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Hydrocortisone improves somnolence without hypotension in the postpartum period

Nada Usta-Makkaoui[1,2], Timothy L. Lacy[1], and Neil Roy Connelly[1,2]

[1] Department of Anesthesiology, Baystate Medical Center, 759 Chestnut Street, Springfield, MA 01199, USA
[2] Department of Anesthesiology, Tufts University School of Medicine, Springfield, MA, USA

Abstract
Hypothalamic-pituitary-adrenal (HPA) axis abnormality and adrenal insufficiency secondary to chronic steroid treatment can be present in the perioperative period. When this occurs in pregnant patients during the peripartum period, the usually expected physiological changes may not be present. The hypotension associated with adrenal insufficiency may be masked by the normal physiological changes of pregnancy and delivery. We report on a patient whose only presenting symptom was mental status changes; this occurred without any significant hemodynamic changes. These mental status changes responded within minutes to a single dose of hydrocortisone. We recommend administering a pharmacological dose of steroid as a maneuver to rule out adrenal insufficiency when faced with a patient with an unexplained altered mental status while other differential diagnoses are considered.

Key words Pregnancy · Complication anesthesia · Epidural medication · Steroids · Adrenal suppression

Introduction

Hypothalamic-pituitary-adrenal (HPA) axis abnormality and adrenal insufficiency secondary to chronic steroid treatment can be present in the perioperative period. When this occurs in pregnant patients during the peripartum period, the usually expected physiological changes may not be present. The hypotension associated with adrenal insufficiency may be masked by the normal physiological changes of pregnancy and delivery. We report on a patient whose only presenting symptom was mental status changes; this occurred without any significant hemodynamic changes. These mental status changes responded within minutes to a single dose of hydrocortisone.

Address correspondence to: N. R. Connelly, Neil.Roy.Connelly@bhs.org
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Case report

A 28-year-old parturient (gravida 8, para 4) at full term was admitted for induction of labor. The patient denied any medical problems except for anemia. The patient experienced an uneventful vaginal birth with epidural analgesia, achieved at the L 2-3 interspace. The labor analgesia had been maintained with bupivacaine 0.1% with fentanyl $2\,\mu g \cdot ml^{-1}$ via a continuous infusion at a rate of $10\,ml \cdot h^{-1}$. The infusion was stopped at the time of delivery. Her blood pressure (BP) during labor was 100–119/55–75 mmHg, and her pulse (P) was 75–114 beats per min (bpm). According to family members, she seemed to be very tired just after giving birth, and was more sleepy than usual. Approximately 1 h after delivery, the patient was transported to the operating room to undergo a postpartum tubal ligation. She was given 15 ml of 2% lidocaine, in incremental doses, through the epidural catheter; a T3 level of anesthesia was achieved. During surgery the patient did not require any sedative medications because she was somnolent, although she remained easily arousable. The patient tolerated the incision and extraction of the left fallopian tube. During surgery, her vital signs remained normal, except for one reading of 80/40 mmHg, which responded quickly to 10 mg of ephedrine. During the procedure on the right fallopian tube, she began to grimace. Because 1 h had passed since the initial dosing of the epidural, an additional 15 ml of 1% lidocaine, in incremental doses, was administered through the epidural catheter. Approximately 15 min following the additional epidural lidocaine, the patient began to shake. She remained sleepy, but when awakened stated that she was cold. Warm blankets were placed on the patient and the shaking was reduced. On transport to the postanesthesia care unit (PACU), the patient again began to shake, but at this time she was less responsive. The patient would only open her eyes when called by her name. Vital signs in the PACU were: BP, 140/75 mmHg; P, 90 bpm; arterial

oxygen saturation (Sa_{O_2}), 100%; and temperature, 36.9°C. The patient's medical record was reviewed at this time, and it was noted that she had received 2 weeks of oral steroid treatment (prednisone tapered from 40 mg·day^{-1} to 5 mg·day^{-1}) for eythema nodosum 2 months prior to delivery. While waiting for a blood work and considering the possible causes of the mental changes in this patient, she was given 100 mg of intravenous hydrocortisone. The patient returned to her normal mental status within 3 min. The patient became fully coherent and had no complaints. Laboratory results revealed a hematocrit of 27%; sodium, 136 mEq·l^{-1}; potassium, 3.7 mEq·l^{-1}; glucose, 106 mg·dl^{-1}; ionized calcium, 1.18 mmol·l^{-1}; and a negative drug screen. The patient was discharged home 2 days following delivery; the remainder of the hospitalization was uneventful.

Discussion

We present a patient who had excessive somnolence and shaking in the immediate post-partum period. Although we considered the possibility of local anesthetic toxicity, the patient was somnolent prior to receiving the lidocaine (300 mg incrementally) for the tubal ligation. One hour later, after receiving an additional 150 mg lidocaine, again incrementally, she experienced some shaking. An additional hour later, in the PACU, the patient's responsiveness was decreased. These symptoms promptly resolved following a single dose of hydrocortisone, making reaction to the lidocaine even more unlikely. The production of glucorticoids by the adrenal cortex is regulated by the adrenocorticotropic hormone (ACTH) secreted by the anterior pituitary gland. The normal cortisol secretory rate in response to minor surgery is 50 mg per day, and about 75–150 mg a day for major surgery; cortisol secretion in the first 24 h after surgery rarely exceeds 200 to 300 mg [1,2].

During pregnancy, maternal ACTH, cortisol, cortisol binding globulin (CBG), and plasma renin activity increase [3,4]. At midgestation, the free unbound active cortisol can reach three fold above the levels of non-pregnant women [5].The rate of cortisol secretion by the adrenals is not increased in pregnancy, but the rate of clearance is decreased [6,7]. This does not result in clinical evidence of hypercortisolism or hyperaldosteronism; the feedback mechanisms of cortisol are regulated at a higher setpoint with a lower suppression by dexamethasone [3]. The fetus is protected from hypercortisolemia by the placenta activity of the enzyme 11β-hydroxysteroid dehydrogenase type 2 [5]. At 33 weeks of gestation, fetal adrenal cortisol production increases. In cases of mild maternal hypocortisolism, adrenal crisis may be avoided until delivery by the transplacental passage of cortisol from fetus to mother to maintain maternal cortisone levels [3]. This might explain the absence of symptoms until delivery in our patient.

Cortisone was first introduced for anti-inflammatory and immunosuppressive purposes in 1948 [7]. Patients taking prednisone 5 mg·day^{-1} or higher have considerable variability in HPA axis suppression; this response does not correlate well with the total dose or duration of therapy [8,9]. Any patient who has received glucocorticoids for more than 5 days, in doses equivalent to at least 20 mg a day of prednisone, is at risk for HPA suppression for up to 1 year [7,10]. It is often not possible to predict the duration of recovery from a prolonged course of glucocorticoid therapy in an individual patient [7,11]. However, if the treatment is less than 5 days, recovery usually occurs in approximately 1 week [12]. When discontinuing or abruptly decreasing the dosage of glucocorticoids, patients can experience vague central nervous system (CNS) symptoms such as nausea, anxiety, lethargy, and sleep disturbances; withdrawal syndrome may involve psychosis [13,14]. This is often referred to as steroid withdrawal syndrome. When CNS symptoms such as nausea, anxiety, lethargy, sleep disturbances, and psychosis are attributed to steroid withdrawal syndrome, they are usually relieved by slowing the tapering schedule or by replacing the glucocorticoid [13]. Most of these symptoms disappear within a few days after glucocorticoid therapy [13,14].

In a case report by Krasner [15], a patient who underwent a change in her steroid therapy from prednisone to a tapering dose of triamcinolone developed uncontrollable shaking, in addition to nausea and dizziness. Following 25 mg of oral prednisone, the patient "felt better almost immediately." In our case, the patient also developed shaking and became minimally responsive. Her symptoms totally resolved within a few minutes after receiving a single 100-mg dose of intravenous hydrocortisone.

Usually the diagnosis of adrenal insufficiency secondary to exogenous corticosteroids requires documentation of either subnormal cortisol levels or cortisol levels that remain inappropriately low despite provocation [16]. The diagnosis of hypoadrenalism secondary to exogenous steroids is difficult in pregnancy [5]. One problem is the lack of gestation-related normative data [5]. It has been recommended that a blood sample for cortisol level should be drawn prior to treatment being given [17]. However, if an adrenal crisis is suspected, it is essential not to delay the treatment while diagnostic tests are performed [17]. In our patient, her neurologic symptoms took only minutes to resolve following a single dose of hydrocortisone. We did not test for a cortisol level in our patient during the time of her mental status changes. However, the response to treatment was an indirect proof of cortisol deficiency, knowing that it was the only treatment given.

In treating an adrenal crisis, appropriate measures to maintain vital signs should be taken. Intravascular hydration should be aggressive and consist of 5% dextrose (to prevent hypoglycemia) in 0.9% saline. Plasma, oxygen, and vasopressor drugs can be given as needed. Narcotics and sedatives should be avoided. Hydrocortisone 100 mg or dexamethasone 4 mg intravenously has been suggested to be given to the established Addisonian patient in crisis or to patients with suspected Addisonian crisis [3,7]. Intravenous infusion of an additional 200 mg of hydrocortisone per day, for a total of 300 mg per day, is indicated. Because the half-life of hydrocortisone is 90 min, continuous infusions have been suggested as being preferable to boluses every 6 h [3,7]. Stress dose glucocorticoid therapy with a soluble hydrocortisone ester should be administered at the initiation of active labor and continued until after delivery, followed by a rapid taper to previous maintenance doses [6,18]. Dexamethasone, methylprednisolone, and prednisone have fewer mineralocorticoid effects than do cortisone and hydrocortisone. Therefore, they may decrease the chance of salt and water retention occurring in the patient receiving glucocorticoid replacement therapy. As an alternative to 100 mg hydrocortisone, one may administer dexamethasone 4 mg, prednisone 25 mg, methylprednisolone 20 mg, or betamethasone 3 mg. There does not seem to be any advantage of one particular glucocorticoid for the treatment of adrenal insufficiency.

Mental status changes can be the sole presenting symptom of adrenal insufficiency. We have presented a patient who had excessive somnolence and shaking in the immediate post-partum period; these symptoms promptly resolved following a single dose of hydrocortisone. We recommend administering a pharmacological dose of steroid as a maneuver to rule out adrenal insufficiency when faced with a patient with an unexplained altered mental status while other differential diagnoses are considered.

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