

The steroid-responsive hiccup reflex arc: Competitive binding to the corticosteroid-receptor?

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Abstract

Hiccups occurring secondary to high-doses of corticosteroids are a well-recognized problem in the field of neurosurgery. Numerous reports of oral, intravenous and intraarticular corticosteroids inducing hiccups exist in the literature. To date, there is only one case of anabolic steroids inducing hiccups. We now present a case of a patient who underwent a suboccipital craniotomy for resection of a cerebellar pontine angle meningioma. Postoperatively the patient was on high doses of Decadron and Oxandrin, an anabolic-anticatabolic agent used to combat the deleterious effects of corticosteroids. The patient suffered intractable hiccups postoperative day one, resistant to Thorazine. Oxandrin was discontinued to assess the possibility of an anabolic steroid-induced singultus. The hiccups resolved within 24 hours. This report validates the previous report on anabolic steroids inducing hiccups and exemplifies the ability for steroids as a class, due to their backbone structural homology, to induce function even as competitive inhibitors.

Abbreviations and Units

mg = milligrams
b.i.d. = twice a day
t.i.d. = three times per day
q = every
hrs. = hours
p.o. = by mouth

Introduction

For years hiccups or singultus have been reported to be associated with high-doses of corticosteroids [1–5]. The mechanisms of action for steroid-induced hiccups are yet to be elucidated. We recently reported the first case of anabolic steroid induced-hiccups in an elite power lifter [6]. We now report on a case of anabolic steroid-induced hiccups associated with concomitant corticosteroid treatment in a postoperative patient. This case demonstrates the partial antagonistic effect of certain steroids and further elucidates the complex molecular mechanisms of steroid-induced hiccups.

Case Report

A 40 year-old male presented to the neurosurgery clinic for resection of a cerebellar-pontine angle mass that was causing progressive hearing loss. Neurologically the patient was intact except for decreased high-pitched hearing in the left ear. The patient was taken to the operating room for a standard suboccipital craniotomy and resection of a cerebellar-pontine angle meningioma. The surgery was uneventful and there were no changes in brainstem-auditory evoked potentials during surgery. Postoperatively the patient was on high doses of Dexamethasone (Decadron) 8 mg p.o. q 6hrs. with a decreasing taper of 2 mg q 48 hours for postoperative edema. He was also on Oxandrolone (Oxandrin) 10 mg b.i.d., an anabolic steroid, to combat some of the deleterious metabolic effects of the Decadron. On postoperative day one the patient began suffering intractable hiccups and was given Thorazine (Chlorpromazine) 50 mg t.i.d. for 24 hours without benefit. Based on previous experience a decision was made to discontinue the Oxandrolone and within 24 hours the hiccups resolved without any other medication alterations. The patient was discharged two days later on a Dexamethasone taper and Oxandrolone. The patient denied any further hiccups at his two week postoperative follow-up examination.

Discussion

The hiccup reflex arc is a complex system involving an afferent, efferent, and central limb. In brief, the afferent limb involves the sympathetic chain from thoracic segments T6-T12, the phrenic and vagus nerves. The efferent limb is primarily the phrenic nerve and it's involvement with the glottis, accessory respiratory muscles and interaction with the brainstem and hypothalamus [2]. The central connection of the afferent and efferent limbs is a nonspecific location between C3-C5 and the brainstem [2,6].

Previous reports have demonstrated that oral, intravenous and intraarticular corticosteroids can induce hiccups [2,3,5]. There is also a report of oral progestins causing hiccups which were thought to occur via corticosteroid receptor pathways [4]. It has been proposed that corticosteroids may lower the synaptic threshold in the brainstem, thus permitting hiccups to arise [7]. Corticosteroids, mineralocorticosteroids and progestins have been shown to bind to steroid-receptors within the efferent limb of the hiccup reflex arc [11–13].

We previously proposed in our case of intractable hiccups occurring in an athlete using supraphysiologic doses of anabolic steroids that stimulation of the corticosteroid receptor was occurring via competitive binding [6]. We postulated that competitive binding to the corticosteroid-receptor within the afferent limb of the hiccup reflex arc was occurring based on the rapid resolution of symptoms after discontinuing anabolic steroids [6]. Interestingly, the athlete in the case was not using Oxandrolone but a more potent oral anabolic-androgenic steroid Methandrostenolone (Dianabol) [6]. The present case further supports our previous theory of androgens competitively binding to the corticosteroid-receptor in the afferent limb of the reflex arc, as symptoms resolved within 24 hours after discontinuing the Oxandrolone [6].

Oxandrolone is both structurally and functionally an anabolic steroid yet it is also considered an anti-catabolic steroid due to its ability to bind competitively to corticosteroid receptors [10]. We routinely place our patients on Oxandrolone postoperatively to combat the deleterious effects of Dexamethasone and to improve wound healing [14,15]. The ability of androgens to bind to corticosteroid receptors is the thesis of this report which is supported by our previous case of androgen-induced hiccups [6,8,10].

Lastly, one may question whether the hiccups could have resulted secondary to brainstem irritation from retraction during the surgical approach to the tumor. The tumor did not encase any of the cranial nerves and there were no changes in brainstem-auditory evoked potentials during the case. Postoperatively the patient had no new deficits and his hearing progressively improved.

Conclusions

It is our general consensus that this case which involves an anabolic steroid that has been shown to competitively bind to corticosteroid-receptors and our previous case of intractable hiccups occurring with anabolic steroids demonstrates that competitive binding to the corticosteroid receptor is a highly plausible explanation [6]. We continue to use Oxandrolone in our postoperative patients to combat the deleterious effects of corticosteroids and hope that this report will educate other physicians on the complicated molecular actions of anabolic steroids.

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