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## Editorial

# Epidural corticosteroid injections: Still credible?



## ARTICLE INFO

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### 1. Widely performed yet not officially recommended

Abundant evidence from the literature indicates that epidural corticosteroid injections (ECSIs) are very widely performed throughout the world to treat patients with back or neck pain. Nevertheless, ECSIs are not recommended by the French High Authority for Health (HAS) as well as by the Food and Drug Administration (FDA). Furthermore, recommendations issued by scientific societies about ECSIs are scarce, as discussed below.

Obstacles to the evaluation of the benefits of ECSIs include the broad diversity of the conditions treated (e.g., low back pain versus nerve root pain), variations in the techniques used, especially injection routes and corticosteroid formulation, as well as the psychological, social, and occupational ramifications of spinal pain. These obstacles explain the fairly small number of high-quality randomized controlled trials.

The rationale for ECSIs lies in the inflammatory component involved in the pathogenesis of spinal and nerve root pain. Studies of nerve root pain due to disk impingement have demonstrated local inflammatory processes including cytokine release by the nucleus pulposus. Elevation of a neuroinflammation marker associated with a response to ECSIs was recently reported in patients with chronic lumbar nerve root pain [1]. However, in patients with spinal stenosis due to osteoarthritis, the role for inflammation is less well established and venous congestion may play a greater role.

Serious neurological adverse effects of ECSIs [2,3], although extremely rare compared to the large number of ECSIs performed, have generated controversy. Many studies have shown that these events are ascribable to the use of particulate corticosteroids (in suspension) injected via the intervertebral foramen or certain other approaches [4,5]. At the cervical spine, 24 cases were identified in a recent literature review [6], whereas two north american studies found slightly higher numbers [7,8]. The FDA database contains 90 cases (excluding cases of arachnoiditis), of which only 18 have been published [9]. The incidence and prevalence of serious neurological adverse events cannot be accurately determined due to the lack of

data on the number of ECSIs but are undoubtedly low, as no cases occurred in several cohorts of several hundred ECSIs [3]. Among particulate corticosteroid preparations, only cortivazol (Altim), a steroid which was marketed only in France and Tunisia, does not cause erythrocyte agglutination [10]. In France, after the removal of the cortivazol from the market, the healthcare authorities and several scientific societies developed guidelines and recommendations about the use of prednisolone acetate (Hydrocortancyl), which is another particulate corticosteroid which was involved in several cases of severe neurological complications [6]. Dexamethasone sodium phosphate is a water-soluble inorganic dexamethasone ester and is the only nonparticulate corticosteroid used for epidural injections. Dexamethasone is widely available in other countries as a pure solution. There is no evidence to suggest that dexamethasone can induce the neurological complications seen with particulate corticosteroids. However, the effectiveness of dexamethasone in solution compared to that of particulate corticosteroids is uncertain [11]. Local lasting of a steroid is likely to be shorter with a solution than with a crystalline preparation. Studies comparing the two types of corticosteroid are few in number and small in size. In France, dexamethasone is not licensed for epidural administration and is available only in hospitals as a preparation that contains sulfites, which can cause allergic reactions. Two French radiology societies (the *Société d'Imagerie Musculo-Squelettique* [S.I.M.S.] and *Société Française de Radiologie*) have advocated the use of this dexamethasone preparation in France for ECSIs [11].

Since the production of cortivazol was stopped, no corticosteroid designed for epidural injection devoid of history of neurological complications, and proven to be effective by extensive studies is available in France. Consequently, the role for ECSIs (notably via the transforaminal approach) to treat spinal pain deserves reappraisal.

### 2. Considerable variability in injection routes

At the cervical and lumbar spine, the epidural space can be reached by the interspinous, interlaminar, and transforaminal routes. Transforaminal injections can be infrapedicular, retroneural, or retrodiscal [12], and none of these three transforaminal routes has been proven safer than the others [13]. At the lumbar spine, the needle can also be inserted through the sacrococcygeal hiatus, although a volume of at least 20 mL is required to reach the L4 and L5 nerve roots [14]. Most of these routes are performed under fluoroscopy or computed tomography (CT) guidance and a contrast are used to check for the location and safety of the injection site. In french practice, exceptions are the lumbar interspinous route, for which identification of anatomical landmarks is sufficient,

**Table 1**  
SR-SFR and SIRIS-SFR guidelines about using prednisolone acetate for epidural injections to treat nerve root pain [6].

Cervical spine	Do not use the transforaminal route and do not inject a particulate corticosteroid, notably prednisolone acetate, via a posterior route.
Lumbar spine	Do not use the transforaminal route for particulate corticosteroid injections especially with prednisolone acetate. The task force recommends the continued use of prednisolone acetate in the licensed indications for spinal injections either via the posterior interspinous route, with or without imaging guidance, or via the interlaminar route under imaging guidance, provided the patient has no history of lumbar spine surgery. In patients with a history of lumbar spinal surgery, prednisolone acetate can be used in licensed indications to treat nerve root pain, provided the injection is not performed at the intervertebral level previously operated on. The vertebral level to be injected should be distant from the surgical site, and selected during a multidisciplinary discussion (imaging studies should be obtained to check that the neural arch and ligamentum flavum at the contemplated injection site are intact). In patients with a history of spinal surgery, the sacrococcygeal hiatus route can be used.
Facet joints	In patients with a history of surgery who require a corticosteroid injection into a facet joint, the injection should be performed at a distance from the surgical site, and the injection site should be selected during a multidisciplinary discussion.

SR-SFR: Spine Section recognized by the French Rheumatology Society (SR-SFR). SIRIS-SFR: Imaging and Interventional Rheumatology Section of the French Rheumatology Society (SR-SFR).

as well as the sacrococcygeal hiatus route, which can be guided by ultrasonography. Ultrasonography to guide lumbar epidural injections is being currently developed.

Nearly all the reported serious neurological adverse events seen after lumbar ECSIs occurred with the use of a particulate corticosteroid [6]. However, studies have shown that the transforaminal route and a history of surgery at the spinal levels where the injection is performed are also associated with an increased risk of severe neurological events.

The rationale for using the transforaminal route is that placing the corticosteroid in contact with the highly vascular spinal ganglion may increase the effectiveness of the injection. However, this hypothesis remains unproven. A prospective nonrandomized study of CT-guided injections found no superiority of the usual anterolateral transforaminal route over the posterolateral transforaminal or indirect transfacet routes at the cervical level [15].

Five to seven metameric radiculomedullary arteries supply the spinal cord by feeding the anterior spinal artery. The radiculomedullary artery that supplies the conus medullaris usually arises from a metameric artery, mostly from T9 to T11 and more frequently from the left side. This artery is known as the artery of Adamkiewicz. When this artery originates above T9, an inferior lumbar artery, which may arise from a lower lumbar or sacral level, consistently contributes to supply the conus medullaris [16]. An inadvertent injury to such variant arteries in the constrained space of the intervertebral foramen [3] is probably responsible for the cases of paraplegia reported after transforaminal injection of a particulate corticosteroid at the lower lumbar spine. The absence of bleeding at the needle hub as well as the injection of a contrast agent before the corticosteroid to check for the absence of vascular opacification do not seem to afford sufficient prevention [17]. The rare occurrence of neurological adverse events after injections into the posterior epidural space, where veins predominate and no spinal cord arteries are present, constitutes a more difficult enigma. One possible explanation is the presence of normal arteriovenous shunts along the course of radicular vessels [18], as well as of perimedullary arteriovenous fistulas. Similarly, the presence of arteriovenous fistulas within epidural scars may explain that a history of surgery at the injected spinal level is associated with a higher neurological risk.

### 3. Efficacy proved only in the short term

ECSIs have been proven effective in many indications, including spinal conditions [19,20]. However, they provide only a short-term relief, and their usefulness in a chronic disorder is therefore questionable. However, in nerve root pain, ECSIs may help the patient during the acute painful period which often lasts only a few weeks, until the spontaneous improvement occurs. This may also explain the lack of difference in efficiency between soluble

#### Box 1: Recommendations issued by the SIMS, FRI, and SFR about epidural corticosteroid injections [11,26].

Strong recommendation: Do not use the transforaminal route to inject particulate corticosteroids (notably prednisolone acetate), given the theoretically increased risk of ischemia in the spinal cord or in the distribution of the vertebral artery, at the cervical, thoracic, and lumbar spine.

When a cervical epidural injection (via the transforaminal or posterior route) or a lumbar transforaminal epidural injection is indicated (inadequate response to conservative treatment or diagnostic injection), currently available data suggest that dexamethasone may be associated with a lower risk of neurological adverse events compared to particulate steroids in patients with no history of spinal surgery.

At the lumbar spine, when an epidural injection via the posterior interlaminar route or the sacrococcygeal hiatus is indicated, either prednisolone acetate (Hydrocortancyl) or dexamethasone sodium phosphate can be used. In patients with prior surgery, the injection site must be at a distance from the surgical site and must be selected during a multidisciplinary discussion, unless the injection is done through the sacrococcygeal hiatus.

SIMS: musculoskeletal imaging society.

FRI: interventional radiology society.

SFR: French radiology society.

(dexamethasone) and particulate corticosteroids [21]. In a retrospective study, however, particulate corticosteroids produced better outcomes [22].

### 4. Recommendations from scientific societies

Although many review articles have been published, there are few recommendations from scientific societies concerning the use of ECSIs [23]. There have been a few responses [24,25] to the FDA's statement that ECSIs are not recommended [9]. Table 1 and Box 1 recapitulate the guidelines from the spine and interventional radiology section of the French Rheumatology Society (*Société Française de Rhumatologie*, SFR) and the recommendations developed by the musculo-skeletal imaging society (*Société d'Imagerie Musculo-Squelettique*, SIMS) and interventional radiology section (*Fédération de Radiologie Interventionnelle*, FRI) of the French Radiological Society (*Société Française de Radiologie*).

### 5. Other treatment options

The main issue is how ECSIs compare with the other available treatment options regarding risks/benefits. However, studies comparing the two treatments are scarce. Prolonged bedrest is known to be deleterious in patients with mechanical spinal disorders.

Consequently, sufficient pain relief must be provided to allow the patient to maintain some physical activity. Level 1 analgesics are often inadequate, and weak or strong opioids must often be given. However, their use should be kept as short as possible as their adverse effects may hinder physical activities. In addition, opioids may cause severe side effects in older patients. Nonsteroidal anti-inflammatory drugs (NSAIDs) may be used as the first-line treatment in severe pain and in the absence of contraindications. Inflammatory pain, including pain at night, supports the use of NSAIDs. Oral steroids is the main alternative. Provided the treatment is kept short, the side effects are usually acceptable. However, the doses used vary widely and are sometimes excessive. Further studies comparing NSAIDs to oral steroid therapy are needed. A few reports of systemic side effects of ECSIs have been published. The use of biotherapies have been proposed based on some pathophysiological arguments, but may result in unacceptable costs.

## 6. Potential side effects of lumbar epidural corticosteroid injections: are they acceptable?

The incidence of serious neurological adverse events after ECSIs is unclear [3]. Nevertheless, when their frequency and severity are compared to those associated with NSAID therapy and spinal surgery, ECSIs do not necessarily emerge as the least safe option. However, the risk of definitive paralysis in a patient with a condition whose natural outcome is usually favorable requires careful selection of fully informed patients. Furthermore, a recent study does not support the cost-effectiveness of lumbar ECSIs [27].

## 7. Cervical epidural corticosteroid injections (ECSIs)

Cervical interlaminar ECSIs are popular in some countries but rarely performed in France. Question is whether French physicians are too cautious. Neurological adverse events after particulate corticosteroid injections are both more common and more severe at the cervical level than at the lumbar spine. They also occur with posterior injection routes, perhaps due to the greater abundance of venous plexuses posteriorly. Therefore, we believe it is not reasonable to continue to use prednisolone acetate at the cervical spine, regardless of the injection route used.

## 8. Conclusion

Lumbar ECSIs are useful in everyday clinical practice and play an important role in the rheumatology and interventional radiology management of back pain. Particulate corticosteroids (prednisolone acetate) should be used only at the lumbar spine via the posterior interlaminar or interspinous lumbar route and only in patients with no history of surgery at the same site. Particulate corticosteroids should not be injected via the transforaminal route, whose relevance will not be assessable until a soluble corticosteroid preparation devoid of neurotoxic and allergy-inducing components becomes available. All healthcare professionals should strive to achieve this objective.

## Disclosure of interest

The authors declare that they have no competing interest.

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