

CASE REPORT - OLGU SUNUMU

## FATAL ANAPHYLACTIC RESPONSE TO INTRAMUSCULAR DICLOFENAC FOR POSTOPERATIVE ANALGESIA

### POSTOPERATİF ANALJEZİ AMACIYLA UYGULANAN INTRAMUSKULER DİKLOFENAK'A BAĞLI FATAL ANAFLATİK REAKSİYON

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#### SUMMARY

*In evidence-based clinical practice guidelines, non-steroidal anti-inflammatory drugs (NSAIDs), unless contraindicated, are recommended for perioperative acute pain control for all patients. They are commonly used for postoperative analgesia alone or in combination with opioids or local anesthetics. As part of a multimodal approach, NSAIDs can reduce pain scores and reduce opioid-related side effects (1); however, they may have serious adverse effects such as anaphylaxis (2). In this manuscript, we report an anaphylaxis case that developed cerebellar ischemia and death after im diclophenac injection for postoperative analgesia.*

**KEY WORDS:** Diclophenac; Anaphylactic Reaction; Postoperative Pain.

#### ÖZET

*Kanuta dayalı klinik uygulamalara ilişkin kılavuzlarda, nonsteroidal antiinflamatuar ilaçlar (NSAİİ), perioperatif ağrı kontrolü için, kontrendike olmadıkça tüm hastalara önerilmektedir. Bu ilaçlar yaygın olarak postoperatif analjezi için yalnız veya opioidlerle veya lokal anestetiklerle kombine olarak kullanılmaktadır. Multimodal yaklaşımın bir parçası olarak, NSAİİ' lar ağrı skorlarını ve opioide bağlı yan etkileri azaltabilir (1); bununla beraber, anaflaksi gibi şiddetli yan etkiler meydana getirebilirler (2). Biz bu makalede postoperatif analjezi için intramuskuler diklofenak enjeksiyonunu takiben serebellar iskemi gelişen ölümcül bir anaflaksi vakasını sunuyoruz.*

**ANAHTAR KELİMELER:** Diklofenak; Anaflaktik Reaksiyon; Postoperatif ağrı.

#### INTRODUCTION

Since non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for postoperative analgesia and the under-reporting problem for adverse drug reactions - in fact, diclophenac associated anaphylaxis is commonly reported in the Netherlands (2) -, we believe that there is a need to review non-steroidal anti-inflammatory drugs (NSAIDs) for postoperative analgesia with regard to their side effects and adverse effects as well as their analgesic efficacy. However, prospective studies are not possible for anaphylaxis because of its unpredictable and dose independent nature and it cannot be modeled.

#### CASE

We report a fatal anaphylaxis case to intramuscular diclophenac in a 45-year-old female patient was given 75 mg diclophenac intramuscularly at the postoperative 8th hour for postoperative analgesia. The patient died

and written consent was obtained from the institutional review board. There was neither atopy nor allergic reactions to any drugs or foods in her medical history. After 20 minutes of diclophenac injection, she complained of itching and respiratory distress. After cardiopulmonary arrest larynx edema was observed during intubation. After cardiac response to CPR, the patient was transferred to the anesthesiology intensive care unit. The patient was comatose, with no spontaneous breathing and with a widespread skin rash observed on the surface of her body. The patient underwent controlled mechanical ventilation. Computerized tomography scans of the brain showed brainstem edema and suggested hypoxic brain injury.

The patient was explored surgically. There was no bleeding or hematoma in the surgical site. Fourteen days after the exposure, the patient died from sepsis and related complications.

## DISCUSSION

NSAIDs, as a sole agent, generally provide effective analgesia for mild to moderate pain. NSAIDs also considered a useful adjunct to opioids for the treatment of moderate to severe pain. NSAIDs are administered orally or parenterally and are particularly useful as components of a multimodal analgesic regimen by producing analgesia through different mechanisms from that of opioids or local anesthetics perioperatively. Diclofenac is one of the most commonly used NSAIDs for postoperative analgesia alone or as part of a multimodal approach to minimize side effects of opioids and for ambulatory surgery (4-5).

In two studies that assessed reporting system data in the Netherlands, Heidjen et al. demonstrated that disproportionately more anaphylactic reactions were reported for diclofenac compared with other NSAIDs in both males and females, suggesting an increased risk of these reactions during the use of diclofenac. A lack of any difference between the two sexes was also demonstrated with regard to diclofenac anaphylaxis. It can be concluded from this study that the use of odds ratios estimated from spontaneous reporting systems was useful only in evaluating drug-drug interactions as the ratios were not affected by under-reporting only in this group (3). Klauw et al classified anaphylaxis cases from hospital records in a drug-associated anaphylaxis study that assessed 20 years of reporting in the Netherlands. Patients were classified as "anaphylaxis probable", "anaphylaxis possible", "anaphylaxis unlikely" or "admission unclassifiable" according to the symptoms and the time interval between exposure and reaction (6). In this study the drugs that caused anaphylaxis more frequently were glafenine, NSAIDs, and certain antibiotics.

The incidence of anaphylaxis is not well documented. However, Kaufman et al in their international study calculated incidence of anaphylaxis among those exposed various drugs, with denominators estimated from exposure rates in the controls and number of hospitalizations. Risk of anaphylaxis following exposure to various drugs during hospitalization, using hospital records, demonstrated that analgesics (including diclofenac) involve relatively a low risk of anaphylaxis (7). In the other hand, the incidence of anaphylaxis during anesthesia is reported as from 1 in 10,000 to 1 in 20,000. Although neuromuscular blocking agents are most frequently incriminated there is a lack of reports of perioperative analgesics (8).

In conclusion, in this case, symptoms characteristic of anaphylaxis were documented through skin, pulmonary and cardiovascular systems. The reaction observed after

20 minutes of exposure indicated a strong causal relationship between diclofenac exposure and anaphylaxis (6). Studies using statistical data from reporting systems in the Netherlands showed that these recording procedures are affected by under-reporting, leading to underestimation of the true prevalence of anaphylactic drug reactions (2,3,6). Therefore, we believe that every case of anaphylaxis should be reported, as the main source for anaphylaxis are the case reports because prospective studies on this subject are not possible, and under-reporting might favour the clinical use of drugs with adverse reactions.

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