A case report of celecoxib-induced generalized edema and hypertension

Selective cyclooxygenase-2 (COX-2) inhibitors like celecoxib and rofecoxib are being increasingly used for the symptomatic treatment of chronic arthritic disorders like osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. This widespread use of COX-2 inhibitors could be attributed to the fact that these agents are highly effective anti-inflammatory agents yet have a lesser propensity for causing gastrointestinal adverse effects. These COX-2 inhibitors despite having a lower ulcerogenic potential are not devoid of renal toxicity. Renal adverse effects of NSAIDs are commonly encountered in elderly subjects and in those with renal, hepatic and cardiac dysfunction.

This case of celecoxib-induced peripheral edema and new onset hypertension is being reported due to the infrequent occurrence of this adverse effect in subjects with normal renal, cardiac and hepatic function and also to highlight that the MEDLINE search on renal and hemodynamic adverse effects of celecoxib has revealed that there are no published case reports in the Indian population on the above subject.

A case report of celecoxib-induced peripheral edema and hypertension is outlined below.

A young adult male aged 40 yr presented with a history of progressive swelling of both feet and the face for about 5-6 days. On enquiry he stated that he was on celecoxib 200 mg once daily as advised (by his physician) for the last 15 days for sacro-iliac joint pain. There was no history of fever, rash, urticaria or respiratory distress. Symptoms suggestive of renal, cardiac, pulmonary or hepatic diseases were also absent. There was no history of any previous hypersensitivity reactions to drugs. The patient was not a known diabetic or hypertensive (as per previous health records BP was 122/74 as on 23/4/03 and a PPBS report of 104 mg/dL dated 16/1/03). He denied history of alcohol consumption.

Clinical examination revealed the presence of pitting edema of the feet extending up to the mid-leg and facial puffiness. The patient was afebrile and some of his vital signs recordings showed supine blood pressure of 158/96 mm of Hg, pulse rate 88/min and body weight 82 kg while the other systemic examination was normal. The patient was extensively investigated and reports of hemoglobin %, total count, differential count, ESR and serum electrolytes—sodium, potassium and chloride—were normal. Fasting and postprandial sugar levels, urea, creatinine, thyroid profile and liver function tests were normal. Routine and culture sensitivity reports of urine examination showed absence of protein, sugar, ketone bodies, casts, RBC, and microorganisms. Straight X-ray (KUB), chest X-ray and ECG were non-contributory. Although the patient was asked to get a urinary sodium excretion done he did not comply with the advice.

The patient was asked to immediately stop celecoxib and to report regularly. Within 3 days of stopping celecoxib there was a gradual reduction of the edema and by the 7th day there was complete subsidence of the edema and the blood pressure reduced to levels between 122/74 to 120/70 mm of Hg. There was also a reduction in his body weight to 80 kg. A provisional diagnosis of celecoxib-induced generalized edema and hypertension was made on the premise that all other etiological factors that could lead to this clinical state were excluded and that the clinical condition completely subsided with dechallenge. As per the causality assessment this could be stated as a probable case of adverse drug reaction to celecoxib.

Studies carried out on patients aged 65 years and above with symptomatic osteoarthritis and hypertension revealed that there was a clinically significant rise of systolic blood pressure (either >20 mm of Hg or systolic BP >140 mm of Hg) in patients who were previously stabilized on antihypertensives (ACE inhibitors, Beta blockers) prior to initiation of therapy with rofecoxib or celecoxib. However, the incidence of this effect was greater with rofecoxib. Clinically significant new-onset hypertension or worsening of edema along with weight gain developed in 4.7% of cases on celecoxib and in 7.7% of cases on rofecoxib.

In another study carried out on patients of debilitating arthritic diseases, the most common adverse event reported with long-term celecoxib use was peripheral edema (2.1%), new-onset hypertension (0.8%) and exacerbation of preexisting hypertension (0.6%). These effects were not found to be dose-related or time-related.

Renal adverse effects like papillary necrosis leading to renal failure have also been reported. Since the adult kidneys have high levels of COX-2 expression in the macula densa and in the associated thick ascending loop cells, inhibition of this enzyme in the kidney could lead to inhibition of the synthesis of the renal prostaglandins resulting in peripheral edema, hypertension and other renal adverse effects.

Although these novel selective COX-2 inhibitors have a better ADR profile than the non-selective agents with regard to GIT, the renal safety and tolerability of these agents war-
rant cautious and judicious use, especially in elderly subjects. Careful monitoring of blood pressure in all subjects who are on these drugs should be undertaken as they may lead to retention of water and sodium, leading to edema, weight gain and rise of BP. The patients should also be suitably instructed to report at the earliest, in case of weight gain, swelling of the legs, facial puffiness and onset of any other new symptom after initiation of the COX-2 inhibitor.

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References

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