

## FAST FACTS AND CONCEPTS #323 CORTICOSTEROID-INDUCED PSYCHIATRIC SYMPTOMS

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**Background** Corticosteroids are used for a wide spectrum of palliative care indications, including pain, nausea, anorexia, fatigue, and depression (1). These agents are known to induce psychiatric adverse drug reactions, ranging from subtle mood changes and memory deficits to frank psychosis (2,3). This *Fast Fact* will focus on the identification and management of corticosteroid-induced psychosis.

**Incidence and Risk Factors** In the published literature, the incidence of corticosteroid-induced psychosis has ranged from 1.8-62%. This vast range reflects a number of clinical phenomena: variation in the clinical definition, the unpredictability of the reaction, poor clinical awareness of the issue, and the lack of standardization for corticosteroid dosing (3-8). Dose may be the most important risk factor for the development of steroid-induced psychosis, particularly when 80 mg of oral prednisone (dexamethasone dose equivalent of 12 mg po) or greater are prescribed (3,9-10). Still, even at lower doses, idiosyncratic psychiatric effects are known to occur. Other risk factors include female sex and older age (8,10,11). Previous diagnosis of mental illness and prior incidence of corticosteroid-induced psychiatric effects may also be risk factors (2-3, 8,10,11).

**Pathophysiology** The mechanism of action of this reaction is not known, however, it may relate to the enhanced dopamine activity triggered by glucocorticoids. Evidence has shown patients receiving long-term corticosteroid therapy may develop decreased hippocampal volumes; it has been postulated that these neuro-anatomic changes may also contribute to the development of psychiatric symptoms (4, 5).

**Clinical Manifestation** Early indicators of steroid-induced psychosis include confusion, perplexity, and agitation that typically occur within the first five days after initiation of treatment (6-7). Patients may go on to develop hallucinations, delusions, and cognitive impairment (2). Duration of psychiatric symptoms is dose and time-dependent; therefore, if clinicians encounter this reaction they should take prompt, appropriate clinical action (see below) (8). Development of acute psychosis in a severely ill individual has many implications on the patient's survival and quality of life, including psychological distress and interference with the patient's ability to meaningfully interact with friends and family members (12).

**Management** If patients are found to have severe symptoms of psychosis, the dose of the corticosteroid should first be tapered to <40 mg/day of prednisone (dexamethasone dose equivalent of 6 mg po), or the lowest dose possible (10,13). It has been reported that 92% of patients who undergo corticosteroid tapers can experience full symptom resolution (6). Caution is advised in aggressive tapering schedules due to the risk of corticosteroid withdrawal. In cases where the corticosteroid cannot be discontinued or significantly reduced, additional pharmacological management may be appropriate. There are currently no FDA-approved medications with an indication for corticosteroid-induced psychosis. As evidenced in case reports, low-dose antipsychotics, such as haloperidol (0.5 to 1 mg/day), olanzapine (2.5-20 mg/day) and risperidone (1-4 mg/day), may lead to symptom resolution within days to weeks (13-17). Use of the mood stabilizer, lithium, has been described to prevent corticosteroid-induced psychosis, but it is associated with more side effects. Therefore, involvement of a consult liaison psychiatry team should be considered when utilizing lithium (18).

**Other Psychiatric-Induced Symptoms** In addition to psychosis, a multitude of psychiatric disorders can arise as adverse effects of corticosteroids. These include, but are not limited to, mood disorders with depressive or manic features and delirium (10). In addition to corticosteroid tapers, the literature provides limited evidence of medication management. Case reports focusing on depressive episodes have shown response to antidepressants, such as fluoxetine 10-40 mg/day, within 7 days, as well as electroconvulsive therapy (ECT) (19). One case report describes the resolution of mania symptoms within 10 hours after initiating quetiapine 25 mg/day (20). The majority of patients will recover from psychiatric symptoms within several weeks after discontinuation or significant dose tapering of the corticosteroid (6).

**Summary** The rare complication of corticosteroid-induced psychiatric symptoms should not impede the prescribing of these agents for appropriate indications, especially when the benefits of therapy would far outweigh the risks. Clinicians should, however, be able to identify and manage these psychiatric effects, as these can significantly inhibit quality of life and meaningful interpersonal interactions for seriously ill patients.

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