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Recurrent hiccups after dexamethasone-containing pain interventions despite a change in injection route and local anesthetic: two cases

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Case Report

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Abstract

Background

Hiccups are an uncommon adverse event after corticosteroid-containing interventional pain procedures. Because most reports describe a single exposure to a mixed injectate, the relative roles of the epidural route, the local anesthetic and the corticosteroid remain uncertain.

Case presentation:

A 71-year-old man received a caudal epidural injection and bilateral L3–L5 medial branch blocks in one session (total dexamethasone 15.2 mg, bupivacaine 28.5 mg). Hiccups began 12 hours later and lasted approximately 24 hours. One month later, bilateral sacroiliac joint injections without an epidural component (dexamethasone 8 mg, lidocaine 80 mg) were followed by hiccups that began at 16 hours and lasted approximately 24 hours. A 56-year-old man underwent, in a single session, left L5–S1 dorsal root ganglion pulsed radiofrequency with a transforaminal epidural injection, a caudal epidural injection and bilateral L3–L5 medial branch radiofrequency thermocoagulation (total dexamethasone 17.25 mg, bupivacaine 22.5 mg). Hiccups began 13 hours later and resolved spontaneously after 28 hours. He reported no hiccups during courses of oral methylprednisolone for subacute thyroiditis in 2022.

Conclusions

In the first patient, recurrence after a non-epidural injection containing a different local anesthetic shows that neither epidural administration nor bupivacaine was necessary for both episodes; dexamethasone was the constant exposure. The second patient's history is compatible with, but does not establish, susceptibility specific to dexamethasone. Before repeat corticosteroid injections, clinicians should ask about hiccups after earlier steroid exposures and record any episode as a possible adverse drug reaction.

Introduction

Hiccups are involuntary contractions of the diaphragm and inspiratory intercostal muscles, terminated by abrupt closure of the glottis. They are generated by a reflex arc with vagal, phrenic and sympathetic afferents, a central network in the brainstem and upper cervical cord that is still poorly defined, and efferent output mainly through the phrenic nerve [1, 2]. Episodes lasting less than 48 hours are usually called acute, those lasting longer are called persistent, and those lasting more than a month intractable [2]. Even brief episodes can be distressing, and when they begin many hours after a procedure their connection with it is easily missed.

Corticosteroids are among the drugs most often associated with hiccups. Dexamethasone in particular has been implicated in patients receiving it as an antiemetic during chemotherapy [3, 4]. In interventional pain medicine, hiccups have been reported mainly after epidural steroid injections [2, 5–7], but also after facet joint and sacroiliac joint injections [5] and after intra-articular joint injections [8–10]. A 2025 review of hiccups after epidural injections identified 23 publications describing 30 patients; onset was most often between 6 and 24 hours after the procedure, and duration was most often less than 2 days [2]. These figures summarize published case reports, in which several patients contributed more than one episode; they do not provide an incidence or a comparison of risk between drugs or routes.

Most reported procedures delivered a corticosteroid together with a local anesthetic, often into the epidural space, so the contribution of each component can rarely be separated. Proposed explanations include changes in cerebrospinal fluid volume or pressure after epidural injection, effects of the local anesthetic, and systemic effects of the absorbed corticosteroid [2, 5].

We describe two men who developed delayed, self-limited hiccups after dexamethasone-containing procedures. In the first, hiccups recurred after a second session in which both the injection route and the local anesthetic had been changed. The second had previously received prolonged oral methylprednisolone and reported no hiccups during that treatment. We discuss what these within-patient observations can and cannot reveal about the trigger.

Case presentations

Case 1

A 71-year-old man presented with low back and leg pain and neurogenic claudication. In 2018 he had undergone L3–L5 posterior instrumentation for lumbar spinal stenosis; the instrumentation was removed in 2019 because of worsening pain. He could walk approximately 100 m with two forearm crutches. No motor deficit or sphincter dysfunction was found. FABER and FADIR tests were positive bilaterally. Lumbar magnetic resonance imaging showed multilevel facet hypertrophy, extruded disc herniations at L4–L5 and L5–S1, and an anteroposterior spinal canal diameter of 8 mm. Pregabalin, duloxetine, other analgesic treatment and physiotherapy had not provided adequate relief.

In a single session, he underwent ultrasound-guided bilateral L3–L5 medial branch blocks and a caudal epidural injection. The caudal injectate (10 mL) consisted of dexamethasone 8 mg (2 mL), 0.5% bupivacaine 3 mL (15 mg) and 0.9% saline 5 mL. A second 10-mL mixture of identical composition was prepared for the medial branch blocks, and 1.5 mL was injected at each of six sites (9 mL in total), delivering dexamethasone 7.2 mg and bupivacaine 13.5 mg on the assumption of uniform mixing. Total exposure in this session was therefore dexamethasone 15.2 mg and bupivacaine 28.5 mg. No sedation, contrast medium or other procedural medication was used.

Hiccups began 12 hours after the procedure. Four hours after onset, the patient attended an emergency department, where he received oral chlorpromazine 100 mg. Relief was temporary, and the hiccups

resolved completely approximately 24 hours after onset.

One month later, ultrasound-guided bilateral sacroiliac joint injections were performed using a 10-mL mixture of 2% lidocaine 4 mL (80 mg), dexamethasone 8 mg (2 mL) and 0.9% saline 4 mL; each joint received 5 mL. No epidural injection, sedation, contrast medium or other procedural medication was used. Hiccups began 16 hours after the procedure and resolved without treatment approximately 24 hours after onset.

Case 2

A 56-year-old man presented with progressive bilateral low back pain and burning, tingling pain extending from the buttocks into both legs, more marked on the left. He had undergone two operations for lumbar disc herniation, and stabilization material had been removed approximately nine years before presentation. Muscle magnetic resonance imaging and electromyography had been performed because of a mildly elevated creatine kinase concentration; no myopathic findings were reported, and electromyography showed neurogenic involvement at L5–S1. Over approximately ten years, gabapentin, pregabalin, duloxetine and carbamazepine had been used sequentially, each providing less than 50% pain relief.

In a single session, he underwent left L5–S1 dorsal root ganglion pulsed radiofrequency with a transforaminal epidural injection, a caudal epidural injection, and bilateral L3–L5 medial branch radiofrequency thermocoagulation. Intravenous midazolam 1 mg was given for sedation, and 2 mL of iohexol contrast medium was injected into the epidural space. The epidural injectate had a total volume of 11 mL and contained dexamethasone 12 mg, 0.5% bupivacaine 3 mL (15 mg) and 0.9% saline 5 mL; of the dexamethasone, 8 mg was given caudally and 4 mg transforaminally. Before thermocoagulation, the six medial branch sites received a combined 6 mL containing dexamethasone 5.25 mg and bupivacaine 7.5 mg. Total exposure was dexamethasone 17.25 mg and bupivacaine 22.5 mg.

Hiccups began 13 hours after the procedure and resolved spontaneously, without medication, 28 hours after onset.

In 2022, the patient had been treated with oral methylprednisolone for subacute (de Quervain) thyroiditis. Treatment started at 40 mg/day with a planned 25% dose reduction every six days. Approximately six weeks later, worsening thyroiditis symptoms led to an increase to 16 mg/day, after which the dose was reduced by 4 mg every two weeks until discontinuation. The patient reported no hiccups during these courses.

Comparison of the three episodes

Table 1 summarizes the exposures and the course of each episode. The two episodes in Case 1 occurred in the same patient and should not be read as independent observations.

Table 1. Exposures and course of the three hiccup episodes in two patients

	Case 1, first episode	Case 1, second episode	Case 2
Procedures (single session)	Caudal epidural injection; bilateral L3–L5 medial branch blocks (ultrasound-guided)	Bilateral sacroiliac joint injections (ultrasound-guided)	Left L5–S1 DRG PRF with transforaminal epidural injection; caudal epidural injection; bilateral L3–L5 medial branch RF thermocoagulation
Epidural component	Yes (caudal)	No	Yes (caudal and transforaminal)
Dexamethasone, total	15.2 mg (8 mg caudal; 7.2 mg medial branch)	8 mg (intra-articular)	17.25 mg (12 mg epidural; 5.25 mg medial branch)
Local anesthetic, total	Bupivacaine 28.5 mg	Lidocaine 80 mg	Bupivacaine 22.5 mg (15 mg epidural; 7.5 mg medial branch)
Injected volume	10 mL caudal; 9 mL medial branch	10 mL (5 mL per joint)	13 mL epidural (11 mL injectate + 2 mL iohexol); 6 mL medial branch
Sedation / contrast	None / none	None / none	Midazolam 1 mg IV / iohexol 2 mL (epidural)
Onset after procedure	12 h	16 h	13 h
Duration (from onset)	Approx. 24 h	Approx. 24 h	28 h
Treatment	Oral chlorpromazine 100 mg; temporary relief	None	None

DRG, dorsal root ganglion; PRF, pulsed radiofrequency; RF, radiofrequency.

Discussion

Both patients developed hiccups 12–16 hours after a dexamethasone-containing procedure, and all three episodes resolved within 24–28 hours of onset. The most informative observation is the second episode in Case 1. The first session combined a caudal epidural injection with medial branch blocks and used bupivacaine, so the episode could not be attributed to a single site or drug. At the second session no epidural injection was performed and lidocaine replaced bupivacaine, but dexamethasone was given again, and hiccups recurred with similar latency and duration. In this patient, therefore, neither epidural administration nor bupivacaine was necessary for both episodes. This does not exclude an epidural contribution to the first episode, an effect shared by amide local anesthetics, or an interaction between a drug and the procedure itself.

Hiccups after non-epidural injections have been reported before. Abbasi and colleagues described eight men with hiccups after interventional procedures that included facet joint and sacroiliac joint injections [5], and hiccups have followed intra-articular corticosteroid injections, including injection of the knee [8,9]. Mengi and Dilbil reported hiccups after each of two intra-articular glenohumeral dexamethasone injections, with no hiccups during subsequent oral methylprednisolone treatment [10]. We therefore do not claim a first description of non-epidural or recurrent hiccups. What these cases add is a within-patient recurrence in which the route and the local anesthetic changed together while the corticosteroid did not, considered alongside a second patient with prolonged earlier exposure to a different corticosteroid without reported hiccups.

Competing explanations

Epidural volume and cerebrospinal fluid dynamics. A transient change in cerebrospinal fluid volume or pressure after epidural injection has been proposed as a trigger [2]. This cannot explain the second episode in Case 1, which followed sacroiliac joint injections alone, although extra-articular spread of the 5-mL volumes could not be assessed without contrast. An epidural contribution remains possible for the first episode in Case 1 and for Case 2, but these episodes began with a latency similar to that of the non-epidural episode, and no measurement of cerebrospinal fluid dynamics was available.

Local anesthetic. Hiccups have occurred after epidural local anesthetic given without a corticosteroid, usually within minutes to a few hours of injection [2,11]. Because both sessions in Case 1 used an amide local anesthetic, a class effect cannot be excluded. However, onset in all three episodes came 12–16 hours after injection, long after the expected duration of local anesthetic action. This timing argues against a direct local anesthetic effect, although it does not rule one out.

Systemic corticosteroid effect. Dexamethasone was the only agent common to all three episodes, and hiccups after systemic dexamethasone are well documented [3,4]. Systemic absorption after local or epidural injection is plausible but was not measured. The latency we observed lies within the range most often reported after epidural steroid injection [2]. Similar latencies strengthen recognition of a post-procedural association, but they do not identify the causal agent and, without drug concentrations, they cannot be taken as evidence of a particular absorption profile. Corticosteroids have been proposed to lower the threshold for synaptic transmission within the central hiccup pathway [2]; this remains a hypothesis rather than an established mechanism.

Individual and molecule-dependent susceptibility. Evidence that susceptibility may be specific to dexamethasone comes from patients receiving chemotherapy. In a retrospective multicenter series of 40 patients with dexamethasone-associated hiccups, rotation to methylprednisolone was followed by complete resolution in 85%, and hiccups recurred in 25 of 34 patients when dexamethasone was reintroduced [3]. In a randomized, single-blind crossover trial in 65 patients with dexamethasone-associated hiccups, methylprednisolone was associated with lower hiccup intensity than dexamethasone, and the difference reversed after crossover [4]. These data come from repeated

antiemetic dosing in patients selected because they had already developed hiccups, so their proportions cannot be transferred to single spinal or intra-articular injections. In the interventional setting, Abbasi and colleagues switched the corticosteroid in some patients, with milder hiccups in at least one [5]. Susceptibility also need not appear at every exposure: one patient tolerated a lumbar epidural steroid injection before developing prolonged hiccups after a cervical one [6].

Case 2 is relevant here. In 2022 he received oral methylprednisolone starting at 40 mg/day, a dose of roughly the same glucocorticoid potency as 7.5 mg of dexamethasone [12], followed by a second taper over several weeks, and he reported no hiccups. This history is compatible with dexamethasone-specific susceptibility, but it is a retrospective patient report. The two exposures were years apart and differed in route, dose, duration, clinical context and concomitant medication. It is therefore not a natural control: it neither excludes a corticosteroid class effect nor shows that methylprednisolone would be tolerated as an injectate.

Other drugs and procedural or clinical factors. Anxiety, air swallowing, gastroesophageal reflux or gastric distension, electrolyte disturbances and concomitant drugs can all provoke hiccups [1,2]. Case 2 also received intravenous midazolam and iohexol contrast medium and underwent radiofrequency procedures, none of which were used in Case 1. Midazolam is among the drugs reported to provoke hiccups [2], but a single 1-mg dose of a short-acting benzodiazepine is an unlikely explanation for onset 13 hours later, and no sedation was used in either session of Case 1. These alternatives were not systematically excluded; laboratory tests and investigations for thoracic or abdominal causes at the time of the episodes were not available. The temporary relief after chlorpromazine during the first episode of Case 1 does not show efficacy, because spontaneous resolution followed.

Taken together, dexamethasone is the most plausible shared trigger, but these observations describe a temporal association and recurrence after renewed exposure rather than a confirmed adverse drug reaction. Spontaneous resolution after a single injection is not a controlled dechallenge, and repetition of a multidrug procedure is not an isolated dexamethasone rechallenge.

Course and patient characteristics

All three episodes lasted less than 48 hours and are best classified as acute (transient) [2]. This contrasts with the persistent courses described after epidural dexamethasone, for example about 60 hours [7] and 12 days [6], and after repeated intra-articular dexamethasone (60 and 72 hours) [10]. Both of our patients were men. A male predominance has been noted in published hiccup case reports [13], in dexamethasone-associated hiccups during chemotherapy (38 of 40 patients in one series, and all 65 participants in the crossover trial, although sex was not an eligibility criterion) [3,4], and among reported patients with hiccups after epidural steroid injection [2]. Two cases cannot support a sex-specific risk estimate or a hormonal mechanism.

Clinical implications

When planning repeat corticosteroid injections, clinicians should ask specifically about hiccups after previous procedures and systemic corticosteroid courses, record any episode as a possible adverse drug reaction, and warn patients that a delayed episode may recur. Case 1 suggests that changing the injection route or the local anesthetic alone may not prevent recurrence. Whether a different corticosteroid would do so after spinal or intra-articular injection has not been tested, and the chemotherapy data do not justify a general recommendation.

Limitations

This report describes two retrospectively documented patients, without a denominator of exposed patients or an untreated comparator. Each session combined several interventions and drugs, and systemic drug concentrations were not measured. Hiccup frequency and severity were not recorded with a standardized instrument, and alternative causes were not systematically investigated. No agent-specific rechallenge or steroid-free comparison was performed, and the absence of hiccups during earlier methylprednisolone treatment in Case 2 rests on patient report.

Conclusion

Delayed, transient hiccups followed dexamethasone-containing pain interventions in two men. In one, recurrence after sacroiliac joint injections with lidocaine showed that neither an epidural route nor bupivacaine was required for repeated episodes. Dexamethasone was the plausible shared trigger, but causality and molecule-specific susceptibility were not established. Careful reconstruction of drug exposures, explicit questioning about earlier corticosteroid reactions, and transparent reporting of alternative explanations are needed to interpret this uncommon event.

Declarations

Ethics approval:

Ethics committee approval was not required for this case report. Under national regulations in Türkiye, ethics committee approval is required for research studies but not for case reports.

Consent for publication:

Written informed consent for publication was obtained from both patients.

Competing interests:

The authors declare no conflicts of interest.

Use of artificial intelligence tools

During the preparation of this manuscript, the authors used ChatGPT (OpenAI) and Claude (Anthropic) for language editing, restructuring of the text and assistance with checking bibliographic details. The tools were not used to generate or interpret clinical data. The authors reviewed and edited all content, verified every reference against the original sources, and take full responsibility for the content of the publication.

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Author Contribution

M.Ç. performed the procedures and followed up the patients. Z.T. and M.Ç. wrote the main manuscript text. Ç.Y. prepared the tables. All authors reviewed the manuscript and approved the final version.

Data availability:

Data sharing is not applicable to this article, as no datasets were generated or analysed.

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