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A Review Of Fluoroquinolone Antibiotics And Their Antagonistic Mechanisms

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Abstract: Now a days fluoroquinolone is mostly preferable for antibiotics. The most commonly detected fluoroquinolone antibiotics in this study were norfloxacin, ciprofloxacin, and lomefloxacin. In this paper we have discussed in details of an overview of fluoroquinolone antibiotics and their antagonistic processes. Fluoroquinolones are broad-spectrum antibiotics with excellent oral bioavailability. They are widely used to treat various infections; however, their prescription is subject to certain restrictions. So, these drugs are safe prescribing of fluoroquinolones requires careful identification of patients with risk factors for toxicity. In the case of an adverse reaction, prompt discontinuation of the drug is advised. Practicing antimicrobial stewardship prefer only when no alternative drugs are available is crucial for minimizing adverse events and combating antibiotic resistance.

Index Terms - antimicrobial stewardship, ciprofloxacin, fluoroquinolones, moxifloxacin, norfloxacin.

I. INTRODUCTION

Fluoroquinolones are broad-spectrum antibiotics with good oral bioavailability. They are indicated for the treatment of urinary tract infections, pneumonia, gastroenteritis, and gonococcal infections. Globally, the use of fluoroquinolones is increasing, which has been linked to rising rates of resistance. However, their use remains relatively low in Australia compared to other countries due to restrictions on government-subsidized prescribing of fluoroquinolones [1]. In Australia, the fluoroquinolones available for systemic use include ciprofloxacin, norfloxacin, and moxifloxacin. Additionally, ofloxacin is available for topical use in treating bacterial keratitis. Ciprofloxacin and norfloxacin demonstrate excellent activity against aerobic Gram-negative organisms, with ciprofloxacin being particularly effective against *Pseudomonas aeruginosa [2]*. Moxifloxacin, on the other hand, offers additional activity against anaerobes and Gram-positive organisms, especially pneumococci, but lacks efficacy against [3]. Fluoroquinolone antibiotics are a potent and effective group of synthetic antibiotics widely used in both human and veterinary medicine. In Lindberg's study [5]-[6] conducted at the Umea sewage treatment plant (STP) in Sweden, fluoroquinolones were quantified in raw sewage water entering the plant, the final effluent, and the digested dewatered sludge [7]. The findings indicated that fluoroquinolones were primarily adsorbed onto sludge. Building on this, the primary objective of the present study was to analyze the presence of fluoroquinolone antibiotics in the influent and effluent of a sewage treatment plant in Shanghai, China, and to examine the behavior of fluoroquinolones across various treatment units [8]. Additionally, the removal efficiencies of fluoroquinolones from the aquatic phase in each unit were evaluated.

In contrast, another study found no significant difference in the risk of aortic aneurysm and dissection between fluoroquinolones and other antibiotics commonly used for severe infections, such as amoxicillin-clavulanate or cephalosporins. However, an increased risk was observed across all infection types, including pneumonia, genitourinary, intra-abdominal, and soft tissue and bone infections [9]. The authors suggested that

the severity of the infection might confound the observed association between fluoroquinolone exposure and aortic disease, particularly since fluoroquinolones are often prescribed for more severe infections and in older patients [10]-[11]. Alternatively, a surveillance bias toward imaging patients with severe infections may have reinforced the observed association between sepsis and aortic aneurysm and dissection [13]. A recent retrospective study assessed the risk of rupture, surgery, and death specifically in patients admitted with aortic aneurysm or dissection, thus minimizing the potential for surveillance bias [14]. The study found a 1.8-fold increased risk of 'aortic death' in patients who had taken fluoroquinolones. However, the comparator group was treated with amoxicillin rather than a broader-spectrum drug, which may have introduced confounding factors related to the range of infections for which the two patient groups were treated [15].

II. MECHANISM OF ACTION AND SPECTRUM OF ACTIVITY

The three systemic fluoroquinolones available for use in Australia are ciprofloxacin, norfloxacin, and moxifloxacin. Additionally, ofloxacin is available for topical use in treating bacterial keratitis. Ciprofloxacin and norfloxacin exhibit excellent activity against aerobic Gram-negative organisms, with ciprofloxacin being particularly effective against Pseudomonas aeruginosa. Moxifloxacin offers additional activity against anaerobes and Gram-positive organisms, particularly pneumococci, but lacks efficacy against P. aeruginosa. Fluoroquinolones exert their antimicrobial effects by inhibiting bacterial topoisomerases II and IV. Antibiotic resistance develops through mutations in these target enzymes.

A. Antagonistic effects

The adverse effects of fluoroquinolones can be minimized by restricting their use to infections that cannot be effectively managed with other antibiotics.

1. **Gastrointestinal Issues:**
   - Nausea and Vomiting: These are common side effects and usually occur at the beginning of treatment.
   - Diarrhea: Can range from mild to severe, and may sometimes be associated with Clostridium difficile infection, leading to colitis.
   - Abdominal Pain: May occur as part of the general gastrointestinal disturbances.
2. **Central Nervous System (CNS) Effects:**
   - Headaches: One of the most common CNS-related side effects.
   - Dizziness and Lightheadedness: Can impair the ability to perform tasks that require concentration.
   - Seizures: Rare but serious, particularly in patients with a history of seizure disorders or those taking medications that lower the seizure threshold.
   - Psychiatric Disturbances: Anxiety, confusion, hallucinations, and vivid dreams may occur, especially in elderly patients.

B. Tendinopathy

Fluoroquinolones are associated with a two- to fourfold increased risk of acute tendinopathy (defined as pain or reduced function without rupture) and tendon rupture. The incidence of this adverse effect may be as high as 2% in patients aged 65 years and older, compared to a background tendon rupture rate of approximately 0.9% in the general population. The onset of tendinopathy is most common within the first month after drug exposure. The Achilles tendon is the most frequently affected, with severe and sudden onset pain being a characteristic clinical presentation. While optimal management of fluoroquinolone-associated tendon. Risk factors for fluoroquinolone-associated tendinopathy are not fully defined. Most studies report a pooled incidence from a range of fluoroquinolones, including those not currently available in Australia. Older age and concomitant corticosteroid use are identified as key risk factors. Corticosteroids are associated with up to a 14-fold increased risk of tendon rupture. The association between tendinopathy and conditions like diabetes or renal failure remains less clear.

C. Aortic aneurysm and dissection

The evidence linking fluoroquinolone use to aortic aneurysm and dissection is conflicting. A meta-analysis based on four observational studies suggested a two- to threefold increased risk, with the number of fluoroquinolone courses required to harm one patient being 1,301. However, observational studies are subject to residual confounding and surveillance bias. To minimize differences in imaging rates between fluoroquinolone-exposed and non-exposed patients, a case-control study of over one million U.S. patients compared the risk of aortic aneurysm and dissection for specific antibiotic indications. When compared to

azithromycin for pneumonia, the risk of aortic aneurysm and dissection was 2.5 times greater, but there was no significant difference when compared to trimethoprim-sulfamethoxazole for urinary tract infections. The absolute rate of aortic aneurysm and dissection was very low, at less than 0.1%. The authors concluded that, for some patients, the benefits of fluoroquinolones may outweigh the rare potential risk of aortic aneurysm and dissection.

D. Peripheral neuropathy

A limited number of observational studies suggest that fluoroquinolones may increase the risk of peripheral neuropathy, manifesting as numbness or pain, by up to 1.5-fold. However, the occurrence of neuropathy in fluoroquinolone-exposed patients remains rare, with an absolute risk increase of just 0.02% per year in a large database study among all patients, and 0.04% per year in those aged 60 years or older. Risk factors for fluoroquinolone-associated neuropathy include increased body mass index, as well as other known causes of neuropathy such as amyloidosis, alcohol abuse, shingles, and Sjögren's syndrome. Notably, the association between neuropathy and fluoroquinolone use persisted even in a subgroup analysis that excluded patients with these underlying conditions.

E. Retinal detachment

Evidence regarding an association between fluoroquinolone use and retinal detachment is conflicting. While a Canadian cohort study reported up to a 4.5-fold increased risk of retinal detachment with current fluoroquinolone use, most subsequent studies, including two recent meta-analyses, have found no increased risk. One possible explanation for the findings of the Canadian study is the inclusion of an older cohort (mean age 61 years), many of whom had undergone cataract surgery, which is a known risk factor for retinal detachment.

F. Gastrointestinal effects

Nausea, vomiting, diarrhea, and taste disturbances have been reported in up to 20% of patients treated with fluoroquinolones. Like all antibiotics, fluoroquinolones carry a risk of Clostridium difficile infection. Fluoroquinolone-resistant C. difficile infections have emerged in response to increased fluoroquinolone prescribing. Hepatotoxicity, with elevation in transaminases, is a known class effect of fluoroquinolones. Severe hepatotoxicity resulting in acute liver failure is extremely rare, with the exception of trovafloxacin, which was withdrawn from the market

III. Conclusion

In conclusion part finally I studied and observed that in the case of an adverse reaction, prompt discontinuation of the drug is advised. In Australia, fluoroquinolone prescribing is restricted to infections resistant to all other recommended drugs. While serious adverse effects are rare, they can be significant, including tendinopathy, aeropathy, neuropathy, arrhythmia, hypoglycemia, and hyperglycemia. Prescribers should be aware of risk factors for fluoroquinolone toxicity, such as patients over 60 years old and those with comorbidities or taking interacting medications. Patients should be vigilant for symptoms like tendon or abdominal pain and report them promptly. Proper patient education and timely drug discontinuation in the event of an adverse reaction are essential considerations when prescribing fluoroquinolones.

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