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ADVERSE DRUG REACTIONS OF OFLOXACIN: A REVIEW FOCUSED ON THE BURDEN AND CLINICAL IMPACT

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Abstract

Adverse drug reactions (ADRs) are a significant cause of illness and death, particularly in countries with limited healthcare resources. Among all drug categories, antimicrobials contribute the highest percentage (28%) of ADRs compared to other medications. Ofloxacin, an antimicrobial agent used to treat various bacterial infections, has an ADR incidence rate of 4.27%. Although this figure may seem small, the combination of ofloxacin with ornidazole for gastrointestinal infections in India contributes to a substantial burden of ADRs. However, research specifically focused on the adverse reactions of ofloxacin has been lacking in recent years. To address this research gap, the objective of this study was to systematically review the adverse drug reactions associated with ofloxacin in both human and animal studies. The authors conducted a comprehensive search of the PubMed and Cochrane Library databases, covering articles related to ofloxacin's adverse drug reactions published. A total of 42 relevant articles were identified and analyzed. The study findings suggest an increasing side effect profile for ofloxacin, indicating the need for cautious and prudent use of this antimicrobial agent. The review highlights the importance of understanding and monitoring the adverse effects associated with ofloxacin to ensure patient safety and promote appropriate prescribing practices. By bridging the research gap regarding the adverse drug reactions of ofloxacin, this article contributes to addressing the need for more comprehensive knowledge in this area. The study's conclusions emphasize the importance of judiciously using ofloxacin due to its increasing side effect profile. This information can guide healthcare providers in making informed decisions regarding the use of ofloxacin, ultimately improving patient care and medication safety.

Keywords: Adverse drug reaction, side effect, antibiotic, ofloxacin.

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INTRODUCTION:

Ofloxacin is a widely used fluoroquinolone antibiotic with broad-spectrum activity against various bacterial infections.[1] While it is generally considered effective and well-tolerated, like any medication, it is associated with a range of potential adverse drug reactions (ADRs) that need to be carefully monitored. This review aims to summarize the known adverse reactions and their clinical significance associated with ofloxacin use.[1]

The significance of adverse drug reactions (ADRs) as a major cause of morbidity and mortality, particularly in regions with limited healthcare resources.[3] It emphasizes that elderly patients, who often receive multiple medications for long-term illnesses, are at a higher risk of hospitalization due to ADRs compared to younger patients. The elderly patient is affected 4 times greater than younger population. The impact of ADRs is particularly pronounced in countries with limited healthcare resources, where the burden of ADR-related hospitalizations is substantial. Elderly patients, who often receive multiple medications for chronic illnesses, are at a higher risk of experiencing ADRs due to age-related changes in drug metabolism and increased medication use.[1-3] The average incidence of ADRs from all drugs in India is stated to be 9.8%, with skin, central nervous system, and gastrointestinal tract being the most commonly affected organ systems. Furthermore, the antimicrobials contribute to the highest proportion (28%) of ADRs, and ofloxacin, a quinolone antimicrobial, is frequently prescribed for various bacterial infections.[5] The molecular properties and approval status of ofloxacin by the FDA are briefly described. Common side effects of ofloxacin, including insomnia, nausea, vomiting, diarrhoea, and headache, are mentioned, along with the incidence rate of ADRs to ofloxacin, which is stated to be 4.27%. The discontinuation rate of ofloxacin therapy due to side effects is also noted as 4% and Approximately 11% of patients in clinical trials encountered adverse effects while using ofloxacin.[4-6] The burden of ADRs associated with the use of ofloxacin in India, particularly for gastrointestinal infections when used in combination with ornidazole. It points out the lack of recent research focusing on the adverse drug reactions of ofloxacin and states that the article aims to address this research gap. Overall, the introduction sets the context by emphasizing the importance of ADRs, particularly in the Indian healthcare setting, and introduces ofloxacin as a commonly used antimicrobial with potential adverse effects that need to be explored in more detail.[1-2]

REVIEW OF LITERATURE:

Methodology:

Identification of Databases: Relevant databases were selected to retrieve pertinent literature. These included PubMed/MEDLINE, Embase, Scopus, Cochrane Library and Google Scholar.

Keywords Selection: The following keywords were chosen to capture relevant studies: "ofloxacin," "adverse drug reactions," "side effects," "adverse effects," "toxicity," "safety," and "clinical impact."

Search Syntax: The keywords were combined using Boolean operators (AND, OR) to create search strings. Examples of search strings used include: ("ofloxacin" OR "ofloxacin adverse effects" OR "ofloxacin adverse drug reactions") AND ("clinical impact" OR "safety" OR "toxicity").

Inclusion and Exclusion Criteria: Studies were included if they reported on the ADRs specifically associated with ofloxacin use. Both clinical trials and observational studies were considered. Studies involving paediatric and adult populations were included. Publications were limited to those available in English.

Screening and Selection: The initial search yielded a large number of articles. Title and abstract screening were conducted to exclude irrelevant studies. Full-text articles of potentially relevant studies were then assessed for eligibility based on the inclusion criteria.

Data Extraction and Synthesis: Relevant data from included studies were extracted, including study characteristics The findings were synthesized to provide an overview of the burden and clinical impact of ADRs associated with ofloxacin use.

Analysis and Interpretation: The extracted data and findings were analysed and interpreted to provide a comprehensive review of the ADRs of ofloxacin, emphasizing the burden and clinical significance of these reactions.

Inclusion criteria:

The authors of the review included a broad range of study types, such as randomized trials, comparative studies, controlled clinical trials, observational studies, and case reports. They also considered studies with or without free full text availability and did not impose any language restrictions. This inclusive approach aimed to gather a comprehensive body of evidence for the review, ensuring a thorough assessment of the adverse drug reactions associated with ofloxacin use.

Exclusion criteria:

The authors specifically excluded studies that did not report adverse drug reactions (ADRs) related to ofloxacin. This encompassed ADRs associated with drugs similar to ofloxacin, such as levofloxacin. Additionally, studies that solely focused on assessing the antibacterial activity of ofloxacin were also excluded. By excluding these types of studies, the authors ensured that their review focused specifically on the ADRs attributed to ofloxacin use, providing a more targeted and relevant analysis.

DISCUSSION:

The authors categorized the adverse drug reactions (ADRs) associated with ofloxacin into various systems or organ-specific groups. These included fatal reactions, gastrointestinal effects, nervous system manifestations, cutaneous reactions, musculoskeletal disorders, hepatobiliary complications, cardiovascular events, renal abnormalities, haematological abnormalities, ocular reactions, and other miscellaneous ADRs. This systematic classification allowed for a comprehensive examination of the different types of ADRs that can occur with ofloxacin use.

Gastrointestinal ADR:

The most frequently reported adverse drug reactions (ADRs) associated with ofloxacin were gastrointestinal disturbances, including symptoms such as nausea, vomiting, and gastric pain.[7] Following gastrointestinal effects, central nervous system manifestations were also commonly observed. Of particular concern, there have been cases of pseudomembranous colitis associated with Clostridium difficile infection that were attributed to the use of ofloxacin. This highlights the importance of monitoring and managing these ADRs to ensure patient safety during ofloxacin treatment.[7-9]

Cutaneous ADR:

A 24-year-old male patient experienced angioedema after receiving a combination of ofloxacin and ornidazole for loose motions.[11] Cutaneous vasculitis was observed in a patient with a diabetic foot infection who was treated with ofloxacin for the condition. In another case, a patient with a urinary tract infection treated with ofloxacin developed intense erythema's followed by sub-corneal pustulation, fever, and neutrophil leucocytosis, leading to a diagnosis of toxic pustuloderma.[13] Fixed drug eruption, which occurred independently as well as with ciprofloxacin and amoxicillin, resulted in toxic epidermal necrosis. Erythema multiforme-like rash

was attributed to the use of ofloxacin.[10,12] In a rare case, a variant of type 2 Lepra reaction known as erythema nodosum leprosum occurred in a patient receiving multi-drug therapy that included ofloxacin. Additionally, type 1 Lepra reaction occurred in a single lesion paucibacillary leprosy patient treated with a single dose of rifampicin, ofloxacin, and minocycline.[14] Sweet's syndrome (acute febrile neutrophilic dermatosis) was triggered in a patient with Crohn's disease following the administration of ofloxacin.[15] These cases highlight various uncommon and rare adverse reactions associated with ofloxacin use, emphasizing the importance of monitoring and recognizing these potential side effects to ensure patient safety.[16-17]

Nervous system ADR:

Headache and insomnia were the predominant central nervous system adverse drug reactions (ADRs) associated with ofloxacin use, while hallucinations, nightmares, confusion, and depression were reported less frequently. However, the consistency of these findings varied, as post-marketing surveillance involving a population of 1.5 million patients indicated that nervous system ADRs ranked first in frequency, followed by hypersensitivity reactions and gastrointestinal disturbances.[2] Sleep disturbances were commonly observed in children receiving ofloxacin treatment. Rare ADRs, such as hallucination, psychosis, and shock, have been reported in post-marketing experiences in Germany.[18-20]

Ofloxacin use has been associated with generalized tonic-clonic seizures, particularly in patients with compromised renal function due to drug accumulation.[22] Status epilepticus, a prolonged epileptic seizure, has also been described in relation to ofloxacin use. Delirium has been reported as an ADR as well. In one case, idiopathic intracranial hypertension developed in a 25-year-old man who was treated with 400mg/day of ofloxacin for 16 months.[25] Ofloxacin has also been implicated in triggering a Tourette-like syndrome in an elderly patient admitted to a community hospital for the management of pneumonia.[21] These diverse central nervous system ADRs highlight the importance of monitoring and recognizing potential neurological effects associated with ofloxacin use. Healthcare professionals should be aware of these rare but serious reactions to ensure timely intervention and patient safety.[23]

Cardiovascular ADR:

While the incidence of torsade's de pointes, a specific type of cardiac arrhythmia, is relatively low for ofloxacin compared to other fluoroquinolones, caution is still advised when using ofloxacin in patients with a prolonged QT interval.[27] The cardiovascular side effects of ofloxacin have been associated with syncope (temporary loss of consciousness) and tachycardia (rapid heartbeat), which can be attributed to the development of dysrhythmia (abnormal heart rhythm). Therefore, healthcare professionals should be vigilant when prescribing ofloxacin to patients with known QT interval prolongation to minimize the risk of cardiac adverse effects.[28]

Musculoskeletal ADR:

Elderly patients who were concurrently administered corticosteroids and ofloxacin experienced complete rupture of the Achilles tendon. A 53-year-old woman exposed to ofloxacin exhibited symptoms of myalgia, arthralgia, and multiple tendonopathy.[29] A systematic review of observational cohort studies shed light on the relationship between ofloxacin use and the occurrence of tenosynovitis. Additionally, acute rhabdomyolysis was associated with ofloxacin use, as evidenced by a significant increase in serum myoglobin levels and the presence of myoglobin in the urine.[30] To summarize, the concurrent use of corticosteroids and ofloxacin in elderly patients resulted in Achilles tendon rupture. Myalgia, arthralgia, and multiple tendinopathy were

observed in a middle-aged woman treated with ofloxacin. A systematic review of observational studies highlighted the association between ofloxacin use and tenosynovitis. Furthermore, acute rhabdomyolysis was confirmed by elevated serum myoglobin levels and the presence of myoglobin in the urine, indicating its association with ofloxacin.[31-33]

Renal ADR:

In 1995, a case of acute renal failure caused by ofloxacin was reported. Ofloxacin was found to induce nephrogenic diabetes insipidus in a young patient who had developed bilateral lobar pneumonia as a secondary infection following influenza.[34] This adverse reaction resulted in impaired kidney function and the development of diabetes insipidus, a condition characterized by excessive thirst and excessive urine production.[35]

Hepatobiliary ADR:

An instance of asymptomatic hepatitis was observed in a case of pulmonary tuberculosis that was resistant to standard treatment.[37] The patient was prescribed an alternative therapy consisting of Pyrazinamide and ofloxacin. In another case, a patient with Wegener's Granulomatosis who was treated with ofloxacin for a productive cough experienced a moderate increase in liver enzymes. A 70-year-old male patient with complaints of prostatic adenoma and UTI, who received ofloxacin antibiotic, it developed fatal sub-fulminant hepatic failure. A case of acute severe hepatitis associated with ofloxacin use was reported in 1991. Furthermore, in a patient with cholestatic hepatitis, sensitized lymphocytes to both trimethoprim/sulfamethoxazole and ofloxacin were demonstrated, indicating a strong association between ofloxacin and cholestatic hepatitis.[34-36]

Fatal ADR:

A case was reported in which a boy experienced anaphylactic shock following the oral administration of ofloxacin.[36]

CONCLUSION:

In conclusion, the review highlighted the various adverse drug reactions (ADRs) associated with the use of ofloxacin. These ADRs were categorized into different systems or organ-specific groups, including gastrointestinal, cutaneous, nervous system, cardiovascular, musculoskeletal, renal, hepatobiliary, and fatal reactions. Gastrointestinal disturbances, such as nausea, vomiting, and gastric pain, were commonly reported, followed by central nervous system manifestations. Cutaneous reactions ranged from angioedema and vasculitis to toxic Pustular derma and fixed drug eruptions. Nervous system ADRs primarily included headache and insomnia, although more serious reactions such as hallucinations and seizures were also observed. Cardiovascular effects, particularly dysrhythmia, were cautioned in patients with a prolonged QT interval. Musculoskeletal ADRs involved tendon ruptures and myalgia/arthralgia. Renal ADRs encompassed acute renal failure and nephrogenic diabetes insipidus. Hepatobiliary ADRs included hepatitis and hepatic failure. Lastly, a case of anaphylactic shock was reported. Overall, recognizing and monitoring these ADRs is crucial to ensure patient safety during ofloxacin treatment and to increase the appropriate and optimal use.

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