Systemic Effects of Epidural Corticosteroid Injection

Wade King, MMed; David C. Miller, MD, MA; and Clark Smith, MD, MPH on behalf of the Spine Intervention Society's Patient Safety Committee

Myth: Transforaminal and interlaminar epidural injections of corticosteroids can be administered without concern for systemic effects because the doses used are small and intermittent.

Fact: The doses of corticosteroids administered in interventional spine procedures have systemic effects, especially when the patient has a steroid-dependent condition such as diabetes mellitus or has multiple exposures to steroids.

Transforaminal and interlaminar epidural injections of corticosteroids are used to treat radicular pain. The presumed rationale is that the corticosteroid suppresses inflammation of the affected nerve root, which is responsible wholly or partly for the generation of pain. Once injected, the corticosteroid is absorbed through the epidural plexus of veins, and can exert systemic effects. The risk of side-effects is dependent on the dose used and the number of injections given over time. The nature of systemic effects depends on the systems affected and the duration of exposure to steroids.

Pharmacology

The corticosteroids used in spinal pain management are glucocorticoids. They act by binding to glucocorticoid receptors, which are present in virtually all human tissues, and control carbohydrate metabolism. Synthetic corticosteroids have substantially higher affinity for glucocorticoid receptors than does natural cortisol [1]. Glucocorticoid drugs have a weak, but not negligible, affinity for mineralocorticoid receptors.

Glucocorticoids are metabolized in the liver to inactive glucuronides and sulfates, and are excreted mainly by the kidneys, but also in feces. The half-lives of glucocorticoids vary, but are of the order of several days. For example, the half-life of dexamethasone is 36-54 hours [2]. The half-lives of these agents determine the durations of their acute side-effects.

Dose

For transforaminal injection of steroids (TFIS) dexamethasone has become the preferred agent, because it does not form particles. Typical doses range from 5mg [3] to 7.5mg [4, 5] and 15 mg [6]. Equivalent doses of other agents, such as triamcinolone or betamethasone have been used in the past. For interlaminar epidural injections similar or larger doses have been used. For either type of procedure, larger doses are sometimes used when more than one nerve root is the target. There are no published data comparing the incidence, severity or duration of systemic adverse effects with different doses of any of the glucocorticoid steroids administered epidurally.Consequently, any inferences drawn about systemic side-effects can only be qualitative in nature.

Systemic Side-Effects

Corticosteroids principally influence the metabolism of carbohydrates, fats, proteins and purine, but they can also affect electrolyte and water balance; they may affect the functions of the central nervous system, of the cardiovascular, renal, endocrine, reproductive and immune systems, as well as of bones and muscles. The short-term systemic effects of corticosteroids reported [7-11] are listed in Table 1.

Long-term systemic side-effects may arise if corticosteroids are administered on a continuing basis, or given repeatedly at intervals too short for the body to have cleared the previous dose(s). Long-term effects may be caused directly by excess glucocorticoid in the circulation or indirectly through suppression of the hypothalamic-pituitary

axis (HPA). Suppression of the HPA, resulting in low serum cortisol, has been seen following a single epidural steroid injection, and may persist anywhere from 2 to 52 weeks [12-15]. Higher doses of epidural methyprednisolone suppress the HPA axis more frequently and for a longer duration than do lower doses [16]. Serial epidural steroid injections may result in higher frequencies of HPA suppression [17]. A recent study showed that of patients presenting to a university pain management center and considered for epidural steroid injections, more than 44% already had significant steroid exposure within the previous six months [18]. The longer-term effects of epidural steroids reported [7-11] include persistence of the short-term effects (Table 1).

Table 1

Glucose metabolism
hyperglycemia
hepatic gluconeogenesis
inhibition of glucose uptake in muscle and adipose tissue
increased appetite
loss of appetite

Nervous system
mood changes
- restlessness or irritability
- euphoria or even mania
- depression

insomnia
vasomotor flushing (face, neck and chest)
headache
malaise
balance disturbance, vertigo
nausea, vomiting
seizures

Cardiovascular system
fluid retention, edema
hypertension
aggravation of arrhythmias

Immunological
allergic reactions
reduced resistance to infection
delayed healing

Other
gastrointestinal effects
- reflux
- heartburn
- gastritis

menstrual irregularities
vaginal bleeding
raised intraocular pressure

Table 1. A list of the short-term systemic side-effects of corticosteroids that can occur after transforaminal or interlaminar epidural administration.

Other longer-term systemic steroid side-effects, which potentially could occur but have not been reported explicitly after epidural injections, include hyperinsulinemia, increased adiposity, hypokalemic alkalosis, reduced gonadal function and infertility, abnormal intraocular pressure, cataracts, osteoporosis, myopathy, and cardiomyopathy (each caused by excess glucocorticoid), and hypoglycemia, hypoinsulinemia, loss of appetite, hyponatremia, hyperkalemia, hypothyroidism (each caused by effects on the HPA). Lymphocytosis or lymphocytopenia, monocytosis or monocytopenia, and eosinophilia or eosinopenia, can also occur.

Implications

The practical implications of the pharmacology of corticosteroids are that unwanted effects should be taken into account when planning the administration of steroids by any route. The risks should be explained to patients before any intervention in which a steroid is to be administered, so they can give properly informed consent. Precautions should be taken for anticipated effects, such as hyperglycemia, in patients with impaired glucose tolerance. If steroid injections are to be repeated, shorter-acting agents should be administered at intervals of not less than two weeks to prevent accumulation of the drug in the body and HPA suppression. If a longer-acting, depot steroid is to be used, a 3-week or even 4-week interval may be appropriate. Injected doses should be in accordance with published data. Every effort should be made to determine if patients have received other glucocorticoid steroids.

Acknowledgements

The authors express appreciation to the other members of the Patient Safety Committee who served as peer reviewers for this FactFinder, in particular Dr. Adrian Popescu and Dr. Byron Schneider, and to Mrs. Belinda Duszynski, who coordinated the project.

References

1. Meikle AW, Tyler FH. Potency and duration of action of glucocorticoids: effects of hydrocortisone, prednisone and dexamethasone on human pituitary-adrenal function. Amer J Med 1977; 63: 200-207.
2. Hardy R, Rabbitt EH, Filer A, Emery P, Hewison M, Stewart PM, Gittoes NJ, Buckley CD, Raza K, Cooper MS. Local and systemic glucocorticoid metabolism in inflammatory arthritis. Ann Rheum Dis 2008; 67: 1204-1210.
3. Thomas E, Cyteval C, Abiad L, Picto MC, Taourel P, Blotman F. Efficacy of transforaminal versus interspinous corticosteroid injection in discal radiculalgia. – A prospective, randomised, double-blind study. Clin Rheumatol 2003; 22: 299-304.
4. Park CH, Lee SH, Kim BI. Comparison of the effectiveness of lumbar transforaminal epidural injection with particulate and nonparticulate corticosteroids in lumbar radiating pain. Pain Med 2010; 11: 1654-1658.
5. Denis I, Claveau G, Filiatrault M, Fugère F, Fortin L. Randomized double-blind controlled trial comparing the effectiveness of lumbar transforaminal epidural injections of particulate and non-particulate corticosteroids for lumbar radicular pain. Pain Med 2015; 16: 1697-1708.
6. Kennedy DJ, Plasteras C, Casey E, Visco CJ, Rittenberg JD, Conrad B, Sigler J, Dreyfuss P. Comparative effectiveness of lumbar transforaminal epidural steroid injections with particulate versus nonparticulate corticosteroids for lumbar radicular pain due to intervertebral disc herniation: a prospective, randomized, double-blind trial. Pain Med 2014; 15: 548-555.
7. Dexamethasone 4.0 mg./ml. injection – summary of product characteristics (SPC). electronic Medicines Compendium. Merck Sharp & Dohme Ltd. 4 December 2013.
8. Gonzales P, Laker SR, Sullivan W, Harwood JE, Akuthota V. The effects of epidural betamethasone on blood glucose in patients with diabetes. PMR 2009; 4: 340-345.
9. Berthelot JM, Le Goff B, Maugars Y. Side effects of corticosteroid injections: what's new? Joint Bone Spine 2013; 80: 363-367.
10. Suh-Burgmann E, Hung YY, Mura J. Abnormal vaginal bleeding after epidural steroid injection: a paired observational cohort study. Am J Obstet Gynecol 2013; 209: 206.e1-6.
11. Kim S. Hwang B. Relationship between bone mineral density and the frequent administration of epidural steroid injections in postmenopausal women with low back pain. Pain Res Manag 2014; 19: 30-34.
12. Burn JMB, Langdon L. Duration of action of epidural methyl prednisolone. A study in patients with lumbosciatic syndrome. Am J Phys Med 1974; 53: 29-34.
13. Jacobs S, Pullan PT, Potter JM, Shenfield GM. Adrenal suppression following extradural steroids. Anesthesia 1983; 8: 953-956.
14. Horani MH. Secondary Cushing's syndrome after a single epidural steroid injection of a corticosteroid. Endocr Pact 2005; 11:408-410.
15. Maillefert J-F, Aho S, Hugeunin M-C, Chatard C, Peere T, Marquignon M-F, Lucas B, Tavernier C. Systemic effects of epidural dexamethasone injections. Revue du Rheumatisme (English edition) 1995; 62: 429-432.
16. Habib G, Jabbour A, Salman J, Hakim G, Haddad H. The effect of epidural methylprednisolone injection on the HPA axis. J. Clin Anesth 2013; 25: 629-633.
17. Kay J, Finding JW, Raff H. Epidural triamcinolone suppresses the pituitary-adrenal axis in human subjects. Anesth Anal 1994; 79: 501-505.
18. Goel AP, Nguyen VH, Hamill-Ruth R. Use of risk stratification tool in identification of potential adrenal suppression preceding steroid injection therapy in chronic pain patients. Pain Medicine 2015; 16: 2226-2234.

SIS MAY 1, 2017