Corticosteroids for Pain of Spinal Origin

Epidural and Intraarticular Administration

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KEYWORDS

• Corticosteroid • Glucocorticoid • Epidural steroid injection • Low back pain
• Lumbar stenosis • Transforaminal • Facet joint • Sacroiliac joint

KEY POINTS

- Epidural steroid injection (ESI) is the most commonly performed outpatient procedure for the treatment of spinal pain worldwide.
- The epidural approach is most often used to optimize the local, anti-inflammatory effects of corticosteroid at the nerve root level in lumbar radiculitis and neurogenic claudication.
- Facet and sacroiliac joint injection of corticosteroid is widely practiced in pain management to target putative peripheral sources of referred, nociceptive chronic low back pain.
- There are a range of widely used corticosteroid formulations with distinct physicochemical properties that may affect outcomes and side effects profiles.
- ESIs offer the advantage of a more localized corticosteroid delivery to the putative anatomic correlate of pain such as the nerve root, thereby decreasing the likelihood of systemic side effects.

INTRODUCTION

Spinal pain syndromes are the leading cause of disability in the United States. The 2010 Global Burden of Disease Study found that the years lived with disability attributed to low back pain (3.1 million) exceeds even that of osteoarthritis (1.9 million).[1] The lifetime prevalence of a single episode of low back pain is estimated at 85%.[2] Corticosteroids are commonly used for a wide range of spinal pain syndromes, such as

Disclosure: None.
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Rheum Dis Clin N Am 42 (2016) 137–155
http://dx.doi.org/10.1016/j.rdc.2015.08.003 **rheumatic.theclinics.com**
0889-857X/16/$ – see front matter

lumbar radiculitis and neurogenic claudication associated with spinal stenosis. In the United States alone, 9 million injections of corticosteroids are administered annually and this rate is increasing steadily.[3] Sustained increase in utilization is likely owing to (1) recent studies demonstrating lack of analgesic efficacy with oral steroid treatment for acute radicular pain, and (2) growing concerns about the therapeutic index of orally administered pain relievers such as nonsteroidal antiinflammatory drugs (NSAIDs) and opioids.[4] Corticosteroids are most often delivered via the epidural route owing to this compartment's proximity to the putative source of pain. Epidural steroid injection (ESI) is the most common outpatient procedure for pain relief worldwide,[3] despite considerable controversy about the clinical indications for and effectiveness and risks of this approach.

BACKGROUND

Synthetic glucocorticoids mimic the mechanisms of endogenous glucocorticoid (cortisol) but have different levels of efficacy, potency, and affinity for glucocorticoid receptors (GRs). These hormones, whether elaborated endogenously or delivered exogenously, are characterized based on their actions in the body as either glucocorticoids (carbohydrate regulating) or mineralocorticoids (electrolyte regulating). When used clinically, the term "corticosteroids" usually designates glucocorticoids, which are administered in ESIs. Corticosteroids are anti-inflammatory agents, and it this mechanism of action that is most often thought to account for the analgesic benefit of this therapy in patients with spinal disorders; however, there is strong experimental evidence for the direct, neural antinociceptive effects of corticosteroids.[5] Corticosteroids have a broad scope of action beyond their analgesic effects. The wide-ranging effects of steroid hormones on fluid and electrolyte balance and function of the immune, cardiovascular, renal, endocrine, musculoskeletal, and nervous systems account for many of the unintended adverse effects of these agents when used as analgesics.[6] Four of the most commonly administered preparations of synthetic glucocorticoids for intraspinal injections include methylprednisolone, triamcinolone, betamethasone, and dexamethasone[7] (**Table 1**). The considerable variation among different glucocorticoid formulations with respect to potency, particle size, tendency to aggregate, pharmacokinetics, and half-life are summarized in **Table 1**.

Owing to the adverse effects associated with the use of high-dose glucocorticoids, highly potent formulations that achieve the same effect at lower doses are in demand. Efficacy of a glucocorticoid refers to the maximal activity (GR transactivation and transrepression as measured in a cell-based reporter assay) that it can achieve (usually at maximal concentration), whereas the potency of a glucocorticoid pertains to the concentration needed to reach one-half of its maximal activity. For 2 glucocorticoids of the same efficacy, a highly potent one will require a lower dose to achieve the same treatment effect.[8] Potency varies widely across corticosteroid formulations. Although there is no consensus on the ideal dose of steroid to be administered in an ESI,[9] the North American Spine Society (NASS) recommends limiting each ESI session to 80 mg of triamcinolone, 80 mg of methylprednisolone, 12 mg of betamethasone, or 15 mg of dexamethasone.[10] Approximately one-fifth the dose of dexamethasone and betamethasone is required to achieve an equivalent effect to that of methylprednisolone or triamcinolone. Notably, a glucocorticoid may have different potencies for transactivation and transrepression. In the case of dexamethasone, gene activation requires a 5-fold higher concentration than for gene repression. This variance allows for the development of highly potent glucocorticoids that can be administered in low doses to achieve repression of inflammation signaling while minimizing other side effects.[9]