CASE REPORT

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Acute Pulmonary Oedema Induced by COX-2 Inhibitors in a Patient with Chronic Pain

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Cyclo-oxygenase (COX) inhibitors are by far the most commonly used analgesics since they are effective for the treatment of pain derived from common causes and are available without prescription. They are absorbed well from the gastrointestinal tract and, with occasional use, adverse effects are minimal. There are two major classes of COX isoenzymes: COX-1 is constitutively expressed and COX-2 is induced in the inflammatory state. COX-2-selective drugs, which were recently introduced for the treatment of arthritis, have been associated with reductions in gastric irritation. Whether COX 2-selective drugs have analgesic efficacy equivalent to that of other NSAIDs remains to be demonstrated.

NSAIDs, particularly COX-2 isoenzyme inhibitors, are among the most frequently prescribed medications for the treatment of chronic noncancer pain, and polypharmacy is a common problem in recipients of these drugs. COX-2 inhibitors appear to have a better gastrointestinal, but not cardiovascular, adverse effect profile than COX-1 inhibitors. Further, rofecoxib in particular is known to cause fluid overload.[1]

1. Case Report

A 64-year-old female patient with a history of hypertension (controlled by diet), hypercholesterolaemia (for which she was taking atorvastatin) and chronic low back pain was started on rofecoxib 25mg daily by her primary-care physician, and experienced a partial improvement in her low back pain condition. Shortly thereafter the patient changed her primary-care provider. The new primary-care specialist started the patient on celecoxib 100mg twice a day. Since the patient felt that celecoxib alone was not enough to control her pain, she used the refills on the prescription provided by the first primary-care provider, taking additional tablets of rofecoxib (usually 25mg daily).

Her chronic low back pain improved over the next month, but the patient started to complain of shortness of breath and bilateral leg oedema, and was admitted to the emergency room with severe respiratory distress. On examination, she was in acute respiratory failure with tachypnoea of 25 breaths/minute, speech dyspnoea, use of accessory muscles and signs of peripheral cyanosis and bilateral +3 pitting oedema. The pulse oximeter showed saturation of 86% and 90% with a rebreathing mask on 100% oxygen. The blood gas analysis was consistent with hypoxia and acute respiratory acidosis. The chest x-ray was consistent with acute pulmonary oedema. The patient was afebrile and her white cell count was within the normal limits. Cardiac enzymes were also within normal limits and no new ECG changes occurred. The ejection fraction was mildly reduced (by 35%) as per 2D ECG, without significant change.

The patient was intubated and mechanically ventilated for 2 days. Aggressive diuresis was started and after gradual improvement she was extubated. ECG recordings at this point did not show any new changes. The ECG was consistent with hypertensive cardiomyopathy and showed an ejection fraction of 40%. Cardiac catheterisation showed diffuse mild

atherosclerosis, and cardiac markers were negative for an acute cardiac event. The patient underwent a successful course of acute inpatient rehabilitation that led to a significant improvement in her functional status and a decrease in her low back pain. She was discharged on celecoxib 100mg daily only, and instructed on the proper use of analgesic tablets.

2. Discussion

COX-2 inhibitors are considered to be a well tolerated and readily available option for patients in pain. Celecoxib has been shown to have fewer adverse effects than ibuprofen and diclofenac in a randomised controlled study,[2] although the advantages were in relation to gastrointestinal (such as gastrointestinal bleeding or intolerance) or renal adverse effects and not to the cardiovascular complications of COX-2 inhibitors.

Rofecoxib has been associated with more fluid retention and oedema than celecoxib in older patients with hypertension.[3] Coadministration of rofecoxib and celecoxib may cause more cardiovascular side effects than each one alone.

In this case, a mildly hypertensive (controlled by diet) older patient with a relatively well preserved ejection fraction experienced major life-threatening acute pulmonary oedema induced by the combination of therapeutic doses of rofecoxib and celecoxib. The patient did not have signs of sepsis or pneumonia and an acute cardiac event was ruled out through investigation of cardiac enzymes. As there was no evidence of infection or deterioration of the ejection fraction on 2D ECG, it was logical to assume that the fluid overload state in this case was related to the concomitant administration of NSAIDs.

3. Conclusion

Caution with the chronic use of COX-2 inhibitors, as well as patient education on the use of these agents, is advocated.

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