In another study (Johnson et al., 2008), the time to resolution of major symptoms and return to normal activity was evaluated in adults with acute bacterial maxillary sinusitis treated with moxifloxacin 400 mg once daily for 10 days. Clinically, more than 85% of patients showed clinical improvement by day 2, increasing to more than 96% by day 4. The study concluded that moxifloxacin rapidly improves the signs and symptoms of acute bacterial maxillary sinusitis.

Salvatore Puglisi et al., 2011, investigated the incidence of chronic maxillary sinusitis of dental origin and evaluated the microbiology of chronic odontogenic and non-odontogenic maxillary sinusitis. Samples were obtained from 59 patients with chronic maxillary sinusitis (47 non-odontogenic, 12 odontogenic). The study found that 20% of

chronic cases were of dental origin. Regarding microbiology, the predominant aerobic bacteria were Staphylococcus aureus and Streptococcus pneumoniae, while the most frequent anaerobes were Peptostreptococcus species and Prevotella species. Haemophilus influenzae and Moraxella catarrhalis were absent in sinusitis associated with a dental origin. The antibiotics moxifloxacin, metronidazole, and clindamycin were the most active against anaerobic bacteria.

A retrospective study (Zirk et al., 2017) analyzed clinical trials of 121 patients with odontogenic maxillary sinusitis who underwent surgery. Bacterial susceptibility profiles were reviewed, as well as surgical reports of foreign material removed from the maxillary sinus or odontogenic foci along with preoperative cone beam CT (CBCT) scans. A predominance of anaerobic bacteria was observed, with 45 anaerobes versus 19 aerobes. The antibiotics that obtained the best results were MXF (86.2%) and Piperacillin/Tazobactam (93.3%), which presented the highest sensitivity rates for the collected bacteria.

Moxifloxacin in Odontogenic Abscesses:

Sobottka's group (Sobottka et al., 2002) evaluated the antimicrobial susceptibility of 87 pathogens isolated from 37 patients with odontogenic abscesses.The most prevalent bacteria were viridans group streptococci and Prevotella species. Considering all bacterial isolates, 100% were susceptible to AMX-AC, 98% were susceptible to MXF, and 75% to CLI.An in vitro study was conducted to determine the susceptibility of oral anaerobes and strict anaerobes to various antibiotics commonly used in dentistry (Thomas I et al., 2007). Resistance to amoxicillin (AMX) was found in 45.3% of the strict anaerobes, and resistance to CLI in 18.6%. All isolates were susceptible to metronidazole (MTZ), and 98.8% were susceptible to AMX-AC.

Strict and opportunistic anaerobes showed high percentages of resistance to AMX and CM, and high minimum inhibitory concentration (MIC) values for azithromycin (AZM) in the absence of recently administered antibiotics. MXF showed greater activity than telithromycin (TLM), similar to that detected for AMX-CLA and MTZ.Warnke et al., 2008, examined the spectrum of oral pathogens found in odontogenic abscesses and their susceptibility to five antimicrobials. In vitro results were compared with clinical observations. Samples were collected from 94 patients (188 isolates total) with odontogenic abscesses. Susceptibility testing revealed that 99% of aerobes and 96% of anaerobes were sensitive to MXF. In comparison, penicillin showed lower sensitivity rates: 61% for aerobes and 79% for anaerobes.

Nawaz et al., 2009, conducted a study in 21 hospitalized patients with severe odontogenic abscesses to evaluate the effect of MXF compared to AMX-AC. The primary clinical outcome was the time to clinical remission, which averaged 6.6 days for MXF and 6 days for AMX-AC. In this pilot study, MXF showed promising results compared to AMX-AC.Cachovan et al., 2010, compared the efficacy and safety of MXF with CLI for the treatment of patients with gingival inflammatory infiltrates and odontogenic abscesses requiring surgical treatment. Patients received a daily dose of 400 mg of MXF or 300 mg of CLI four times daily for five days. Among patients with abscesses, 15 were treated with MXF and 16 with CLI. Faster favorable clinical responses were observed with MXF in both patients with abscesses and infiltrates, along with a lower incidence of adverse effects, particularly gastrointestinal, compared to CLI.

Another in vitro study (Sobottka et al., 2012) sought to identify common oral pathogens found in odontogenic infections and assess their susceptibility to AMX-AC, CLI, doxycycline (DOX), levofloxacin (LVF), MXF, and penicillin (PEN). A total of 205 isolates were cultured from 71 patients, with viridans group streptococci predominating. Ninety-eight percent of the pathogens were susceptible to MXF, 96% to AMX-AC, 85% to LVF, 67% to PEN, 60% to CLI, and 50% to DOX. The authors concluded that the high *in vitro* activity of MXF aligned well with its clinical effectiveness in treating odontogenic abscesses.

Arambula et al., 2015, compared the use of MXF with CLI and ceftriaxone (CEF) in hospitalized patients with odontogenic abscesses or cellulitis. They evaluated length of stay and hospital discharge, along with antimicrobial susceptibility assessment. Microbiological results showed that MXF and CEF obtained significantly better results than CLI. The strains tested were highly sensitive to MXF (97.5%) and CEF (92.5%) compared to CLI (62%). No statistically significant differences were observed in hospital stay duration among the treatment groups.

Luri Mochalov et al., 2023, analyzed purulent exudates from 13 patients with acute odontogenic intraoral lesions (abscesses) to determine sensitivity to antibacterial agents. Bacteriological studies showed that the Streptococcus

genus predominated in 69% of cases. The isolates showed significant resistance to tetracycline and doxycycline, with the fluoroquinolones moxifloxacin and ciprofloxacin being most effective.

Moxifloxacin in Post-Extraction Bacteremia:
Regarding post-extraction bacteremia, Tomas's group (Tomas et al., 2004) studied the most prevalent pathogens in the bloodstream following tooth extractions and their sensitivity to routinely used antibiotics. Most streptococci isolated from the bloodstream were susceptible in vitro to penicillin, ampicillin, amoxicillin, and moxifloxacin. There was a high percentage of streptococci resistant to erythromycin and clindamycin. All bacterial isolates showed a low minimum inhibitory concentration (MIC) of MXF.

Diz Dios et al., 2006, evaluated the efficacy of oral prophylactic treatment with AMX, CLI, and MXF in preventing bacteremia after tooth extractions in 221 patients. Streptococcus species were the most prevalent bacteria. Regarding antibiotics, AMX and MXF showed high efficacy in reducing the prevalence and duration of post-extraction bacteremia, whereas CLI demonstrated significantly lower efficacy.

Discussion:-

Maxillary Sinusitis Several in vitro studies have demonstrated the efficacy of moxifloxacin (MXF) against the microorganisms responsible for maxillary sinusitis, obtaining promising results that position MXF as an effective alternative in the treatment of this condition. The importance of this finding lies in the fact that MXF, as a broad-spectrum fluoroquinolone, can replace or complement penicillin, especially in cases of resistance or intolerance to this antibiotic.

Regarding microbiology, Zirk et al. (2019) reported a higher prevalence of anaerobic bacteria than aerobic bacteria in sinus infections (45 anaerobes versus 19 aerobes). The antibiotics that showed the greatest activity in this study were MXF, with 86.2% effectiveness, and piperacillin/tazobactam, with 93.3%. Similarly, Salvatore Puglisi et al. (2011) identified the predominant aerobic bacteria as Staphylococcus aureus and Streptococcus pneumoniae, while Peptostreptococcus and Prevotella species were among the most common anaerobes. In this context, MXF, along with metronidazole (MTZ) and clarithromycin (CLI), proved to be the most active antimicrobials against the isolated bacteria, supporting their empirical use in the treatment of maxillary sinusitis.

From a clinical perspective, comparative studies have analyzed the efficacy of MXF versus amoxicillin with clavulanic acid (AMX-AC), a widely used treatment for sinusitis. Rakkar et al. (2001), in a trial with 475 patients, observed similar results in terms of clinical resolution and adverse effects, reporting nausea in 11% of patients treated with MXF versus 5% with AMX-AC, and diarrhea in 3% versus 10%, respectively. Furthermore, Johnson et al. (2008) demonstrated that, although both drugs were effective, MXF achieved clinical improvement more quickly, with over 85% of patients improving by day 2, increasing to over 96% by day 4.

Odontogenic abscesses and cellulitis:-
In the management of odontogenic abscesses and cellulitis, antibiotic treatment is a fundamental component that must be complemented by the elimination of the causative infectious focus.(18) Historically, penicillins have been the first-line antimicrobials in these cases, followed by clindamycin and cephalosporins as second-line alternatives.(19) However, a significant increase in the rate of bacterial resistance has been reported in the current literature, especially against clindamycin (CLI). This represents a significant fact that could compromise both the efficacy of treatment and the clinical outcome of these conditions.

Due to this problem, other alternatives have been explored, including moxifloxacin (MXF), an antibiotic from the fluoroquinoline family that has shown promising results in in vitro studies, even comparable to amoxicillin with clavulanic acid (AMX-AC) and superior to clindamycin. The importance of moxifloxacin in this context lies in its broad spectrum of activity, good tissue penetration, and high susceptibility rates in microorganisms isolated from odontogenic abscesses.

Several studies support this efficacy. Thomas et al. (2007) conducted an in vitro study evaluating the susceptibility of oral anaerobes and strict anaerobes to various antibiotics used in dentistry. They found resistance to amoxicillin (AMX) in 45.3% of strict anaerobes and resistance to CLI in 18.6%. All isolates were susceptible to metronidazole (MTZ), and 98.8% to AMX with clavulanic acid. Furthermore, strict and opportunistic anaerobes showed high

percentages of resistance to AMX and clindamycin, while MXF showed activity similar to that detected for AMX-CLA and MTZ, suggesting its potential as an effective alternative.

In another microbiological study, Sobottka (2002) isolated pathogens from odontogenic abscesses and found that 100% of the microorganisms were sensitive to AMX-AC, 98% to MXF, and 75% to CLI, concluding that MXF was superior to CLI against these pathogens. Warnke et al. (2008) reported similar results, demonstrating that sensitivity to MXF in odontogenic abscess samples exceeded 99% for aerobes and 96% for anaerobes, reinforcing its efficacy in the treatment of these infections.

In comparative clinical studies, the effectiveness of MXF has been assessed against commonly used antibiotics in dentistry. The results are encouraging, as MXF has shown similar efficacy to AMX-AC in the remission of clinical symptoms, thus supporting the in vitro findings. Furthermore, its use has been compared with CLI and cephalosporins, with favorable results. For example, Al Nawas et al. and Limeres et al. compared the use of AMX-AC with MXF, observing that both groups had positive outcomes with no statistically significant differences in outcomes.

Regarding the comparison between MXF and CLI, Cachovan et al. (2010), in a pilot study, demonstrated that MXF produced better clinical outcomes, with less pain and fewer adverse effects, primarily gastrointestinal, compared to clindamycin. Furthermore, the higher degree of treatment adherence in patients treated with MXF can be explained by its dosage, which requires administration every 24 hours, in contrast to AMX-AC, which must be taken every 8 or 12 hours depending on the dosage. This ease and convenience of administration can significantly improve treatment adherence.

Post-extraction bacteremia:-

Tomas et al. demonstrated in an in vitro study that most streptococci isolated from the bloodstream after tooth extractions are highly susceptible to penicillin, ampicillin, amoxicillin, and moxifloxacin. However, a high percentage of streptococci resistant to erythromycin and clindamycin was observed, consistent with other in vitro studies. Clindamycin, which for years has been the alternative option to beta-lactams in patients with hypersensitivity, has seen its efficacy reduced due to the increase in resistant strains (Diz Dios et al).

Moxifloxacin has consistently shown to be effective against oral streptococci isolated, exhibiting high sensitivity and low minimum inhibitory concentrations (MICs), surpassing the effectiveness of clindamycin. Microbiological reports indicate that the main agent isolated in odontogenic infections is streptococcal species, with both amoxicillin and moxifloxacin having the best results.

Proper management of post-extraction bacteremia through rational use of antibiotics is essential to prevent systemic complications and facilitate a rapid and safe recovery. In this context, moxifloxacin appears to be a promising alternative, particularly in patients with hypersensitivity to beta-lactams.

Conclusions:-

The consistent results obtained with MXF in both clinical and microbiological studies, comparable to those obtained with AMX-AC, make it a potential alternative to penicillins for antimicrobial treatment of maxillofacial infections. Its role in odontogenic abscesses is particularly important due to its broad spectrum, good tissue penetration, and high sensitivity rate against causative microorganisms.

Proper management of post-extraction bacteremia through rational use of antibiotics is essential to prevent systemic complications and ensure safe, effective recovery. In this context, moxifloxacin appears to be a promising alternative in in vitro studies, especially in patients with hypersensitivity to beta-lactams.

However, further prospective randomized clinical studies with larger sample sizes are needed to evaluate the clinical efficacy of MXF for the management of odontogenic abscesses and severe maxillofacial infections. This will allow us to create a plausible clinical protocol that considers MXF as an alternative for these infectious conditions and as prophylaxis for post-extraction bacteremia in patients with beta-lactam hypersensitivity.

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