

ADVERSE DRUG REACTION

Indomethacin induced psychosis

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Abstract

Indomethacin is a commonly prescribed non-steroidal anti-inflammatory drug. While its adverse effects on gastrointestinal and renal systems are well described, its central nervous system effects are less well known. This case report describes an elderly man, prescribed indomethacin for gout, who presented with psychosis.

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Case report

An 88 year old man developed gout and was prescribed indomethacin 50 mg four times a day. The next day his wife noted him to be withdrawn and low in mood. On the sixth day the patient was admitted to hospital with agitation and was convinced that his life was about to end.

In 1995 the patient was referred to hospital with olfactory hallucinations. He was certain that his wife was responsible for the foul smell, which he described as rotting fish. This problem led to strained relations between the couple. The patient was receiving indomethacin 25 mg three times per day for treatment of gout and the resolution of olfactory hallucinations coincided with its discontinuation. Investigations including electroencephalography and computed tomography were normal. There was no previous psychiatric history but he suffered with migraine, transient ischaemic attacks, and had had a mild stroke.

On arrival at hospital the patient was alert but agitated and physically aggressive. He was mistrustful and was petrified of being harmed by people around him. The systemic examination was unremarkable and there were no clinical signs of gout. Investigations including biochemical and inflammatory markers were normal. Computed tomography of the head showed cerebral atrophy consistent with the patient's age.

Indomethacin was discontinued after admission and he required a small dose of haloperidol for control of his behavioural symptoms. He recovered over the next two days and on discharge, was alert, orientated, and cognitively intact.

A month later the patient was readmitted with identical symptoms. He had another flare up of gout and was treated with indomethacin 50 mg four times per day. He initially became withdrawn and very low in mood. On the sixth day he developed paranoid ideas about his personal safety and later became aggressive. Upon

arrival at hospital he had clear consciousness but was agitated, aggressive, and mistrustful of people. Examination was unremarkable, though this time there was evidence of gout involving the left first metatarsal joint.

Investigations showed no evidence of infection or any biochemical abnormality. Indomethacin was discontinued and the psychosis responded well to haloperidol. The gout was treated with colchicine with rapid resolution of symptoms. Five days later the patient was asymptomatic and was discharged home.

The patient had no behavioural problems during six months of follow up. He had another flare up of gout but showed no psychotic symptoms. The acute symptoms of gout were treated with colchicine and later the serum uric acid concentration remained under control with allopurinol.

Discussion

The central nervous system (CNS) side effects of indomethacin include cognitive dysfunction, depression, depersonalisation, hallucination, and psychosis.¹⁻⁴ Though psychosis is less common it is the most serious CNS side effect of indomethacin. The adverse effects are more common in the elderly but could be missed due to lack of awareness and the presence of other pathologies such as dementia.

Indomethacin induced psychosis was first described by Carney in 1977.⁴ He reported a case where an elderly woman developed paranoid jealousy of her husband along with visual and olfactory hallucinations. Since then a few other case reports have been published.⁵⁻⁶ There are marked similarities in all published reports as most patients were elderly and had no previous psychiatric history. The symptoms of olfactory and visual hallucinations with paranoia developed after exposure to indomethacin and resolved completely after its discontinuation. Though most published reports have described these adverse reactions with indomethacin, similar problems have been noted with other non-steroidal anti-inflammatory drugs.⁷⁻⁹

The precise mechanism causing psychosis with indomethacin remains unclear. The molecular structure of indomethacin has similarities with serotonin as both of them have an indole moiety, which may explain the development of psychosis.¹⁰ Others have suggested effects on prostaglandins and neurotransmitters.¹¹ There is also evidence of decreased cerebral blood flow with indomethacin, which coincides with its peak levels and hence may contribute to adverse CNS effects.¹²

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Learning points

- The central nervous system effects of indomethacin are less well known
- The risk of psychosis is higher in older patients
- Indomethacin should be used in low dose and with caution in the elderly

Our case report has remarkable similarities with previously published literature. However our case is unique in that the patient had specific symptoms on three occasions after exposure to indomethacin, which were resolved with its discontinuation. It is plausible that a higher dose of indomethacin may have contributed to a more severe reaction during his recent hospital admissions, suggesting a possible relationship of adverse CNS reactions with the dose. Rapid resolution of symptoms after the discontinuation of indomethacin and lack of behavioural problems during follow up makes our diagnosis more robust.

To date 14 cases of psychosis associated with the use of indomethacin have been reported to the Committee on Safety of Medicines/Medicine Control Agency (Committee on Safety of Medicines; personal communication). A high index of suspicion is required to

detect this adverse effect and to prevent expensive investigations and prolonged hospital stay. More studies are needed to study the CNS effects of non-steroidal anti-inflammatory drugs in a growing elderly population. Until more information is available, indomethacin should be used in low dose and with caution in elderly people.

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