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Original Contribution

The effect of epidural methylprednisolone acetate injection on the hypothalamic-pituitary-adrenal axis☆,☆☆

George Habib MD, MPH (Chief, Rheumatology Clinic)[a,b,*], Adel Jabbour PhD (Head, Central Laboratory)[c], Jameel Salman MD (Attending Anesthesiologist)[d], Geries Hakim MD (Chief of Orthopedics)[e], Henry Haddad MD (Chief of Anesthesiology)[d]

[a]*Rheumatology Clinic, Nazareth Hospital, Nazareth 16000, Israel*
[b]*Deputy, Department of Medicine, Carmel Medical Center, Haifa, Technion Faculty of Medicine, Haifa 34362, Israel*
[c]*Central Laboratory, Nazareth Hospital, Nazareth 16000, Israel*
[d]*Department of Anesthesiology, Nazareth Hospital, Nazareth 16000, Israel*
[e]*Department of Orthopedics, Nazareth Hospital, Nazareth 16000, Israel*

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Abstract

Study Objective: To evaluate the effect of an epidural corticosteroid injection of 80 mg and 40 mg of methylprednisolone acetate on the hypothalamic-pituitary-adrenal axis and on back pain.

Design: Randomized, single-blinded prospective study.

Setting: Operating room of a university-affiliated hospital.

Patients: 42 patients with low back pain due to radiculopathy.

Interventions: Group 1 received an epidural corticosteroid injection of 80 mg of methylprednisolone acetate, and Group 2 received an epidural corticosteroid injection of 40 mg of methylprednisolone acetate. All study patients underwent a stimulation test of one μg of adrenocorticotropin hormone (ACTH), and their pain levels were graded just prior to and following the epidural corticosteroid injection on weeks one, 3, and 4.

Measurements: Serum cortisol of the ACTH stimulation tests and back pain levels were rated using a visual analog scale (VAS). Serum cortisol levels lower than 18 ng/mL 30 minutes following the ACTH stimulation test were considered to be secondary adrenal insufficiency.

Main Results: 21 patients were enrolled in each group. The rate of secondary adrenal insufficiency in Group 1 was ~86%, ~ 22%, and ~17% of patients versus ~53% (P = 0.024), 15% (P = 0.874), and ~12% (P = 0.715) of Group 2 patients at weeks one, 3, and 4, respectively. About 62%, 56%, and 39% of Group 1 patients had a favorable clinical response as opposed to ~47% (P = 0362), 35% (P = 0.21), and ~6% (P = 0.049) of Group 2 patients at weeks one, 3, and 4, respectively.

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* Correspondence: George Habib, MD, MPH, Rheumatology Clinic, Nazareth Hospital, P.O.Box 11, Nazareth 16000, Israel. Tel.: +972 4 602 8888; fax: +972 4 602 8844.
E-mail address: gshabib@gmail.com (G. Habib).

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Conclusions: Epidural corticosteroid injection of methylprednisolone acetate in both groups was associated with very high rates of secondary adrenal insufficiency, but significantly more so in Group 1 at week one. This suppression was transient, with recovery of the gland in most patients noted over the ensuing weeks. An epidural corticosteroid injection of 80 mg had higher rates of favorable clinical response than a 40 mg injection, but significantly more so at week 4 only. This favorable response waned over a few weeks in both groups.

1. Introduction

Epidural corticosteroid injection is a common procedure performed in pain clinics [1]. Its main indication is persistent radiating back pain due to radiculopathy [2]. Different types of corticosteroids and different doses have been used; however, usually 80 mg of methylprednisolone acetate is used. It was reported also that doses of 40 mg of methylprednisolone have comparably favorable results [3].

The mechanism of action of the injected corticosteroids in the epidural space is still illusive and some studies have shown no significant clinical difference following the injection of local anesthetic alone versus local anesthetic and corticosteroids [4,5].

There are relatively very few reports on the systemic effects of epidural corticosteroid injection, including the effect on the hypothalamic-pituitary-adrenal axis [6-9]. Suppression of this axis with secondary adrenal insufficiency is a real consideration whenever an individual is subjected to depot steroid compounds, including epidural corticosteroid injection. The few studies about the effect of epidural corticosteroid injection on the hypothalamic-pituitary-adrenal axis included steroids from different types and in some with multiple doses. However, there is only one report in the English literature with a relatively small number of patients about the effect of epidural methylprednisolone acetate injection on the hypothalamic-pituitary-adrenal axis [10], in which a dose of adrenocorticotropin hormone (ACTH) of 250 μg rather than one μg was used as a stimulation test.

Traditionally, insulin-induced hypoglycemia or overnight metyrapone test were used to evaluate the integrity of the hypothalamic-pituitary-adrenal axis. These tests might have serious adverse effects and the corticotropin analog stimulation test is considered safer, faster, and less expensive [11]. Currently, most studies show superiority of the one μg (so called "low dose") ACTH stimulation test over the high dose (250 μg) test in evaluating secondary adrenal insufficiency [12,13]. It is more sensitive but less specific. However, there is still debate about the definition of secondary adrenal insufficiency. Most reports agree that a serum cortisol level of 18 ng/mL obtained 30 minutes following the low-dose ACTH stimulation test as the cutoff level for secondary adrenal insufficiency [13,14].

In this study, we prospectively evaluated the effect of an epidural corticosteroid injection of both 80 mg and 40 mg of methylprednisolone acetate on the hypothalamic-pituitary-adrenal axis and on back pain in patients presenting to a pain clinic.

2. Materials and methods

The study was approved by the Helsinki Committee at the Nazareth Hospital, and all patients enrolled gave their written, informed consent. Consecutive patients attending the pain clinic who were candidates for epidural corticosteroid injection, were asked to participate in our study. If they agreed and met the inclusion criteria and had no exclusion criteria, patients were randomized to two groups: Group 1 and Group 2 on an alternating pattern (first pt allocated to Group 1, second pt to Group 2, third pt to Group 1, eg (systematic assignment). Groups 1 and 2 patients had an epidural corticosteroid injection of 80 mg and 40 mg of methylprednisolone acetate (Pfizer VN/SA, Brussels, Belgium), respectively, and underwent stimulation test using one μg of ACTH (Tetracosactide Acetate; Alliance Pharma PLC, Chippenham, UK) just prior to the epidural corticosteroid injection (day-0), and one (week-1), 3 (week-3), and 4 weeks (week-4) later. Week 2 was skipped so as to increase compliance. The ACTH stimulation test was performed at 09:00 hour with the patient in supine position, following an overnight fast for at least 8 hours, and having had no special physical activity during the morning prior to the test.

Just before the epidural corticosteroid injection, blood was obtained (time-0) for serum cortisol levels through a 22-gauge intravenous (IV) catheter (Venflon™), then μg (one mL) of ACTH was injected, flushing the IV catheter with 2 mL of normal saline, and more blood was obtained for cortisol level after 30 minutes (time-30) following a 3 mL dead space of blood obtained through the Venflon.

The researchers were aware of the dose of the methylprednisolone acetate in both groups, but patients were not. Inclusion criteria included patients older than 18 years, low back pain due to radiculopathy of at least one month's duration that did not respond to physical therapy or nonsteroidal anti-inflammatory drugs (if not contraindicated), and ability to give written, informed consent. Exclusion criteria were having had an epidural corticosteroid, systemic, intra-articular, and/or intramuscular injection; nasal spray, eye drops, or inhalation of steroid compounds during the previous three months; evidence of acute illness (inflammatory or noninflammatory); inflammatory back pain; uncontrolled hypertension; uncontrolled diabetes; anticoagulant treatment; bleeding tendency; allergy to corticosteroids; and/or pregnancy.

All of the patients were asked to grade the level of their back pain just prior to and at follow-up visits (wk-1, wk-3,