Cervical Foraminal Versus Interlaminar Epidurals: Risks, Benefits, and Alternatives

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Abstract The goal of cervical epidural corticosteroid injections is to ameliorate pain from cervical radiculopathy. Controversy remains regarding the use and optimal delivery route of epidural medications in the cervical spine. The purpose of this review article is to compare the risks and benefits associated with cervical interlaminar and transforaminal epidural injections, and to describe alternatives to their use.

Keywords Transforaminal epidural injection · Interlaminar epidural injection · Spine intervention · Cervical spine · Corticosteroid · Radiculopathy · Risk

Introduction

The majority of patients with cervical radiculopathy can be managed conservatively, with approximately 10–20 % eventually having surgery [1, 2]. Recurrence rates as high as 30 % are observed in patients treated both surgically and conservatively [2, 3]. The primary goal of conservative treatment of acute radicular pain is to ameliorate the

symptoms and improve function while the favorable natural history runs its course. For this purpose, epidural corticosteroids in various forms have proven beneficial [4–8]. These injections are commonly used to treat radicular pain from disc herniation and degenerative stenosis. Failure of non-invasive conservative care with continued functional limitations is a relative indication for this treatment.

There are two commonly used approaches for cervical epidural injections: interlaminar and transforaminal. An interlaminar injection (occasionally called “interspinous” or inappropriately called “translaminar” or “intralaminar”) accesses the epidural space via a posterior approach between the lamina. The first description of cervical interlaminar epidural injections appeared 80 years ago [9].

Transforaminal injections in the cervical spine were more recently developed as a more target-selective alternative, and initially were presumed to provide advantages for safety and effectiveness [10–12]. A cervical transforaminal injection requires placement of a needle into the neuroforamen from an anterolateral approach. By targeting the anterior epidural space at a single level, transforaminal injections do provide more localized medication delivery [13, 14], and they are particularly target specific for foraminal and extraforaminal disc herniations [15, 16].

Debate continues on the ideal cervical epidural injection approach. This dispute arises from issues surrounding effectiveness and safety. The comparative effectiveness of these two approaches has never been determined in a prospective randomized trial, and each technique risks similar minor and serious complications [10, 17•, 18–20, 21•, 22–29]. Despite the absence of evidence for a superior technique, authors have voiced strong opinions on which injection to use in practice [30]. This chapter will discuss and compare the known risks of each approach, outline the currently published evidence for their clinical use, and review available alternatives.

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Cervical Transforaminal Injection Risks

The story of cervical transforaminal injections over the past quarter century contains important lessons for physicians evaluating new treatments. In the beginning, interventionists were happy to adopt a new cervical epidural approach since the serious risks inherent to cervical interlaminar epidural injections were well known by the time this new approach entered the scene. Early promotion of cervical transforaminal injections as a safer and more target selective alternative rapidly impacted practice patterns [31]. In the following years, reports of serious morbidity and death dispelled all myths about the improved safety of this approach [23, 25]. Many abandoned the procedure while others continued only after initiating additional safety measures.

In the hands of experts, minor complications occur in a small percentage of cases—from 0.32 to 1.6 % in two studies, each involving more than 1,000 injections [18, 32]. Reported serious complications involve different central nervous system infarctions resulting in anterior spinal artery syndrome [19, 20], quadriplegia [22], ischemic stroke [23, 24], and death [25, 26]. A recent literature review and a survey of pain physicians each highlighted the occurrence of these serious events [21•, 33]. Still, their actual incidences remain unknown since none have been recorded in any of the large published series [18, 32, 34]. Initially, different mechanisms were postulated to explain these observed neurologic infarcts. Needle-induced vessel trauma with dissection or spasm was initially suggested [19, 22], and a single case of arterial dissection was documented in a post-mortem examination [26]. Over time, evidence grew supporting another primary mechanism—inadvertent injection of particulate corticosteroids into a radiculomedullary artery or the vertebral artery resulting in microembolic ischemia [20, 24, 25, 35]. Studies of vascular anatomy demonstrate abundant collateral circulation making vasospasm of a single radicular artery an unlikely culprit [36], microscopic measures of corticosteroid particle size demonstrated the potential for an embolic shower infarction at the arteriole level [25, 27], and observations from two independent animal studies confirmed the presence of microembolic ischemia caused by intra-arterial injection of certain corticosteroids [37, 38••]. Thus, efforts to maximize the safety of cervical transforaminal injections have centered on reducing the risk of inadvertent intravascular injection.

Vascular uptake of contrast appears in one third of cervical transforaminal injections [39•, 40•] with the highest frequency observed in the upper cervical levels [40•]. Fortunately, the vast majority of these observations involve intravenous injection. Rates of inadvertent arterial injection are not as well documented with few published

estimates. Radicular artery uptake was observed in 2/354 injections in one center, for an incidence of 0.56 % [41•]. Incidental vertebral artery injection was estimated to have an incidence of 0.016 % in a purely informal analysis [30].

Although the risk associated with arterial injection exceeds that of venous injections, all vascular injections should be avoided. The neuroforamen is a dangerous and costly site for an IV injection of corticosteroids, not to mention the resulting loss of diagnostic accuracy and therapeutic potential. It is also important to note that arterial injections, in some instances, may only be recognized by the subsequent venous washout and therefore mistaken as a more benign venous injection [42].

Cervical Transforaminal Risk Reduction

Several methods have been proposed to avoid inadvertent vascular injection, and investigations have shown some to be more beneficial than others. Table 1 summarizes the evidence specific to cervical transforaminal injections. Detecting potential vascular injections was an early area of focus. Aspiration for blood with a syringe was shown to have good specificity but regrettably low sensitivity [43]. Therefore, it is useful if positive, but not if negative. Image confirmation of contrast distribution can also improve safety. Using intermittent fluoroscopy to identify cervical injection contrast patterns caused experienced physicians to miss nearly 50 % of the inadvertent vascular uptake that was observed using live fluoroscopy [44]. So, careful observation of the dynamic spread of contrast under live fluoroscopy is required to maximize the detection of accidental vascular injections. In another center, digital subtraction angiography (DSA) was shown to increase the rate of vascular detection from 18 to 33 % [39•]. If the above techniques fail, the routine use of an anesthetic test dose appears to be safe and capable of uncovering potentially dangerous intravascular injections, with a positive test in just 0.56 % of injections in one multicenter study [41•].

Needle selection and placement are also important to consider. At different times short-bevel and blunt-tip needles were recommended as potentially safer alternatives [45–47]. A later prospective study revealed no advantages in vascular injection risk using short-bevel needles [48•]. Animal studies have demonstrated that large-gauge blunt-tip needles are less likely than sharp needles to enter blood vessels and produce bleeding [46, 49], but this advantage was less noticeable with blunt-tip needles in sizes that are more likely to be used in the spine (22 and 25-gauge). This finding was confirmed in a prospective study of patients undergoing lumbar transforaminal injections that found no difference in inadvertent vascular injection rates between the sharp beveled needles, whitacre needles and blunt-tip

Table 1 Methods to reduce the risk of inadvertent vascular injection during transforaminal injections are shown in this table along with supporting citations; methods with known accuracy to detect vascular

injections are listed first, followed by methods without defined accuracy but with evidence of some benefit in formal research; finally, methods not yet formally tested are listed

Methods with known vascular detection accuracy in the cervical spine		
Test	Sensitivity (%)	Specificity (%)
Aspiration for blood [43]	46	97
Intermittent fluoroscopy [44]	54	90
Live fluoroscopy [40•]	99	100
Methods with other impacts defined by research		
Test	Details	
Anesthetic test dose	Positive in 0.75 % of cervical injections following live fluoroscopy to confirm contrast spread [41•]	
Digital subtraction (DSA)	Increases rate of detection of vascular uptake [39•]	
Needle size	Anesthetic test dose negative in 146 consecutive cervical injections confirmed using DSA [41•]	
Needle type	22-Gauge needles may cannulate cervical radicular arteries [51]	
Needle location	No difference in cervical injection vascular rates between various quinke needle gauges [48•]	
Needle location	In animals, advantages of blunt-tip needles are isolated to large [18, 20] gauges [46, 47]	
Needle location	No difference in vascular injection rates during lumbar transforaminals using quinke, chiba, whitacre and blunt-tip needles [48•, 50]	
Needle location	Posterior foramen to avoid vertebral artery, however intraforaminal vertebral artery anomalies are present in 7.6 % of patients [52•].	
Needle location	Mid foramen depth to avoid larger radicular arteries and deep cervical arteries in and near the outer foramen [36]	
Corticosteroid	Corticosteroids with particles consistently smaller than red blood cells do not cause the ischemic injuries observed from larger-particle steroids when intentionally injected into the vertebral arteries of animals [37, 38••]	
Methods suggested but not formally tested		
Test	Details	
Dissection risk screen	High risk suggests alternate methods be considered	
Minimizing sedation	Patients are more able to provide feedback about potential complications	
Extension tubing	Used to avoid manipulation and movement of the needle between contrast and corticosteroids	

needles [50]. At one time larger gauge needles were considered less likely to result in inadvertent vascular injection, however even the small radicular arteries can be cannulated by a 22-gauge needle [51]. Furthermore, needle gauge does not impact the observed vascular rates in cervical injections [40•], although it did impact the type of vascular injections observed. Specifically, larger gauge needles are more likely to produce vascular contrast patterns that appear simultaneous to the expected epidural injection [40•]. Since this specific type of vascular pattern is more difficult for physicians to detect [44], this finding favors the use of smaller gauge needles.

Needle placement in the posterior foramen is intended to avoid the vertebral artery, yet this region is not always safe. Radiographic studies show that intraforaminal vertebral artery anomalies are present in 7.6 % of patients [52•], and this can place the vertebral artery in the intended path of the needle [36]. Thus, a careful review of advanced imaging

is advised before placing a needle for a cervical transforaminal injection. While shallow placement in the foramen is sometimes considered, a cadaveric study showed that radicular arteries are larger and thus more likely to be cannulated in the outer foramen [36]. Plus, other deep cervical arteries with occasional feeder branches to the radicular arteries are more likely located here. As a result, the ideal depth of needle placement remains the mid-foramen (Fig. 1).

Currently, some safety methods are based on common sense alone, including patient screening for dissection risk factors, minimizing sedation, and avoiding needle manipulation after contrast confirmation by injection through extension tubing [25, 53]. Manipulating a needle to change from a contrast-filled syringe to a corticosteroid-filled syringe risks moving the needle tip. Accidental needle movement, even very small distances that are undetectable by the human hand, can be sufficient to move the needle

Fig. 1 *Left image* is an AP fluoroscopic view of a left C6–C7 transforaminal injection with epidural and peri-radicular contrast displacement. The image also shows ideal needle depth with the tip of the needle at the mid-point between two imaginary *vertical lines*. The first imaginary line corresponds with the lateral edge of the lateral

pillar and the second with the uncinat line. Image on the *right* is from a C7–T1 interlaminar injection. This image demonstrates the contralateral oblique view of needle tip placed into the epidural space along with epidural contrast displacement

from outside to inside a vessel lumen. Thus, the results of a contrast injection may not apply to the distribution of medications injected after swapping syringes on the needle hub. To avoid this, an extension tube is connected to the needle hub thru which all medications are injected without manipulating the needle. Although procedural competency is difficult to measure objectively, it is common sense that practitioners must ensure they have adequate training and experience to perform these potentially dangerous injections [54]. Indeed, one study did show that experience was positively associated with accuracy of detecting incidental vascular injections [54].

In the end, the ability to prove risk reduction by each of these methods is limited by the extremely low incidence of these complications. An extremely large prospective trial will be required to demonstrate the effectiveness of any single safety method. Ethical concerns limit the feasibility of such a trial. Recently, a case report questioned the accuracy of some of these tests by detailing a case of paraplegia following a lumbar transforaminal epidural injection performed using several of the above safety measures [55•].

Thus, as a final measure of safety, dexamethasone has become the corticosteroid of choice for cervical transforaminal injections. Since its particles are smaller than red blood cells [25, 56], it can avoid microembolic ischemia even if injected intra-arterially [37, 38••]. Further support for using dexamethasone in cervical transforaminal epidural injections comes from a small prospective randomized trial comparing it to a commonly used large-particulate corticosteroid with no significant differences in outcomes between the two treatment groups [57].

Cervical Interlaminar Injection Risks

To date, the largest study of cervical epidural injection risk is a retrospective survey of International Spine Intervention Society instructors who reported on a combined 5,968 cervical epidural steroid injections, 73 % interlaminar and 27 % transforaminal [18]. While the overall complication rate was higher in the interlaminar group (0.52 vs. 0.32 %), the difference was not statistically significant. No serious complications were reported in either group. This study's retrospective nature likely underestimates the true incidence of complications. Another retrospective chart audit of 345 interlaminar epidural injections also uncovered only minor and transient complications, but with a higher overall rate of 16.8 % [58]. This difference is explained by the inclusion of several complications not reported in the larger study. The specific minor complications reported and their incidences include: neck pain (6.7 %), non-positional headache (4.6 %), insomnia (1.7 %), vasovagal reaction (1.7 %), facial flushing (1.5 %), dural puncture (0.3 %), and fever the night of the procedure (0.3 %). These side effects and complications are similar to those seen in lumbar interlaminar injections.

Cervical interlaminar epidural injections have a time-honored track record, more than three times that of cervical transforaminal injections. Consequently, serious complications resulting from cervical interlaminar epidural injections have long been recognized. Published reports document cases of epidural hematoma with various neurologic involvement [59•, 60, 61], spinal cord injury [62], and death [29]. Closed-claims data demonstrates that a large number of unreported cases also exist [17••]. The actual incidence of

these events is unknown. Here again, none have been reported in a large published case series [18], but their continued appearance is one factor that led many to use the transforaminal approach when it was introduced.

Cervical interlaminar injections are most often administered at the C6–C7 or C7–T1 interspaces because the dorsal epidural space above this is scant [63, 64, 65]. Unfortunately, lateral imaging of the lower cervical spine can be obscured by shoulder anatomy, making it difficult to confirm the needle tip position. This has resulted in inadvertent needle advancement and injection into the spinal cord producing a permanent myelopathy [62]. A study of cervical injections for chronic pain in the American Society of Anesthesiologists' closed-claims database found that direct needle trauma and injection during interlaminar epidural injections was responsible for a greater number of spinal cord injuries than any other mechanism, including incidental arterial injection during transforaminal procedures [17]. Interestingly, the spinal cord injured patients were five times more likely to be unresponsive from sedation during the procedure.

Like transforaminals, interlaminar injections also have a vascular mechanism underlying potential catastrophic injuries, however the exact mechanisms differ. Excluding a major vascular malformation, the dorsal epidural space is void of arterial communication to central nervous system tissues, so arterial injection is not a major concern. What is of concern is the creation of a symptomatic hematoma [59, 60, 61, 66, 67]. Hematomas are more commonly reported in patients receiving continuous instead of single-shot epidural anesthesia [68]. Currently, there are no published estimates of the risk of epidural hematoma from single-shot epidural anesthetics, or in patients receiving epidural corticosteroid injections.

Even with proper technique and optimal needle placement, an epidural hematoma can occur following an interlaminar injection. On the other hand, needle placement in the cervical foramen has not been linked to symptomatic epidural hematoma formation. Certainly foraminal venous bleeding must occur in some transforaminal injections. Possibly, excess blood in the foramen flows preferentially into the extraforaminal tissues instead of building pressure in the spinal epidural space, whereas bleeding in the dorsal epidural space has no such escape. Because of this, some consider transforaminal injections a better option in any patient with increased bleeding risk, although here caution is also warranted.

Cervical Interlaminar Risk Reduction

Risk mitigation strategies for interlaminar epidural injections have focused on reducing epidural bleeding and

maximizing needle visualization. With percutaneous epidural access, there are two known risk factors for a spinal hematoma: continuous access for medication infusions, and disordered clotting. No other procedure or patient-related details are known to play a role, including needle type and gauge, practitioner experience, midline versus paramedian approach, etc. Thus, screening for and managing potential bleeding risk factors remains the only safety measure to minimize hematoma risk. To this end, the American Society for Regional Anesthesia and Pain Medicine has produced specific guidelines for treatment of patients undergoing neuraxial anesthetic procedures [69]. It is beyond the scope of this chapter to outline these risk factors and their recommended management, however it is important to note that hematomas can occur even when these guidelines are closely followed [70].

Cervical interlaminar injections are ideally performed using image guidance. In the study of closed-claims data, the on-site reviewers indicated that the appropriate use of radiographic guidance would have prevented the spinal cord injury in 45 % of cases [17]. Traditionally a lateral view is used to monitor needle depth, however shoulder anatomy can obscure this view. To improve visualization of needle tip depth and avoid inadvertent intradural and intramedullary placement, alternate imaging strategies were recently described. Depending upon the specific needle orientation and trajectory, the “contralateral oblique view” (Fig. 1) may provide superior information regarding needle depth [71]. Currently, many experienced practitioners are adopting this approach.

A few additional items deserve mention. The blood aspiration test during interlaminar injections, as with transforaminal injections, can produce false negative results [72, 73]. Excessive sedation should be avoided since a minimally responsive patient cannot provide the feedback that might indicate contact with the dura and its contents [17, 64, 74]. Some even argue that patients should not be sedated during these injections [74]. Finally, as with transforaminal injections, a careful review of advanced imaging before the procedure is useful to evaluate the available dorsal epidural space and to help plan the optimal needle trajectory.

Comparative Benefits and Risks

Relative to lumbar radiculopathy, cervical radiculopathy treatments are poorly researched and thus more controversial. In the lumbar spine, evidence suggests that epidural injections are effective in reducing pain and need for surgery. In addition, randomized controlled trials demonstrate that outcomes of lumbar transforaminal injections are superior to lumbar interlaminar injections [11, 12]. Currently, the

efficacy of cervical epidural injections, both interlaminar and transforaminal, remains unknown because neither has been tested against a placebo. Additionally, these two approaches have never been directly compared so their comparative effectiveness is unknown. Although the evidence is limited, it is not completely lacking.

There is one published randomized trial on cervical interlaminar injections. This study compared them to intramuscular corticosteroid injections, with superior results observed in the interlaminar injection group [8]. This finding supports the theory that a more target specific and higher concentration of corticosteroids produces better results. Of concern to some is that interlaminar injections are often delivered at sites distal to the known pathology, reducing their target specificity. Still, some studies have shown that just 2 cc of contrast can spread from the lower cervical spine up to the C2 level [75, 76]. In routine practice, compared to transforaminals, interlaminar epidurals involve larger injectate volumes containing less concentrated corticosteroids. Carried to its logical conclusion, the target specific theory would suggest a preference for transforaminal injections. While evidence supports this argument in the lumbar spine [11, 12], it has never been demonstrated in the cervical spine.

To overcome the lack of site specificity with interlaminar injections, an epidural catheter can be inserted and passed thru the epidural space to a target site [77]. Since interlaminar epidural injections have been shown to fail to deliver medications to the site of pathology in up to 74 % of patients [78] this practice seems logical on the surface. Regrettably, it also increases the risks inherent to interlaminar injections. Passage of a catheter provides additional opportunity for trauma to epidural veins and increases hematoma risk, much like continuous epidural access for medication infusions. Plus, multiple prospective studies have demonstrated that the standard interlaminar approach is effective in reducing pain and need for surgeries [8, 79–82, 83••].

For transforaminal epidural injections there are two published randomized trials. The first compared results of injections using small particle to large particle corticosteroids with equal benefits in the two groups [57]. The second study compared transforaminal injections of anesthetic and corticosteroid to transforaminal injections with anesthetic and saline [84]. While the authors concluded that no differences were observed between the two groups, there are serious problems with this study. The methods used to obtain the outcomes information is not defined, and the outcomes questionnaire used to measure success is not described. Thus, it is difficult to draw any conclusions from this study. As a result, the current best evidence comes from several prospective cohort studies. These have consistently demonstrated clinical benefits following cervical

transforaminal injections [53, 83••, 85]. In one study, the majority of patients recovered after a single injection [85].

When a decision is made to proceed with a cervical epidural injection, selecting between an interlaminar and transforaminal approach can be challenging. A proper risk–benefit analysis requires a comparison of both the effectiveness and the risks. Since comparative effectiveness data is lacking in the cervical spine, the risk–benefit profile rests on the risk side of the equation. Unfortunately, a clear decision cannot be made here either. Studies comparing risks associated with these two injections have found no significant differences [18]. Serious morbidity and death are rare complications documented with each procedure [17••, 30]. The incidence of these major complications remains unknown so any claim that one procedure is safer than the other is utterly unfounded. What is clear is that research during the past several years has focused more on improving the safety of transforaminal injections, but this does not guarantee superior safety relative to interlaminar injections. Because of these known risks, combined with the short supply of evidence, epidural injections are not considered first-line treatment for cervical radiculopathy. One must first consider the alternatives.

Alternatives

Fortunately, the natural history of cervical radiculopathy is favorable. The majority of individuals improve within several weeks or months without the aid of epidural injections [1]. Time spent educating and counseling patients about the expected course is of great value. It relieves fears and helps patients understand the benefits of a conservative treatment approach.

Medical management often starts with nonsteroidal anti-inflammatory drugs. Evidence of their effectiveness for neck pain relief is sparse [86, 87], and they do carry risks of renal, cardiovascular and gastrointestinal complications [88–90]. Opioid pain medications and muscle relaxants are known to help in the short-term [91, 92]. However, they produce drowsiness in approximately one third of patients, and can impair driving [93]. Long-term use of opioids is highly controversial. Many other pain-modifying drugs have been used in clinical practice, including tricyclic antidepressants and anti-epileptic drugs. More recently, duloxetine has received an FDA indication for osteoarthritis pain so its use is on-label for radiculopathy stemming from degenerative spine disease.

Systemic corticosteroids, oral and parenteral, are sometimes used. Surprisingly, this practice has never been shown to benefit patients with cervical radiculopathy. As detailed above, intramuscular corticosteroid administration is inferior to interlaminar epidural injection based on a single

randomized trial [8]. Another well-designed placebo controlled randomized trial found that oral corticosteroids were no better than placebo in the treatment of lumbar radiculopathy [94]. No other evidence exists to support or refute the use of systemic corticosteroids.

Other alternatives include physical therapy, mobilization, traction and acupuncture. Here again, data is sparse [95]. A randomized clinical trial of patients with chronic cervical radiculopathy compared surgery to physical therapy and cervical collar treatments finding no differences in pain, muscular strength or sensory loss at 4 months [96, 97]. A systematic Cochrane review of mobilization for neck pain found that mobilization combined with exercise is beneficial for persistent mechanical neck disorders, however there was insufficient evidence to draw conclusions for cervical radiculopathy [98]. Cervical traction is occasionally used as a supplement to manual therapy and exercise, however results from a multicenter randomized trial showed no additional benefit when traction was added to a multimodal treatment program [99]. Acupuncture is frequently used but there is no clear demonstration of its effectiveness in cervical radiculopathy [100].

Overall, the literature regarding non-invasive treatments for cervical radiculopathy is lacking. In fact, the evidence is less than that supporting epidural injection. Given the known favorable course of the disease, and the low risks associated with these alternative treatments, they still deserve first consideration. Epidural injections should be reserved for patients with the most severe symptoms who fail an initial course of more conservative treatment.

Conclusion

Current evidence regarding the conservative and interventional treatment of cervical radiculopathy provides limited guidance. While evidence supporting epidural corticosteroid injections exceeds that for non-invasive conservative measures, the risks associated with epidural injections and the generally favorable course of cervical radiculopathy support initial use of the conservative measures. While cervical epidural injections have a low incidence of minor complications, severe morbidity and death are rare complications associated with existing techniques, transforaminal and interlaminar. Currently, an evidence-based argument cannot be made to support the selection of one injection approach over the other. Methods to improve the safety of each approach have been described and studied, and practitioners need to understand their respective utility and limits.

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- Of importance
- Of major importance

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