

ISOLATED PERIORBITAL EDEMA ASSOCIATED WITH NAPROXEN: A CASE REPORT

SULE SAHIN ONAT,* ZUHAL OZISLER, OZLEM TASOGLU

Ankara Physical Medicine and Rehabilitation Training and Research Hospital, Departments of Physical Medicine and Rehabilitation, Ankara, Turkey

*Author for Correspondance: sahinulester@gmail.com

This paper is available online at www.jprhc.in**ABSTRACT**

Hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs), resulting in urticaria and angioedema, is being observed with increasing frequency partly due to the large size of the exposed (at risk) population. Prevalence rates range from 0.1–0.3%. Facial angioedema constitutes the most common form of clinical presentation, and one-third of the patients show a mixed clinical pattern of cutaneous (urticaria and/or angioedema) and respiratory symptoms which include upper respiratory tract edema, rhinorrhea, cough, breathlessness and tearing. But to the best of our knowledge there is no isolated periorbital edema reported to date due to naproxen in the literature. In this report, a 62-year-old woman who developed reversible bilateral periorbital edema after naproxen ingestion was presented. The periorbital edema due to NSAIDs was discussed.

KEYWORDS: Naproxen, periorbital edema**INTRODUCT ON**

Periorbital edema is defined as an acute vascular reaction involving the dermis and subcutaneous tissue in the periorbital region¹. This localized edema is caused by increased dilatation and permeability of the capillaries leading to extravasation of serous fluid. It can be secondary to a wide variety of causes such as infection, inflammation and drugs. Periorbital edema as a part of diffuse facial edema has been reported in patients taking aspirin²⁻⁴, ibuprofen⁵, and naproxen⁶ in the literature. Here we want to describe a patient who developed reversible isolated periorbital edema after naproxen use.

CASE REPORT

A 62 year old woman with a history of knee osteoarthritis was referred to our clinic with swelling around the eyes. She was prescribed 750 mg/day naproxen orally for knee osteoarthritis. She had no known drug allergies. There was no history of any unprescribed drug or herbal medication use and she had a negative atopic status. After three doses of naproxen, she had swelling around bilateral eyes (Figure 1). However, there was no erythema, itching, pain, tearing, pus formation nor difficulty breathing and pretibial edema during the reaction. Her primary care physician instructed to discontinue naproxen and prescribed 8 mg oral chlorpheniramine maleate and 40 mg parenteral methylprednisolone. The periorbital edema recovered within a day (Figure 2).

After a detailed medical history, other causes of periorbital edema, such as infections or autoimmune diseases were eliminated. Laboratory findings were normal. Further questioning revealed 650 mg/day acetaminophen ingestion didn't result a similar reaction. Two weeks later, with a premedication of 120 mg terfenadin twice a day, naproxen 500 mg was restarted and this time no adverse reaction occurred.

D SCUSS ON

Isolated periorbital edema due to analgesics in a similar manner was reported in 4 cases with aspirin and a case with ibuprofen in the literature²⁻⁶. In a single-blind, placebo-controlled, drug challenge study of 240 patients with a history of NSAID intolerance, Quiralte et al. discovered positive responses to the challenge in terms of isolated periorbital edema in 52 of 80 patients (65%)⁷.

Katz et al reported two patients who developed periorbital edema caused by aspirin sensitivity². The first patient was a 26-year-old man, who experienced itching in his eyes advancing into bilateral periorbital edema, after ingestion of 62.5 mg aspirin. The second patient was an 18-year-old man who developed periorbital edema after ingesting 125 mg aspirin. Before aspirin rechallenge, two patients were pretreated with terfenadine 120 mg orally and then were able to tolerate 500 mg aspirin without any reactions. Both of the patients had no history of atopy. The authors concluded that the reaction was

histamine mediated due to the effective pretreatment with terfenadine. Price and colleagues described the case of a 30-year-old man who was developed pruritus and periorbital edema following 673 mg aspirin, although his blood pressure, heart rate, respiratory rate, and spirometric measures remained stable within normal limits. Whether the patient had an atopic status or not wasn't reported³. Rafiq reported a 38-year-old man who suffered localized swelling around the eyes with concurrent pressure sensation, stinging, blurred vision and increased lacrimation after 600 mg aspirin. He denied having chest tightness, difficulty breathing or any other systemic symptoms. A few hours later, after chlorpheniramine maleate 8 mg and prednisone 30 mg orally, his symptoms started to improve.

Palungwachira et al. presented a 29-year-old woman receiving no concurrent medications who developed bilateral periorbital edema after ingestion of ibuprofen 200 mg orally. The patient was successfully treated with terfenadine.⁵ Also, Balas et al. reported an 80-year-old woman with a history of osteoarthritis and hypertension who was referred to the pharmacotherapy clinic for investigation of a possible adverse drug reaction. Her medication regimen included fosinopril sodium 40 mg orally daily for hypertension, which was started two years ago. After ingesting two doses of naproxen, the patient began experiencing itching, swelling, and erythema around the eyes. She discontinued the medication. Then the patient was prescribed ibuprofen. After ingesting two doses of ibuprofen 600 mg orally, she experienced a similar adverse reaction, at which point she was instructed to discontinue the medication.⁶ Our case is similar to the patient described by Balas et al as the type of reaction that have occurred, but Balas's case had itching and erythema besides periorbital edema. To the best of our knowledge this is the first case in the literature where naproxen use caused isolated periorbital edema.

It is proposed that naproxen's inhibition of cyclooxygenase and subsequent reduction of prostaglandin synthesis led to an increased production of or increased the sensitivity to leukotrienes (or both). Leukotrienes are mediators of bronchoconstriction, tissue edema, and mucous secretion, thereby induce the symptoms described (e.g. shortness of breath, dyspnea). A number of different cutaneous hypersensitivity reactions occurring after NSAID administration have been recognized.⁸ These reactions include urticaria, angioneurotic edema, erythema multiforme, Stevens-Johnson syndrome, maculopapular eruptions, vasculitis, fixed drug eruptions, toxic epidermal necrolysis, erythema nodosum, allergic and photoallergic contact dermatitis⁹. Many of these are due to a single drug, and most likely mediated by immunological mechanisms including immediate-type hypersensitivity (IgE-mediated), immune complexes or T cell-mediated cytotoxicity. Overall, the most frequent NSAID adverse reaction observed in the skin is facial angioedema¹⁰. It has also been recognized that NSAIDs can aggravate skin lesions in up to one-third of patients with active chronic urticaria, but they do not appear to induce any eruptions during symptomless periods of the disease.



Figure 1: The periorbital edema of patients before treatment



Figure 2: The decreased periorbital edema of patients after treatment

CONCLUSION

NSAID-induced periorbital edema is relatively uncommon, clinicians should be cognizant of its possibility. Alternative agents should be used in patients with a history of this disorder. Antihistamine therapy before NSAID administration may also be considered.

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