Steroid-induced psychosis

Iresha Perera, Fesochi Atulayo, Malcolm Forbes

CASE

A retired teacher, aged 74 years, with a history of treated hypothyroidism and no psychiatric history, presented to our service after urgent referral from her rheumatologist. She had been diagnosed with giant cell arteritis one month before our involvement and had been taking prednisolone 50 mg daily since diagnosis. On initial review in a community clinic, she presented with irritable affect, insomnia, persecutory delusions and delusions of reference, auditory hallucinations and impaired insight. An initial diagnosis of steroid-induced psychosis was made and olanzapine 2.5 mg daily was commenced. Inadequate adherence to the antipsychotic regimen and deteriorating mental state resulted in hospital admission and an increase in olanzapine to 5 mg daily. Tocilizumab was prescribed weekly as the prednisolone dose reduction was expedited. Over the subsequent week, the patient refused all medications and the *Mental Health Act*[1] was used to compel treatment given the risk of serious psychiatric deterioration and permanent visual loss. After recommencing treatment, the patient made a full recovery from her psychotic symptoms and suffered no permanent sequelae from giant cell arteritis. Following discharge from hospital, olanzapine was continued for two weeks before tapering and cessation, with sustained remission from psychotic symptoms 12 months later.

QUESTION 1

How common is the use of oral glucocorticoids in Australia?

QUESTION 2

What side effects are associated with glucocorticoids?

QUESTION 3

How does steroid-induced psychosis present?

QUESTION 4

What is the management of steroid-induced psychosis?

QUESTION 5

What is the expected outcome and prognosis?

QUESTION 6

Are there any options for prevention?

ANSWER 1

Oral glucocorticoids have potent anti-inflammatory and immunosuppressive properties and are used in the treatment of several common conditions. They are frequently prescribed, with 2,042,346 prescriptions made via the Pharmaceutical Benefits Scheme/Repatriation Pharmaceutical Benefits Scheme (PBS/RPBS) in 2022.[2]

ANSWER 2

Despite their efficacy, the adverse effects of oral glucocorticoids sometimes restrict their use. Short-term use is associated with infection, venous thromboembolism, and fracture.[3] Long-term use is associated with chronic diseases including diabetes mellitus, cardiovascular disease, myopathy, cataracts and osteoporosis.[3]

Serious psychiatric conditions – major depressive episodes, mania, delirium and psychotic disorders – develop in approximately 6% of patients who receive oral glucocorticoids.[4] Older age (>50 years) is a risk factor for the development of psychiatric complications.[5] Oral glucocorticoids might increase the risk of suicidal behaviour and completed suicide. A 2021 Danish population-based, case-control study found oral glucocorticoid initiation was associated with a seven-fold increased risk of suicide in cancer patients and a two-fold increased risk

of suicide in patients treated for other medical conditions, with a clear dose–response relationship.[6] The absolute risk increase associated with glucocorticoid prescription remains very low.

ANSWER 3

Steroid-induced psychosis is the most severe neuropsychiatric presentation associated with oral glucocorticoid use.[4] Its pathogenesis remains unknown. The condition can present insidiously with insomnia, irritability, anxiety, mood lability and overvalued ideas before the development of frank psychotic symptoms including delusions, hallucinations and grossly disorganised behaviour. These symptoms typically occur within two weeks of the initiation of high-dose glucocorticoid treatment.

ANSWER 4

There have been no randomised trials to guide optimal management of steroid-induced psychosis, but the available evidence (retrospective cohort studies, case-control studies and case series) recommends a taper and cessation of glucocorticoids. If this is not possible, the glucocorticoid dose should be reduced to less than the equivalent 40 mg/day of prednisolone. Psychotic symptoms respond to second-generation antipsychotic medications, with most published cases reporting use of olanzapine 2.5–20 mg daily. This is best administered nocte as it has a sedative effect, and high-dose glucocorticoids are often associated with disruption of diurnal rhythm.

ANSWER 5

Response to antipsychotic treatment is typically complete and usually occurs within two weeks of treatment initiation.[4] There have been no longitudinal studies of patients who have suffered with steroid-induced psychosis to report on long-term cognitive and psychiatric outcomes, but anecdotal evidence suggests full recovery.

ANSWER 6

There have been several pharmacological agents trialled for prophylaxis of neuropsychiatric complications of oral glucocorticoid use, with mixed results. Case reports indicate positive results with both olanzapine and lithium.[7]

All patients and their carers should be advised about the potential for psychiatric complications associated with high-dose glucocorticoid use. Education about these risks might facilitate early recognition and timely intervention (Box 1). If steroid-induced psychosis is suspected, risk assessment, tapering and discontinuation of the glucocorticoid, and early psychiatric consultation, is recommended.

Box 1. Potential risk factors for serious adverse neuropsychiatric effects

Age >50 years

History of severe depression, mania or psychosis

Family history of serious mental illness or adverse effects from prednisolone treatmment

High dosage (≥40 mg per day of prednisolone or equivalent)

Key points

- Glucocorticoids are an occasional iatrogenic cause of mild insomnia, depressed mood and mood elevation.
- The incidence of steroid-induced psychosis, the most serious neuropsychiatric complication of glucocorticoid use, is unknown.
- Patient education about the small but significant risk of serious mental disorders associated with the use of high-dose glucocorticoids is recommended, particularly in those who have other potential risk factors.

Authors

Iresha Perera MBBS, Psychiatry Registrar, University Hospital Geelong, Barwon Health, Geelong, Vic

Fesochi Atulayo MD, Psychiatry Registrar, University Hospital Geelong, Barwon Health, Geelong, Vic

Malcolm Forbes MBBS, MP, GCEpi, FRANZCP, CertPOA, Consultant Psychiatrist, University Hospital Geelong, Barwon Health, Geelong, Vic; Research Fellow, The Institute for Mental and Physical Health and Clinical Translation (IMPACT), School of Medicine, Barwon Health, Deakin University, Geelong, Vic; Clinical Tutor, Department of Psychiatry, The University of Melbourne, Melbourne, Vic

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Correspondence to:
malcolmpforbes@gmail.com

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correspondence **ajgp@racgp.org.au**