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A Case Report

Death due to Diclofenac Sodium: A Case Report

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Abstract :

Introduction: Diclofenac sodium, a commonly used non-steroidal anti-inflammatory drug (NSAID), is generally regarded as safe for postoperative analgesia. However, rare but severe hypersensitivity reactions such as anaphylaxis have been reported. This case report describes a fatal adverse event following intravenous administration of diclofenac.

Case report: A 43-year-old female patient who underwent a total laparoscopic hysterectomy for uterine fibroids was prescribed injection diclofenac by intravenous route. Shortly after initiating a 75 mg diclofenac infusion, the patient developed a burning sensation, erythema, shortness of breath, and generalised pruritus, followed by unconsciousness and cardiovascular collapse. Despite immediate discontinuation of the infusion and administration of emergency medications, including chlorpheniramine, hydrocortisone, adrenaline, and inotropes, the patient did not recover and succumbed to cardiac arrest approximately 24 hours later. The reaction was categorised as a serious and life-threatening adverse drug reaction (ADR) and reported to the pharmacovigilance system. Causality assessment using the WHO-UMC scale suggested a "possible" link with diclofenac, and the event was classified as Level 7 (lethal) according to Hartwig's severity assessment.

Conclusion: This case highlights the potential for severe anaphylaxis following intravenous NSAID use, emphasising the need for heightened clinical vigilance, thorough drug history evaluation, and emergency preparedness during perioperative analgesic administration.

Keywords: adverse event; diclofenac sodium; hypersensitivity; NSAIDs; pharmacovigilance; WHO-UMC scale.

Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for their antipyretic, anti-inflammatory, and analgesic properties.[1] Diclofenac sodium is a commonly used NSAID for acute and chronic pain management as well as postoperative analgesia.[1,2,3] Diclofenac works by inhibiting cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) enzymes.[4] Diclofenac is a non-selective NSAID with relative preferential inhibition of COX-2 compared with COX-1.[1]

Diclofenac is used for long-term symptomatic treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, pain, primary dysmenorrhea, and acute migraine.[5-7] It is available in multiple oral formulations, topical gels, ophthalmic solutions, and transdermal patches.[2,8,9]

Possible adverse reactions of diclofenac comprisedyspepsia, diarrhoea, constipation, nausea, and vomiting, as well as stomach bleeding and ulcers, rash, urticaria, photosensitivity

reactions, acute renal failure, analgesic nephropathy (with prolonged use), and bone marrow and liver damage.[3,10]

Anaphylaxis after oral, intramuscular, and rectal administration of diclofenac has been reported previously,but with IV diclofenac, very few cases have been reported.[5,11-13]This case report describes a life-threatening anaphylactic shock caused by intravenous infusion of diclofenac sodium injection.

Case Description

A 43-year-old female patient was admitted with complaints of excessive per-vaginal bleeding for the past four months. On evaluation, she was diagnosed with multiple uterine fibroids and was planned for surgical management. The patient subsequently underwent total laparoscopic hysterectomy on 13 September 2024, and the procedure was uneventful.

Following surgery, intravenous diclofenac sodium (75 mg diluted in 100 mL normal saline) was administered as an infusion for postoperative analgesia.

Within approximately 2 minutes of initiating the diclofenac infusion, the patient developed a sudden-onset burning sensation and generalised erythema, accompanied by shortness of breath and generalised pruritus.

Recognising a possible hypersensitivity reaction, the diclofenac infusion was immediately discontinued.

Emergency medications were administered promptly, including injection chlorpheniramine (Avil) 2 mL intravenously and injection hydrocortisone 100 mg intravenously. However, the patient rapidly deteriorated and lost consciousness shortly thereafter.

The patient initially developed symptoms suggestive of anaphylaxis, including erythema, pruritus, and respiratory distress. Rapid progression to cardiovascular collapse necessitated cardiopulmonary resuscitation (CPR). On examination, the pulse was not palpable and blood pressure and oxygen saturation were not recordable.

Immediate bag-and-mask ventilation was initiated, and an urgent call to the anaesthetist was made. The patient was subsequently intubated, and CPR was started. As the patient was pulseless at that stage, adrenaline 1 mg was administered intravenously and repeated after four minutes according to Advanced Cardiac Life Support (ACLS) guidelines.

Inotropic support with dopamine and noradrenaline was initiated. Sodium bicarbonate was also administered to correct metabolic acidosis.

Following these interventions, a central pulse was regained and recorded at 160 beats per minute, although the patient's hemodynamic response remained poor. She was managed with continued ventilatory and inotropic support.

Despite aggressive resuscitative measures and supportive management, the patient's clinical condition continued to deteriorate. She subsequently developed cardiac arrest on 14 September 2024. Cardiopulmonary resuscitation was attempted but remained unsuccessful, and the patient was declared dead at 12:30 PM on 14 September 2024, approximately 24 hours after the initial reaction.

The cause of death was recorded as cardiorespiratory arrest secondary to severe anaphylactic shock due to NSAIDs (diclofenac) in a postoperative case of total laparoscopic hysterectomy.

The event was classified as a serious and life-threatening adverse drug reaction. According to the WHO-UMC causality assessment scale, the reaction was categorized as possible due to the temporal association between diclofenac administration and onset of symptoms, absence of alternative explanations, and improvement after withdrawal of the suspected drug. The reaction was categorised as Level 7 (lethal) according to Hartwig's severity assessment scale. The adverse drug reaction was subsequently reported to the National Coordinating Centre through the VIGIFLOW pharmacovigilance reporting system.

Discussion

Diclofenac sodium is a widely used non-steroidal anti-inflammatory drug (NSAID) with analgesic, antipyretic, and anti-inflammatory properties. Its pharmacological action is primarily mediated by inhibition of cyclooxygenase (COX) enzymes, particularly COX-1 and COX-2,

thereby decreasing the synthesis of prostaglandins involved in pain and inflammatory pathways.[1] Although diclofenac is generally considered safe and effective for postoperative analgesia, it is also associated with a range of adverse effects, including gastrointestinal toxicity, renal impairment, and hypersensitivity reactions.[3,10,13]

Hypersensitivity reactions to NSAIDs are relatively uncommon but may occasionally present as severe or life-threatening events. These reactions may occur through immunological mechanisms (IgE-mediated hypersensitivity) or through non-immunological mechanisms related to cyclooxygenase inhibition, leading to increased leukotriene production and activation of mast cells and basophils.[13] This process can lead to manifestations such as urticaria, angioedema, bronchospasm, orsystemic anaphylaxis. Importantly, these reactions may occur even in individuals without prior exposure to the drug.[14,15]

In the present case, the patient developed burning sensation, erythema, generalised pruritus, and respiratory distress within two minutes of initiating intravenous diclofenac infusion, which rapidly progressed to cardiovascular collapse. The rapid onset of symptoms strongly suggests an acute hypersensitivity reaction, possibly mediated by mast cell degranulation. Intravenous administration of drugs is known to produce more rapid and severe systemic reactions, as the drug directly enters the circulation and immediately interacts with immune effector cells**.**

Similar cases of diclofenac-induced hypersensitivity reactions have been reported in the literature. Gulrez et al. described a case of severe anaphylactic reaction following intravenous diclofenac administration that required emergency management.[6] Likewise, Singh et al. reported an anaphylactic reaction to intravenous diclofenac in a postoperative patient, emphasising that such reactions can occur even in patients with no previous history of drug allergy.[7] Another report by Colak et al. documented anaphylaxis following intra-muscular diclofenac administration, highlighting that parenteral routes of administration may increase the risk of severe systemic reactions.[14] Additionally, Sahoo et al. reported a case of anaphylactic shock following intramuscular diclofenac, further demonstrating the potentially fatal nature of this adverse drug reaction.[11]

In the present case, the patient initially developed symptoms suggestive of anaphylaxis, including erythema, pruritus, and respiratory distress, which rapidly progressed to cardiovascular collapse. At the time of clinical assessment, the patient was pulseless, necessitating immediate cardiopulmonary resuscitation. Therefore, adrenaline 1 mg was administered intravenously according to Advanced Cardiac Life Support (ACLS) guidelines, which is the recommended dose for cardiac arrest. Despite prompt discontinuation of diclofenac and administration of emergency medications including antihistamines, corticosteroids, and inotropic support, the patient's condition deteriorated and ultimately resulted in a fatal outcome.

The causality of the adverse drug reaction was assessed using the WHO-UMC causality assessment scale, which categorised the association between diclofenac administration and the adverse event as “possible.” This classification was based on the clear temporal relationship between drug administration and onset of symptoms, the known potential of NSAIDs to cause hypersensitivity reactions, and the absence of other identifiable causes. Furthermore, the reaction was classified as Level 7 (lethal) according to Hartwig's severity assessment scale, indicating the most severe form of adverse drug reaction.

This case highlights the importance of careful monitoring during administration of parenteral NSAIDs, particularly in postoperative settings where multiplemedications are administered within a short time interval. Although diclofenac is widely regarded as safe and is commonly used for postoperative analgesia, clinicians should remain vigilant regarding the possibility of rare but severe hypersensitivity reactions, even in patients without a known history of drug allergy. Early recognition of anaphylaxis symptoms and immediate initiation of appropriate resuscitative measures are essential for improving patient outcomes.

Furthermore, this case underscores the crucial role of pharmacovigilance systems in detecting and reporting rare adverse drug reactions. Documentation and reporting of such cases to national pharmacovigilance programs contribute to a better understanding of drug safety profiles and help clinicians remain aware of uncommon but serious adverse events associated with commonly used medications.

Conclusion

This case illustrates a rare but catastrophic adverse reaction to intravenous diclofenac resulting in fatal anaphylactic shock. It underscores the need for heightened awareness of potential NSAID hypersensitivity, even in patients without a known history of drug allergy. Medical professionals must exercise caution when administering NSAIDs, particularly in intravenous form, and ensure prompt recognition and management of anaphylaxis. This case advocates for considering safer alternatives or conducting allergy risk assessment when feasible, especially in a perioperative setting.

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