

Psychiatric Manifestations in Orthopedic Patients on Celecoxib Therapy

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Abstract

Introduction: The Cyclooxygenase-2 (COX-2) enzyme is responsible for the synthesis of prostaglandin which is responsible for inflammation and pain. Celecoxib a cyclooxygenase-2 inhibitor was first used as a non-steroidal anti-inflammatory drug in 1999. Celecoxib is as effective as NSAIDs but causes less ulceration of the gastrointestinal tract, hence it is commonly used. It has been widely used in patients with osteoarthritis and rheumatoid arthritis. We present 3 cases of temporary psychiatric disorders associated with consumption of celecoxib, two of the patients presented with auditory hallucinations while one was diagnosed to be having depression. None had pre-existing psychiatric disorders or consumed alcohol or substance of abuse. All 3 patients recovered from their temporary psychiatric disorders after stopping celecoxib. **Discussion:** It is important to be aware of the psychiatric side effects when prescribing the drug for prolonged periods.

Keywords: Celecoxib, cyclooxygenase-2, psychotic disorder, drug, hallucinations, depression

INTRODUCTION

The Cyclooxygenase-2 (COX-2) enzyme was discovered by Daniel Simmons in 1988. This enzyme is responsible for the synthesis of prostaglandin which is responsible for inflammation and pain. Celecoxib is a cyclooxygenase-2 inhibitor. Celecoxib was first used in 1999. Following the CLASS (Celecoxib Longterm Arthritis Study) study, celecoxib was widely accepted. This was later followed by the SUCCESS (Successive Celecoxib Efficacy & Safety Study) study. Celecoxib is as effective as NSAIDs but causes less ulceration of the gastrointestinal tract, therefore it is commonly used. It has been approved for use in patients suffering from osteoarthritis and rheumatoid arthritis. We present 3 cases of temporary psychiatric disorders associated with consumption of celecoxib, two of which were auditory hallucinations and one was a case of depression. These 3 patients were seen at the orthopedic outpatient clinic with various conditions and were prescribed with celecoxib. All patients recovered from their psychiatric symptoms after discontinuing celecoxib.

Case report 1

A 52 yr old Malay gentleman, a retired police officer with bilateral carpal tunnel syndrome was seen in the orthopedic clinic. As his discomfort was quite severe he was prescribed with oral celecoxib 200 mg once a day for his pain relief. He tolerated the medication well for the first 2 weeks. At the beginning of the third week he started having auditory hallucinations which was gradual in onset and progressively got frequent. He began hearing voices asking him to run out of his house. They were clear voices of people talking to him. He was fully conscious during the episodes of hearing the voices. The voices were present during most parts of the day. When celecoxib was discontinued, the hallucinations gradually disappeared over 2 days. The patient never had any psychiatric history or family history of psychiatric disorders. There was no increase in the dosage of celecoxib before the psychotic episode. The patient denied taking any alcohol or other drugs. He was evaluated by a senior consultant psychiatrist to rule out any pre-existing psychiatric disorders. A final diagnosis of celecoxib induced psychotic disorder was made.

Case report 2

A 48 year old female lecturer who was suffering from prolapsed intervertebral disc was prescribed oral celecoxib 200mg daily to provide pain relief. Two and half months after taking celecoxib, she started to gradually have auditory hallucinations. She heard voices calling her frequently most of the days. She too never had any history of psychiatric illness prior to the symptoms. All her symptoms subsided 4 days after discontinuing celecoxib. There was no increase

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in the dosage of celecoxib before the psychotic episode. The patient denied taking any alcohol or other drugs. She was evaluated by a senior consultant psychiatrist and a final diagnosis of celecoxib induced psychotic disorder was made.

Case report 3

A 48 year old female nurse who was suffering from prolapsed intervertebral disc was prescribed with oral celecoxib 200 mg daily for pain relief. In addition to celecoxib, she was also prescribed Tab Methycobal 500 micrograms tds. After 2 months there was a gradual change in her behavior. She started crying frequently for no apparent reason and became depressed. She had no apparent reason to feel depressed but could not control her emotions. It was as if her emotions were being set to a state of sadness. She could not be cheered up. However there were no other associated symptoms such as sleep and appetite disturbances, guilt or hopelessness. There was no increase in the dosage of celecoxib or methylcobal before the psychotic episode. The patient denied taking any alcohol or other drugs. She was examined by a psychiatrist and advised to discontinue her medications. A month after discontinuing celecoxib she completely recovered. She did not require any anti depressants.

DISCUSSION

These 3 reports demonstrates psychiatric disorders induced by celecoxib. One patient had the manifestation after a duration of 2 weeks while the other 2 had developed symptoms after about 2 and a half months. All of them were normal prior to the consumption of celecoxib. Only one patient was consuming another additional drug, methylcobalamine in addition to celecoxib. It is unlikely that this could have triggered off the psychiatric disturbance. None of them had any change in diet. In 2 patients with auditory hallucinations the recovery was rather rapid while in the patient who had depression the recovery was slightly prolonged. None of the patients were on any psychiatric medications before, during, or after the episodes of the symptoms. All of them were also not dependent on illicit substances or alcohol throughout the symptoms.

Psychiatric manifestations of celecoxib have been reported in a 78 year old lady, she experienced auditory hallucinations, which resolved when celecoxib was discontinued.^[1] Psychiatric manifestations such as depression, psychosis, agitation & delirium have been reported with the use of NSAIDS.^[2] Ibuprofen has been reported to cause paranoid psychosis.^[3] MacKnight C. *et al* reported celecoxib and rofecoxib induced delirium in a 81 yr old lady.^[4]

Cyclooxygenase-2 (COX-2) may play an important role in modulating neural responses. COX-2 and arachnoidic acid metabolites may be involved in selective loss of neural connection as suggested by COX-2 induction seen after seizures and stimulation with glutamate. It is possible that the use of COX-2 inhibitors may help to improve this neural connections resulting in the various hallucinations. Ironically celecoxib together with risperidone has been found to have significant antipsychotic effects when compared to using risperidone on its own.^[5] The exact mechanisms for celecoxib induced psychosis is still unclear. More research needs to be done to determine the role of COX-2 in the brain and how celecoxib and other NSAIDS causes these psychiatric manifestations. For orthopedic surgeons who frequently use celecoxib, it is important to be aware of the psychiatric side effects of celecoxib when prescribing the drug, especially for prolonged periods.

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