

# Corticosteroid-Induced Psychosis After a Single Transforaminal Epidural Steroid Injection

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## ABSTRACT

**Introduction:** Neuropsychiatric symptoms are a well-described side effect of systemic corticosteroid therapy and can range from mild to severe.

**Case Presentation:** We describe a case of substance-induced psychosis following epidural injection of 10 mg dexamethasone. Three days after the procedure, the patient developed symptoms including anger, hostility, insomnia, paranoia, and delusions. Symptoms resolved between 7 and 17 days.

**Discussion:** In the past 50 years, there have been several case reports of severe neuropsychiatric effects following intraarticular or other interventional pain injections with various corticosteroids. More recent reviews have identified possible risk factors, including corticosteroid dose, patient age, sex, and history of neuropsychiatric disorder, among others, although these conclusions are not duplicated across all studies.

**Conclusion:** Recommendations for practice include patient and family education on possible adverse effects of corticosteroid administration, utilization of minimum effective doses for interventional procedures, and the consideration of close follow-up and multidisciplinary coordination, especially in high-risk patients.

## INTRODUCTION

Corticosteroids are commonly utilized by interventional pain medicine specialists for their anti-inflammatory properties. Neuropsychiatric effects of systemic corticosteroid therapy have been described for decades and range from relatively benign, brief disturbances (eg, mood elevation, insomnia) to depression, mania,

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delirium and psychosis.<sup>1-3</sup> The incidence of severe neuropsychiatric symptoms after a single parenteral injection is a much more rare event. Even within the subset of severe neuropsychiatric effects, mood disorders such as depression or mania are more common than psychotic disorders.<sup>3-4</sup> Here, we present a case of substance-induced psychotic disorder following a single dose of epidural corticosteroid.

## CASE PRESENTATION

A 49-year-old white man with chronic low back pain and unilateral radicular pain presented for evaluation in the Pain Management Clinic. He denied resting motor or sensory deficits. His pain regimen included home-based physical therapy, scheduled pregabalin, and oral opioids. He

had previously undergone a transforaminal epidural steroid injection (ESI) with time-limited improvement of his symptoms. Past medical history included anxiety treated with lorazepam as needed up to 1.5 mg daily, diabetes not requiring pharmacologic intervention, and alcoholic cirrhosis status post liver transplant. Physical exam revealed tenderness to palpation over the lumbar vertebral bodies and paraspinal musculature, exacerbation of low back pain by facet-loading maneuvers, positive straight-leg raise on the right, and decreased sensation to pinprick in the right S1 dermatome. Magnetic resonance imaging of his lumbar spine was obtained previously and demonstrated diffuse disk degeneration with moderate foraminal narrowing and compression of the right S1 nerve root.

The patient underwent a right L5/S1 transforaminal epidural steroid injection under fluoroscopic guidance with injectate consisting of 1 mL dexamethasone 10 mg/mL and 0.5 mL lidocaine

**Table.** Selected Reports of Severe Neuropsychiatric Symptoms Following Interventional Corticosteroid Administration

Authors	Pain Intervention(s)	Symptom(s)	Corticosteroid(s)	Time Course	Previous Neuropsychiatric History
Baloch <sup>7</sup> 1974	41-year-old man undergoes bilateral intraarticular injections of shoulder	Excitability, garrulousness, irritability, hostility, delusions	Methylprednisolone 40 mg each side (80 mg total)	Onset: morning after injections, precise timing not reported Resolution: 72 hours	Delusions with systemic corticosteroid therapy
Fishman et al, <sup>8</sup> 1996 (A)	57-year-old woman undergoes celiac plexus block	Spending spree, grandiose thoughts, pressured speech, poor judgment	Triamcinolone 100 mg	Onset: 25 hours Resolution: 4 days	Mania with systemic corticosteroid burst as well as intraarticular shoulder injection
Fishman et al, <sup>8</sup> 1996 (B)	52-year-old woman undergoes celiac plexus block	Euphoria, insomnia, sexual proclivity, irritability	Triamcinolone 100 mg	Onset: 41 hours Resolution: 7 days	Mania with systemic corticosteroid administration (IV and orally)
Robinson et al, <sup>9</sup> 2000	75-year-old woman undergoes intraarticular injection of left hip	Paranoid delusions, visual and auditory hallucinations	Methylprednisolone 80 mg	Onset: 26 hours Resolution: 3 days	Negative
Benjamin et al, <sup>10</sup> 2008	67-year-old man undergoes cervical epidural, medial branch block x4, trigger point injection x4, tendon injection	Racing thoughts, anger, agitation, pressured speech, paranoia	Methylprednisolone 80 mg, triamcinolone 20 mg, additional unknown quantities	Onset: ~ 7 days Resolution: ~ 7-10 days	Negative
Samala and Ciocon, <sup>11</sup> 2011	82-year-old woman undergoes intraarticular injections of bilateral knees	Visual hallucinations, confusion	Methylprednisolone 40 mg each side (80 mg total)	Onset: 3 days Resolution: 3 days	Anxiety and depression
Lally et al, <sup>12</sup> 2017	82-year-old woman undergoes intraarticular injection of left knee	Persecutory delusions, auditory hallucinations	Methylprednisolone 80 mg	Onset: 48 hours Resolution: 4 days (partial), 7 days (complete)	Baseline moderate dementia

Abbreviation: IV, intravenous.

10mg/mL. He reported immediate improvement in his low back pain and was discharged from the ambulatory surgery center to home. On postintervention day 3, the patient's sister contacted his primary care physician (PCP) via phone with the concern that the patient was acting "strangely." Reported symptoms included mood swings, anger, hostility, confusion, insomnia, acute worsening of his baseline anxiety, paranoia, feelings of abandonment, and a preoccupation with "a hole in his heart." He was instructed to transiently increase his lorazepam dosage and short-term follow-up was arranged with the patient's alcohol and other drug abuse (AODA) counselor. On postintervention day 6, the patient became acutely intoxicated with alcohol after 8 years of sobriety and was combative with family members. He was transported by ambulance to the Emergency Department for evaluation. Aside from a mild transaminitis, his evaluation was negative and he was discharged to home once sober. On postintervention day 7, he was evaluated in clinic by his PCP. His neuropsychiatric symptoms continued, and he was prescribed quetiapine as needed for insomnia. Short interval follow-up was arranged both with the patient's PCP and with Health Psychology. On post-intervention day 17, he was again seen in clinic by his PCP; by this time, his neuropsychiatric symptoms had resolved. He was started on a serotonin and norepinephrine reuptake inhibitor (SNRI) and a referral was placed to Psychiatry for a more comprehensive evaluation of his baseline anxiety disorder.

## DISCUSSION

Neuropsychiatric symptoms are well described in patients receiving chronic systemic corticosteroid therapy. Depending on the specific definitions employed, reported prevalence ranges from less than 1% to 60%.<sup>3,5-6</sup> Though not precisely quantified, the incidence of severe neuropsychiatric side effects following a single parenteral injection of corticosteroid is thought to be much more rare. A PubMed review identified several case reports of significant psychiatric symptoms following intraarticular or other interventional pain injection with a variety of corticosteroids.<sup>7-12</sup> (See Table.) Based on the relative paucity of reported cases, it seems clear that severe corticosteroid-induced neuropsychiatric symptoms are rare after a single parenteral injection. Given the potential severity of symptoms, it would be beneficial for clinicians to identify which patients are at increased risk for adverse effects.

Corticosteroid-induced side effects are thought to be dose-dependent. Evidence from the Boston Collaborative Drug Surveillance Program showed an increasing prevalence of psychiatric symptoms with higher doses of corticosteroid: 1.3% in subjects receiving less than 40mg prednisone per day (mg/d), 4.6% in subjects receiving 41 mg/d to 80 mg/d, and 18.4% in subjects receiving more than 80 mg/d.<sup>13</sup> Subsequent studies have verified the increased marginal risk with a daily dose exceeding 40 mg prednisone or equivalent.<sup>6</sup>

Unfortunately, there are limited data to support clinical factors

predisposing patients to corticosteroid-induced neuropsychiatric symptoms, and many purported risk factors have not been duplicated across studies. These investigations have been thoroughly treated in a number of review articles, the conclusions from which can be summarized as follows: risk for corticosteroid-induced neuropsychiatric symptoms may be increased by female sex, hypoalbuminemia, increasing age, and cytochrome p450 inhibition.<sup>5,14-16</sup>

Patient history of neuropsychiatric disorder has long been suspected as a predisposing factor for substance-induced psychotic disorder. However, investigations of this relationship have yielded mixed results. Most recently, Fardet et al (2012) performed a retrospective review of 786,868 outpatient prescriptions of systemic corticosteroids over 18 years in the United Kingdom and identified 10,220 incident cases of severe neuropsychiatric disorders; patients with previous history of neuropsychiatric disorder were at elevated risk for substance-induced neuropsychiatric outcomes in this dataset.<sup>6</sup> These findings contrast previous investigations that suggest neither history of neuropsychiatric comorbidities nor history of corticosteroid-induced neuropsychiatric symptoms increase risk for future corticosteroid-induced neuropsychiatric symptoms, although these previous studies were based on much smaller cohorts (eg, 14 patients by Hall et al, 1979; 13 patients by Clark et al, 1953).<sup>2,17</sup> Based on the totality of evidence, and given the orders-of-magnitude increase in study subjects investigated by Fardet et al, we are inclined to view history of neuropsychiatric disorder as a potential independent risk factor for corticosteroid-induced neuropsychiatric symptoms.

As it relates to the presented case, the patient had no history of psychosis but did suffer from a neuropsychiatric disorder in the form of anxiety. Moreover, he described a personal history of adverse reaction to high-dose systemic corticosteroids administered around the time of his liver transplant; these symptoms included mild agitation and exacerbation of his underlying anxiety state, although he did not experience symptoms consistent with substance-induced psychosis at that time. In addition, the patient experienced no neuropsychiatric symptoms 12 weeks earlier following his first ESI with injectate including 15 mg dexamethasone, a finding that speaks to the relative unpredictability of adverse neuropsychiatric effects. Despite this unpredictability, recurrent corticosteroid-induced neuropsychiatric effects are a common theme in published case reports of severe adverse outcomes (Table); patients with such a history may therefore warrant treatment by clinicians as having a high risk for recurrence.

Uncertainties surrounding patient-specific risk factors notwithstanding, the data clearly suggest a dose-dependent relationship. Specifically, it seems that daily doses in excess of 40 mg prednisone represent a threshold for increased risk, although these findings are based on investigations of chronic systemic therapy. If the same threshold is applied for single-dose interventional injection, 40 mg prednisone is equipotent to 32.5 mg methylprednisolone or

triamcinolone, and to 6 mg dexamethasone.<sup>18</sup> Opinions differ on dosing strategies for epidural pain procedures, but typical doses of corticosteroid are likely to exceed this threshold despite some evidence of equal efficacy at lower dosages.<sup>19-20</sup> And although a complete discussion is well beyond the scope of this review, demonstrated lasting effects from injectate of local anesthetic alone<sup>21</sup> would allow for complete avoidance of these significant, albeit rare, neuropsychiatric effects.

Timing of injections may also be important due to the theoretical concern for “dose-stacking” that could increase risk for corticosteroid-induced psychiatric effects. Short interval corticosteroid injections are generally not favored by pain medicine physicians, due to concern for paradoxical progression of joint space disease as well as transient suppression of the hypothalamic-pituitary-adrenal axis.<sup>22</sup> The 2013 Update to Evidence-Based Guidelines for Interventional Techniques in Chronic Spinal Pain recommends a frequency of epidural interventions no less than 2 months apart for a given region (cervicothoracic vs lumbosacral), or at least 1 to 2 weeks if performed on different regions.<sup>23</sup>

It may be prudent to discuss the possibility of substance-induced neuropsychiatric effects as part of the informed consent process prior to procedures that involve the injection of a corticosteroid, especially in patients who are identified as high risk. This discussion should include the possibility of exacerbating existing mood disorders, as well as the possibility of provoking new disturbances altogether. Involvement of family members at this stage would seem appropriate, given the possibility of impaired insight on the part of the patient should severe neuropsychiatric symptoms develop. Short-term follow-up with the patient’s pain physician or PCP, either via phone or in person, may also allow for untoward effects to be recognized early.

Though not reviewed here, pharmacologic strategies for the prevention or treatment of corticosteroid-induced psychiatric effects have been previously described (eg, West and Kenedi, 2014<sup>16</sup>). These contingency plans are not dissimilar to those put in place for diabetic patients to help manage transient increases in blood glucose related to parenteral corticosteroid administration. It may be reasonable for high-risk patients to have plans in place with their PCP or mental health provider to manage these effects, should they arise.

## CONCLUSION

Neuropsychiatric side effects of systemic corticosteroid therapy are well described. Though significantly more rare, cases of neuropsychiatric symptoms, including psychosis, have also been reported following a single administration of parenteral corticosteroid. Higher doses of corticosteroid confer increased risk for these symptoms, with equivocal marginal risk associated with a history of neuropsychiatric disorder, female sex, hypoalbuminemia, advanced age, and CYP inhibition.

Among the reviewed case reports of severe neuropsychiatric symptoms following a 1-time procedural injection, a history of corticosteroid-induced neuropsychiatric symptoms is a common theme. These reports suggest that physicians may wish to consider such patients as higher risk for similar adverse outcomes. Recommendations for practice include patient and family education on possible adverse effects of corticosteroid administration, utilization of minimum effective doses for interventional procedures, and the consideration of close follow-up and multidisciplinary coordination, or even pharmacologic pretreatment in selected circumstances.

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