Prospective Study

Immediate and Acute Adverse Effects Following Transforaminal Epidural Steroid Injections with Dexamethasone

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Free full manuscript: www.painphysicianjournal.com **Background:** Transforaminal epidural steroid injections (TFESI) are widely used for the conservative treatment of radicular pain. The use of dexamethasone in TFESIs is relatively new; therefore, immediate and acute adverse effects that it may cause are not fully updated.

Objective: To evaluate immediate and acute adverse effects following TFESI with dexamethasone.

Study Design: Prospective, observational study.

Setting: A spine center affiliated with a rehabilitation hospital.

Methods: One hundred fifty consecutive patients receiving TFESI for the management of radicular and axial spinal pain at the cervical, lumbar, and sacral levels with dexamethasone using fluoroscopic guidance with digital subtraction technology were enrolled. The occurrence of adverse effects in patients in the 2-week time period following interventions was monitored through a set of questionnaires followed up by phone calls scheduled for 1 day, day 3, and day 14. Intensity and duration of side effects were recorded.

Results: Of the 150 patients enrolled, 31 patients (19.5%) experienced adverse effects within the first 30 minutes following the intervention. The most common adverse effects were numbness and tingling in the limb, which developed in 19 patients (11.95%) followed by perineal pruritus that occurred in 7 cases (4.4%). Patients also reported experiencing adverse effects within the 3 days following intervention; most complained of headaches, insomnia, hiccups, flushing, and increased radicular pain. No major complications were noted.

Limitations: The sample size enrolled might be too small to perceive possible rare side effects related to the procedure. The 2-week follow-up period is a limitation for evaluating late side effects.

Conclusions: This study offers provision to interventionalists that TFESI with dexamethasone when performed by experienced hands and with proper technique has minor self-limited transient adverse effects that can be easily managed. Patients should be made aware of these adverse effects and their management. Further larger studies are needed to validate the safe use of dexamethasone and the safety of transforaminal epidural injections.

Key words: Transforaminal epidural steroid injection, complications, dexamethasone

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ransforaminal epidural steroid injections (TFESI) are widely used for conservative treatment of radicular pain (1-6). These injections have become highly recognized and accepted as a

conventional method of treatment, given that they are performed in accordance with the current available guidelines (7-9).

Dexamethasone is a steroid known to have no

particulates and therefore it has been recently advocated to be the drug of choice for use in TFESI (10-12). It has been substantially utilized as a treatment in various medical specialties for over 50 years and side effects regarding its oral and intravenous administration are appropriately identified (13,14). However, because the use of dexamethasone in TFESI is relatively a new practice, immediate and acute adverse effects that it may cause through this route of administration are not fully updated.

This study was considered to investigate the possible immediate and acute adverse effects after TFESI with dexamethasone in a prospective way.

METHODS

This study was conducted at a spine center in a major university affiliated hospital after the hospital institutional review board approved the protocol in accordance with the Declaration of Helsinki. Patients who met the inclusion criteria signed an informed consent that described the trial with its risks, benefits, alternatives, and objectives as per the institutional review board protocol. One hundred and fifty consecutive patients with radicular and axial pain were included in this prospective, single-arm, observational study. Each patient received TFESI in the cervical, lumbar, or sacral level. All the participants of this study initially consulted the spine center for management of painful spinal conditions. All patients underwent imaging with magnetic resonance imaging (MRIs) or computed tomography (CTs) (if MRIs were contraindicated) of the spine. The participants were first treated with conservative management, including medications and/ or physical therapy. However, when conservative treatment proved unsuccessful, they were recommended treatment of TFESI.

Inclusion Criteria:

- Providing informed consent to participate in the study
- At least 18 years of age
- Imaging findings of intervertebral disc pathology
- Axial back or neck pain
- Radicular leg or arm pain
- Lack of response to conservative management including medications and/or physical therapy.

Exclusion Criteria:

- Severe allergy to injectants
- History of steroid psychosis

- Tumor or tumor metastasis in the involved spinal area
- Infection at the injection site
- Coagulopathy
- Unstable spinal fracture or spinal instability
- Pregnancy
- Patients unable to provide informed consent.

Prior to the performance of each procedure, baseline data collected were age, diagnosis of the spine pathology and its level, gender, body mass index, presence of depression, medications used, history of allergies, history of diabetes, and prior spinal surgery or prior spine injections.

All procedures were performed by a fellowshiptrained interventional physiatrist (OEA), with over 9 years of experience in performing TFESI. All procedures were performed in an outpatient hospital ambulatory setting. Two independent physicians monitored patient complications. Only single dose vials were used and medications were withdrawn only after patients were on the fluoroscopy table, ready for the procedure. A General Electric OEC 9900 Elite fluoroscopy equipped with Digital Subtraction (DS) suite was used.

Medications used were Omnipaque 300 (30 mL vial), lidocaine 1% preservative free (5 mL vial), and preservative-free dexamethasone 10 mg/mL (1 mL vial-AAP Pharmaceuticals, Inc.). Medications were not mixed and each medicine was withdrawn in an individual syringe.

Twenty-five gauge 3.5 inch Quincke spinal needles were used for cervical injections. Twenty-two gauge (3.5 or 5 inches in length depending on patient body habitus) Quincke spinal needles were used for lumbar and sacral injections. Five mL Luer lock syringes were used for lumbar and sacral procedures and 3 mL Luer lock syringes and 5 inch tubing were used during cervical injections. Cervical injections were performed with the patients placed in a lateral position, head supported by a pillow, and placed in a neutral position. The needles were introduced under an oblique view, abutting the superior articular processes and slightly introduced forward into the inferior and posterior portion of the foramina. In lumbar injections, the patients were placed in a prone position and the needles were introduced to the 6 o'clock position under the pedicles and the positioning was confirmed in an antero-posterior view. For sacral injections, the needles were introduced to the foramina using a lateral to medial approach using antero-posterior viewing, and entering the foramina at the superior and lateral quadrant portion. Once the needles were positioned at the neural foramina, the stylets were withdrawn and blood in the hub (flash) was evaluated. This was followed by aspiration. One mL of contrast medium was subsequently injected to confirm needle placement. Once transforaminal flow was identified, an additional 0.5 mL to 1 mL of contrast was injected under DSA evaluating for missed vascular penetration with the other methods. As an added layer of safety, a lidocaine test was used (a test dose of lidocaine 1% was injected, 0.5 mL in cervical and 1 mL in lumbar injections and patients were monitored for alterations in sensation, motor weakness, or unusual metallic taste) prior to injecting preservative-free non-particulate dexamethasone 10 mg/mL (2 mL for lumbar and sacral injections).

Extension tubings were not used in lumbar injections as the needles were of a larger gauge and more sturdy. The larger gauge needles were stable in the foramina on connecting the different syringes of different medications in comparison with the 25-gauge needles in the cervical spine which can move easily on changing syringes. Additionally, the needles in the lumbar levels occasionally required the performer to apply physical pressure to maintain the position in the foramina depending on patient's girth and body habitus. The radiographic field in the cervical spine is much smaller and as the performer injects the contrast live under fluoroscopy his or her hand will be in the field if extension tubing is not used.

In lumbar injections, we did not obtain lateral views, as we do not recommend relying on lateral views while performing lumbar and thoracic TFESI as in the process of obtaining lateral views the appropriate depth of the needles is not assessed. Needle penetration into the central canal may occur which results in an intradural injection. Additionally obtaining lateral views significantly increases the radiation exposure to the patients and staff.

All the vascular injections detected in our study were venous in nature. The veins are characteristically serpiginous, of varying caliber, flowing longitudinally and transversely crossing the midline or moving out of the vertebral canal. Venous injection is of no consequence other than the need to be recognized and the needle to be repositioned. However radicular artery injection, especially through the artery of Adamkiewicz present at the lower thoracic or upper lumbar region, demonstrates contrast filling, medially flowing and travelling cephalad in the midline (anterior spinal artery). This would be best visualized using digital subtraction technology (15).

The occurrence of any side effect was recorded immediately after the injection and through structured follow-up phone calls (at one day, 3 days, and 2 weeks post-injection).

Data was categorically computed as "yes" or "no" regarding the presence or absence of adverse effects. The number of events was quantitatively computed and the frequency was presented in terms of percentage.

Chi-square tests were conducted to compare the categorical data of multiple baseline categories with the occurrence of side effects or not. For all comparisons, the significance level (alpha) admitted was lower than 0.05. Stata/SE 10.0 for Windows software (College Station, TX, USA) was used for the statistical analysis.

RESULTS

With the total of 150 patients enrolled in the study, 122 patients (81.3%) had lumbar TFESI and 28 cervical injections (18.6%). All cervical injections were single levels injections. Among the 122 lumbar injections, 86 patients (70.5%) received single level TFESI and 36 patients (29.5%) received 2 level or bilateral TFESI. Among the 150 patients, 109 patients (72.6%) were enrolled in the study for management of radicular pain and 41 (27.3%) were being treated for degenerative disc disease with discogenic axial pain. Thirty-nine (26%) patients had an injection less than 3 months prior to the study and were enrolled to receive a repeated injection. Fifty-one patients (34%) had a spinal injection more than 3 months prior to the study for any reason. Sixty patients (40%) had no prior spinal injections. Detailed patients' demographic characteristics and TFESI characteristics are demonstrated in Tables 1 and 2. There was no follow-up drop out during the study period. Thirty-one (20.66%) patients had vascular penetration detected by one of the methods used. Five (3.33%) were cervical injections, 13 (8.66%) at the sacral level, and 13 (8.66%) at the lumbar level.

Thirty-one patients (20.6% of total patients) described immediate effects after having injection: 15 patients (48.38%) reported numbness, 7 patients (22.58%) reported groin, genital, or perineal pruritus, 4 patients (12.9%) reported tingling sensations, and one patient (3.22%) reported weakness, general discomfort, low heart rate, shaking, and facial "warmth." We did not incorporate any immediate spinal or radicular pain that occurred before lidocaine was injected into the results as this effect is considered to be part of the procedure itself rather than an adverse effect.

During the first 3 days following the injections, patients reported increased radicular pain, increased pain at the injection site and the spine, lightheadedness, nausea, headache, heartburn, paresthesia, slight imbalance, rash, insomnia, hiccups, numbness, and hyperactivity/euphoria as side effects. No major complications were noted. A total of 121 minor side effects were reported by 71 patients (47.33%) during the first phone call (after one day of TFESI) and 29 side effects were reported by 20 patients (13.3%) after 3 days of TFESI.

After 2 weeks, only 2 patients (1.3%) complained of side effects after TFESI. One patient complained of an increase in radicular pain that started one week after the first injection when the patient was participating in physical activity, and another patient reported high blood sugar. The detailed occurrence and frequency of side effects are shown in Table 3.

On further review of the results, we noted that patients with a diagnosis of depression prior to injections developed more adverse effects (P = 0.042) especially numbness immediately after the injection (P < 0.001).

	Number of patients = 150
Age in years (Mean ± SD)	54.15 ± 15.48
Gender (Male/Female)	56/94
Body Mass Index in Kg/m2 (Mean ± SD)	27.80 ± 5.61 (Kg/m2)
Patients with obesity	36 (24%)
Patients with depression	27 (18%)
Number of medications in use (Mean ± SD)	6.10 ± 3.91
Patients with history of allergies	23 (15.33%)
Patients with diabetes	14 (9.33%)
Patients with prior spinal surgery	9 (6%)
Patients with no prior spine injections	60 (40%)
Prior spinal injection (more than 3 months)	51 (34%)
Prior spinal injection (less than 3 months)	39 (26%)

Half of the patients who underwent 2 levels or bilateral TFESI injections had at least one adverse effect vs. one third of the patients that underwent single level TFESI, however this was not statistically significant (Table 4).

All other variables, such as previous injections, use and number of medications, prior allergies, diabetes, dose of dexamethasone, dose of lidocaine, side, gender, body mass index, level of the procedure, vascular flow detection, and prior surgeries, were not statistically significant in relation to adverse effects (Table 5).

Discussion

To our knowledge, this is the first study evaluating side effects and complications of TFESI with dexamethasone performed with fluoroscopic guidance using digital subtraction and a strict protocol to prevent vascular penetration. We recognize that we are using a higher dose of dexamethasone in comparison to celestone or depo medrol doses, as it's a non-particulate steroid and has a very short half-life. The doses of dexamethasone or other frequently used steroids are not established and we believe that studies are needed to evaluate the most appropriate doses of steroids to be used. We have been using these doses of dexamethasone, 20 mg for lumbar TFESI and 15 mg for cervical TFESI, for several years. These doses are also widely used by spine interventionalists frequently performing transforaminal epidural injections.

In our study we attempted to provide all possible measures that we believe can eliminate devastating neurologic injury. We followed Scanlon et al's (16) recommendations of a test dose of lidocaine.

Patients were monitored for one minute after the lidocaine test injections, as Baker et al (17) noted that it would be expected that neurologic changes to occur quickly and should be easily appreciated in less than 30 seconds after local anesthetic injection. Karasek and Bogduk (18) described a patient developing quadriparesis developing within 60 seconds after 0.8 mL of lidocaine 2% was injected during a C6-C7 transforaminal

Table 2.	Transforaminal	epidural	steroid injections	(TFESI)	characteristics.

	Lumbar	Sacral	Cervical	Total
Single Level	68	18	28	114 (76%)
Two Level or Bilateral	16	20	0	36 (24%)
Total	84	38	28	150 (100%)
Radiculopathy (Lumbar Central Stenosis, Foraminal Stenosis)	69	14	26	109 (72.6%)
Discogenic pain (Degenerative Disc Disease/Disc Displacement)	12	24	5	41 (27.3%)

Side effect	Immediately after TFESI	One day after TFESI	3 days after TFESI	2 weeks after TFESI	
Number of patients	31 (20.6%**)	71 (47.3%**)	20 (13.3%**)	2 (1.3%**)	
Total reports	31	121	29	2	
Numbness	15 (48.38%)	5 (4.13%)	1 (3.44%)	0	
Pruritus (genital, perineal, groin area)	7 (22.58%)	0	0	0	
Shaking	1 (3.22%)	0	0	0	
Decrease of heart rate	1 (3.22%)	0	0	0	
Weakness	1 (3.22%)	0	0	0	
General discomfort	1 (3.22%)	0	0	0	
Increased pain at injection site	- *	21 (17.35%)	1 (3.44%)	0	
Headache	0	17 (14.04%)	3 (10.34%)	0	
Insomnia	NA	17 (14.04%)	3 (10.34%)	0	
Increased radicular pain	- *	11 (9.09%)	7 (24.14%)	1 (50%)	
Heart burn	0	8 (6.61%)	1 (3.44%)	0	
Increased spine pain	_ *	6 (4.95%)	3 (10.34%)	0	
Nausea	0	6 (4.95%)	2 (6.89%)	0	
Hyperactivity/euphoria/anxiety	0	6 (4.95%)	2 (6.89%)	0	
Tingling	4 (12.9%)	6 (4.95%)	1 (3.44%)	0	
Rash/flush	1 (3.22%)	5 (4.13%)	0	0	
Hiccups	0	3 (2.48%)	2 (6.89%)	0	
Imbalance	NA	2 (1.65%)	1 (3.44%)	0	
Elevation of heart rate	0	2 (1.65%)	0	0	
Muscle spasms/cramps	0	2 (1.65%)	1 (3.44%)	0	
Lightheadedness	0	1 (0.82%)	1 (3.44%)	0	
Pain on the other limb	0	1 (0.82%)	0	0	
Warm sensation on the limb	0	1 (0.82%)	0	0	
Cold sensation on the limb	0	1 (0.82%)	0	0	
Elevation in blood sugar	NA	0	0	1 (50%)	

Table 3. Occurrence and frequency of side effects.

*: not considered because it may be caused due to the nature of the procedure itself. **: percentage of total participants. NA: Not applicable

injection. The metallic taste in the mouth is noticed in intravascular injections of various medications including contrast and it is an adjunct in identifying vascular penetration. Following the lidocaine test, the injection of dexamethasone was performed over 30 – 60 seconds.

We are advocates of the performance of transforaminal epidural injections as we believe they are effective in managing spinal pain, especially radicular. This is due to the unique medication delivery site at the disc and nerve interface, which provides more targeted use of medications and improved outcomes (3,6,19-21). Botwin et al (22) found that TFESI achieved ventral flow in 100% of injections. These injections are performed through the needle introduction into "the safe triangle" at the 6 o'clock position inferior to the pedicle. Table 4. Side effects and number of levels per procedure. Qi square analysis of side effects after 2 or single level injections was not significant (P = 0.409).

	Side eff	Total	
	Ν	Y	
Single level	87	27	114
Two level	25	11	36
Total	112	38	150

Vascular evacuation of the therapeutic medication preventing it from reaching its target occurs in 11% of caudal ESI and interlaminar ESI, and in only 2% of TFESI (23,24). Therefore, the instillation of corticosteroids into the anterior epidural space, maximally reaching the targeted intervertebral disc, is best accomplished by the transforaminal approach rather than the interlaminar or caudal techniques. The purpose of our study is not to establish the exact amount of therapeutic doses of steroids or to compare transforaminal injections to the various types of epidural injections; however, anatomically installing the steroids in the disc/nerve interface is the goal of a successful TFESI. Our study objective is also not to compare dexamethasone injections to particulate steroids injections, and we are not establishing the efficacy of a particular steroid over the others. We do not use particulate steroids in transforaminal injections due to numerous known reports of devastating spinal cord and cerebral infarcts after transforaminal injections in the past decade (12,16,25-37). There are multiple theories explaining the different causes of these infarcts (38) with the leading hypothesis being that inadvertent intra-arterial injection of particulate corticosteroid creates an embolus (12,32,38,39) causing a down-stream infarct. The role of particulate steroids was also evaluated, with different particle sizes identified (11,34) with dexamethasone identified not to have particles under laser microscope (11). In a study by Okubadejo et al (40), 11 pigs underwent intravascular injections of depomedrol, dexamethasone, or prednisolone into the vertebral artery. All the pigs injected with depomedrol failed to gain consciousness after the injection, the other 2 groups recovered with no deficits.

A variable that generates discussion as a possible cause of intravascular injections is the type and size of needle used during TFESI, particularly at the cervical level. Quincke needles are widely used, particularly among interventionalists frequently performing cervical transforaminal injections (41). We performed our study using these needles. Blunt-tip needles were popularized to reduce the chances of arterial penetration. However, there are recent reports that dispute that blunt needles eliminate intravascular entry and prevent vasospasm or vessel injury (42,43). More recently, in their review, Atluri et al demonstrated that there was no correlation between the variable type or size of needles and vascular complications in lumbar transforaminal injections (44).

Since the emergence of complication reports and the publication of Scanlon et al's survey (16) to spine interventionalists on complications of cervical transforaminal injections, a heightened awareness of the risks of TFESI has developed. The use of dexamethasone in TFESI has expanded widely for its safety. More recently, the US Food and Drug Administration (FDA) expedited a drug safety announcement concerning the use of steroids in the epidural space (45). Even though dexamethasone is cited as one of the steroids in the alert, we did not identify specific adverse effects or complications.

We conducted this study in an effort to evaluate the acute complications encountered with the use of dexamethasone along with the prudent vascular penetration prevention measures described above, for minimizing risks of major complications after TFESI. The confirmation of intravascular injection with DSA increased the detection rate of vascular penetration. DSA detected an additional 5.26% of the intravascular needle placements, following the traditional methods (41).

Dexamethasone sodium phosphate is of a rapid onset of action and of short duration compared to other less soluble preparations. At equipotent doses, dexamethasone almost lacks the salt-retaining properties in hydrocortisone. Dexamethasone sodium phosphate suspension is used intravenously very commonly for treatment of multiple systemic conditions and gained popularity amongst spine interventionalists (13).

Huston et al (46) prospectively studied acute side effects and complications of TFESI, but there was no DS used and the medications used were celestone 6 mg and lidocaine. Their analysis of 350 consecutive cervical and lumbar transforaminal injections identified no significant complications. Lutz et al (6) found no dural punctures or other major complications in 50 patients that underwent lumbar transforaminal epidural injections. Botwin et al (20) reviewed complications in 322 transforaminal lumbar epidural injections done in 207 patients. They reported the complete absence of postdural puncture headache. The most common complication found in their study was headaches, occurring in 3.1% of patients. These headaches were transient and resolved after 24 hours. There was no intrathecal pattern noted when epidurograms were reviewed. In our study, 17 (10.69%) of the patients complained of headache, 3 (1.8%) of which lasted for 3 days; the others resolved in 24 hours.

One interesting side effect noted was temporary perineal pruritus occurring immediately after dexamethasone injection. This was not noted with prior epidural injection studies using different steroids. It is possible that it is due to the rapid injection of the medicine, due to an unrecognized vascular injection, or both. This causes momentary discomfort to patients, who might also be surprised by its occurrence and question whether it is related to the procedure. We are currently not aware of any other side effects associated; however, further evaluation may be relevant due to the possibility of unrecognized systemic injection or absorption. Pruritus after intravenous (IV) injection of dexamethasone is a known side effect described initially in the literature in 1972 by Czerwinski et al (14), who performed a randomized, controlled, double-blinded clinical trial in which healthy volunteers underwent IV infusion of dexamethasone. Anogenital pruritus was observed in patients that received dexamethasone with an onset varying from 15 seconds (bolus group) to 5 minutes (slower infusion speed), lasting seconds to minutes.

In 1986, Baharav et al (47) reported 7 cases of what they described as a "severe itching, burning sensation and squeezing pain in the perineal region" in oncology patients who received a 12 mg bolus of IV dexamethasone as an antiemetic agent during chemotherapy. The authors emphasized the obscure nature of the observed reaction, which was endorsed by Thomas (48) who conducted a literature review in the same year and published it in the same journal. Additionally, he emphasized that similar reactions had already been reported with IV infusion of other steroid drugs such as prednisolone and hydrocortisone since 1962. Andrews and Grunau (49) in odontology and Zaglama et al (50) and Taleb et al (51) in oncology also reported similar symptoms. All of them reported the reaction observed with a bolus infusion of IV dexamethasone in a dose that ranged from 8 to 100 mg. The description of symptoms were similar: severe pruritus, tingling, prickling, itching, and burning sensation in the perineum or genital area, beginning rapidly and never lasting less than 30 seconds or more than 6 minutes. Perineal pruritus following dexamethasone IV injection remains poorly understood. It is suggested could be related to the phosphate ester of the dexamethasone sodium phosphate (52).

We previously reported a patient who had an immediate episode of severe pruritus all over the body after a left L5 transforaminal epidural injection that lasted for one minute. Contrast was not used in this patient due to severe allergy and despite no blood flash and negative blood aspiration, it is possible that a vascular injection could have occurred (53). In the current study, we found pruritus complaint in the perineal area in 7 (4.6%) procedures. There were no signs of vascular penetration in any of these patients.

In regards of hiccups, a number of case reports

(54-56) have linked epidural steroid injections to the occurrence of hiccups but none was with the use of dexamethasone. In our study, 3 (10.69%) of the patients reported hiccups, 2 (1.8%) of which lasted for 3 days; the other resolved in 24 hours. While hiccups are usually benign, severe attacks may lead to exhaustion, eating difficulties, and affect quality of life (57). Several authors reported dysphonia following steroid injections (58-60) but none of them as well used dexamethasone. The mechanism of dysphonia after peripheral steroid injection is unknown but thought to result from vascular uptake of the steroid. In our cohort of patients no dysphonia was found.

In this study, 8 (5.3%) patients reported heartburn after the injection. Except for one patient that continued to experience heartburn for 3 days, the other 7 patients felt improvement of the symptom within one day. Glucocorticoid oral intake is a possible cause of peptic ulcer disease including bleeding and perforation. This is of particular concern when there is the concomitant use of non-steroidal anti-inflammatory drugs. To the best of our knowledge no report of peptic ulcers was ever described to be caused by epidural injections.

We found 5 (3.33%) patients to experience facial flushing. One of them started to have symptoms minutes after the injection. Botwin et al (61) found that 3 out of 139 patients (2.3%) who received epidural steroid injections experienced facial flushing. Cicala et al (62) found facial flushing in 18 of 204 patients (9.3%) receiving cervical epidural corticosteroid injections. De Sio et al (63), in a larger study on steroid epidural injections, reported that patients who had taken diphenhydramine subsequently to the appearance of the side effect seemed to experience a slightly shorter duration of reaction compared with patients who did not take it once a reaction had occurred.

A diagnosis of depression prior to the injection was shown to increase the frequency of developing adverse effects, especially numbness immediately after the TFESI. Since the trial was not powered to this analysis, it is hard to know if it's because of the use of antidepressants or because these patients are more sensitive to medications or if they are hyper-vigilant to their symptoms. We don't believe that numbness is caused by dexamethasone as it does not have significant anesthetic properties to our knowledge. All adverse effects improved in 3 days in this group of patients.

One diabetic patient had elevated blood glucose level of 15 points that lasted for one week. Steroids can affect the metabolism by exerting an anti-insulin action in peripheral tissues and raise the plasma glucose levels. This poses a risk for uncontrolled insulin dependent patients, even though the effects of the steroids injections on the blood sugar level usually last less than one week (13).

The injections had a number of minor side effects that did not last more than 3 days. One patient had increased radicular pain for 2 weeks. These minor complications noted are either related to the procedure itself or due to the medications. We generally advise the patients to use diphenhydramine or other allergy medications at night for flushing and insomnia. We also recommend acetaminophen 500 mg every 6 hours as needed for headache and pain and prochlorperazine orally 5 mg every 6 hours if needed for hiccups. We recognize that it is possible that the ominpaque 300 and lidocaine 1% used might have contributed to the immediate adverse effects, occurring on the day of the injections, but it is not likely that the side effects occurring later are related. In this study, there were no serious complications noted.

CONCLUSION

This study offers a provision to interventionalists that TFESI with dexamethasone when performed by experienced hands and with proper technique have minor transient adverse effects. These complications are self-limited, managed easily, and patients should be aware of all possible methods of treatment and side effects in advance. Up to the writing of this manuscript, we are not aware of vascular complications occurring after the use of dexamethasone in TFESI. Further larger studies are needed to validate the use of dexamethasone and the safety of TFESI. We advise against the use of particulate steroids given the evidence implicating their role in central nervous system infarcts following inadvertent intra-arterial administration. We advocate watching carefully for all signs of vascular penetration to minimize the occurrence of major complications.

References

- Delport EG, Cucuzzella AR, Marley JK, Pruitt CM, Fisher JR. Treatment of lumbar spinal stenosis with epidural steroid injections: A retrospective outcome study. Arch Phys Med Rehabil 2004; 85:479-484.
- Cooper G, Lutz GE, Boachie-Adjei O, Lin J. Effectiveness of transforaminal epidural steroid injections in patients with degenerative lumbar scoliotic stenosis and radiculopathy. *Pain Physician* 2004; 7:311-317.
- Vad VB, Bhat AL, Lutz GE, Cammisa F. Transforaminal epidural steroid injections in lumbosacral radiculopathy: A prospective randomized study. Spine (Phila Pa 1976) 2002; 27:11-16.
- Buenaventura RM, Datta S, Abdi S, Smith HS. Systematic review of therapeutic lumbar transforaminal epidural steroid injections. *Pain Physician* 2009; 12:233-251.
- Schaufele MK, Hatch L, Jones W. Interlaminar versus transforaminal epidural injections for the treatment of symptomatic lumbar intervertebral disc herniations. *Pain Physician* 2006; 9:361-366.
- Lutz GE, Vad VB, Wisneski RJ. Fluoroscopic transforaminal lumbar epidural steroids: An outcome study. Arch Phys

Med Rehabil 1998; 79:1362-1366.

- Windsor RE, Storm S, Sugar R, Nagula D. Cervical transforaminal injection: Review of the literature, complications, and a suggested technique. *Pain Physician* 2003; 6:457-465.
- Malhotra G, Abbasi A, Rhee M. Complications of transforaminal cervical epidural steroid injections. Spine (Phila Pa 1976) 2009; 34:731-739.
- Rathmell JP. Toward improving the safety of transforaminal injection. Anesth Analg 2009; 109:8-10.
- Cohen SP, Maine DN, Shockey SM, Kudchadkar S, Griffith S. Inadvertent disk injection during transforaminal epidural steroid injection: Steps for prevention and management. *Pain Med* 2008; 9:688-694.
- Benzon HT, Chew TL, McCarthy RJ, Benzon HA, Walega DR. Comparison of the particle sizes of different steroids and the effect of dilution: A review of the relative neurotoxicities of the steroids. *Anesthesiology* 2007; 106:331-338.
- Tiso RL, Cutler T, Catania JA, Whalen K. Adverse central nervous system sequelae after selective transforaminal block: the role of corticosteroids. Spine J 2004; 4:468-474.

- El Abd O. Steroids in spine interventions. In: Slipman CW DR, Simeone, FA, Mayer, TG (eds). Interventional Spine: An Algoritmic Approach. 1. Elsevier Inc, Philadelphia, 2008, pp 155-156.
- Czerwinski AW, Czerwinski AB, Whitsett TL, Clark ML. Effects of a single, large, intravenous injection of dexamethasone. *Clin Pharmacol Ther* 1972; 13:638-642.
- Bogduk N, Dreyfuss P, Baker R, Yin W, Landers M, Hammer M, Aprill C. Complications of spinal diagnostic and treatment procedures. *Pain Medicine* 2008; 9:S11-S34.
- Scanlon GC, Moeller-Bertram T, Romanowsky SM, Wallace MS. Cervical transforaminal epidural steroid injections: More dangerous than we think? Spine (Phila Pa 1976) 2007; 32:1249-1256.
- Baker R, Dreyfuss P, Mercer S, Bogduk N. Cervical transforaminal injection of corticosteroids into a radicular artery: A possible mechanism for spinal cord injury. *Pain* 2003; 103:211-215.
- Karasek M, Bogduk N. Temporary neurologic deficit after cervical transforaminal injection of local anesthetic. *Pain Med* 2004; 5:202-205.
- 19. Riew KD, Yin Y, Gilula L, Bridwell KH,

Lenke LG, Lauryssen C, Goette K. The effect of nerve-root injections on the need for operative treatment of lumbar radicular pain. A prospective, randomized, controlled, double-blind study. J Bone Joint Surg Am 2000; 82-A:1589-1593.

- 20. Botwin KP, Gruber RD, Bouchlas CG, Torres-Ramos FM, Sanelli JT, Freeman ED, Slaten WK, Rao S. Fluoroscopically guided lumbar transformational epidural steroid injections in degenerative lumbar stenosis: An outcome study. Am J Phys Med Rehabil 2002; 81:898-905.
- Slipman CW, Lipetz JS, Jackson HB, Rogers DP, Vresilovic EJ. Therapeutic selective nerve root block in the nonsurgical treatment of atraumatic cervical spondylotic radicular pain: A retrospective analysis with independent clinical review. Arch Phys Med Rehabil 2000; 81:741-746.
- Botwin K, Natalicchio J, Brown LA. Epidurography contrast patterns with fluoroscopic guided lumbar transforaminal epidural injections: A prospective evaluation. Pain Physician 2004; 7:211-215.
- Sullivan WJ, Willick SE, Chira-Adisai W, Zuhosky J, Tyburski M, Dreyfuss P, Prather H, Press JM. Incidence of intravascular uptake in lumbar spinal injection procedures. Spine (Phila Pa 1976) 2000; 25:481-486.
- 24. Furman MB, O'Brien EM, Zgleszewski TM. Incidence of intravascular penetration in transforaminal lumbosacral epidural steroid injections. *Spine (Phila Pa* 1976) 2000; 25:2628-2632.
- 25. Houten JK, Errico TJ. Paraplegia after lumbosacral nerve root block: Report of three cases. *Spine J* 2002; 2:70-75.
- 26. Huntoon MA, Martin DP. Paralysis after transforaminal epidural injection and previous spinal surgery. *Reg Anesth Pain Med* 2004; 29:494-495.
- Somayaji HS, Saifuddin A, Casey AT, Briggs TW. Spinal cord infarction following therapeutic computed tomographyguided left L2 nerve root injection. Spine (Phila Pa 1976) 2005; 30:E106-E108.
- Glaser SE, Falco F. Paraplegia following a thoracolumbar transforaminal epidural steroid injection. *Pain Physician* 2005; 8:309-314.
- Quintero N, Laffont I, Bouhmidi L, Rech C, Schneider AE, Gavardin T, Dizien O. [Transforaminal epidural steroid injection and paraplegia: Case report and bibliographic review]. Ann Readapt Med Phys 2006; 49:242-247.
- 30. Kennedy DJ, Dreyfuss P, Aprill CN, Bog-

duk N. Paraplegia following imageguided transforaminal lumbar spine epidural steroid injection: Two case reports. *Pain Med* 2009; 10:1389-1394.

- Brouwers PJ, Kottink EJ, Simon MA, Prevo RL. A cervical anterior spinal artery syndrome after diagnostic blockade of the right C6-nerve root. *Pain* 2001; 91:397-399.
- Ludwig MA, Burns SP. Spinal cord infarction following cervical transforaminal epidural injection: A case report. Spine (Phila Pa 1976) 2005; 30:E266-E268.
- Muro K, O'Shaughnessy B, Ganju A. Infarction of the cervical spinal cord following multilevel transforaminal epidural steroid injection: Case report and review of the literature. J Spinal Cord Med 2007; 30:385-388.
- 34. Rozin L, Rozin R, Koehler SA, Shakir A, Ladham S, Barmada M, Dominick J , Wecht CH. Death during transforaminal epidural steroid nerve root block (C7) due to perforation of the left vertebral artery. Am J Forensic Med Pathol 2003; 24:351-355.
- McMillan MR, Crumpton C. Cortical blindness and neurologic injury complicating cervical transforaminal injection for cervical radiculopathy. *Anesthesiology* 2003; 99:509-511.
- Suresh S, Berman J, Connell DA. Cerebellar and brainstem infarction as a complication of CT-guided transforaminal cervical nerve root block. *Skeletal Radiol* 2007; 36:449-452.
- Beckman WA, Mendez RJ, Paine GF, Mazzilli MA. Cerebellar herniation after cervical transforaminal epidural injection. *Reg Anesth Pain Med* 2006; 31:282-285.
- Glaser SE, Shah RV. Root cause analysis of paraplegia following transforaminal epidural steroid injections: The 'unsafe' triangle. Pain Physician 2010; 13:237-244.
- Jasper JF. Role of digital subtraction fluoroscopic imaging in detecting intravascular injections. *Pain Physician* 2003; 6:369-372.
- 40. Okubadejo GO, Talcott MR, Schmidt RE, Sharma A, Patel AA, Mackey RB, Guarino AH, Moran CJ, Riew KD. Perils of intravascular methylprednisolone injection into the vertebral artery. An animal study. J Bone Joint Surg Am 2008; 90:1932-1938.
- El Abd OH, Amadera JE, Pimentel DC, Pimentel TS. Intravascular flow detection during transforaminal epidural injections: A prospective assessment. Pain

Physician 2014; 17:21-27.

- Smuck M, Leung D. Inadvertent injection of a cervical radicular artery using an atraumatic pencil-point needle. Spine (Phila Pa 1976) 2011; 36:E220-E223.
- Gharibo C, Koo C, Chung J, Moroz A. Epidural steroid injections: An update on mechanisms of injury and safety. Techniques in Regional Anesthesia & Pain Management 2009; 13:266-271.
- Atluri S, Glaser SE, Shah RV, Sudarshan G. Needle position analysis in cases of paralysis from transforaminal epidurals: Consider alternative approaches to traditional technique. *Pain Physician* 2013; 16:321-334.
- 45. US Food and Drug Administration: FDA Drug Safety Communication: FDA requires label changes to warn of rare but serious neurologic problems after epidural corticosteroid injections for pain. April 23, 2014. www.fda.gov/downloads/ Drugs/DrugSafety/UCM394286.pdf.
- 46. Huston CW, Slipman CW, Meyers JS, Yang ST, Anghel BN. Side effects and complications of fluoroscopically guided nerve root injections. Arch Phys Med Rehabil 1996; 9:937.
- Baharav E, Harpaz D, Mittelman M, Lewinski UH. Dexamethasone-induced perineal irritation. N Engl J Med 1986; 314:515-516.
- Thomas VL. More on dexamethasoneinduced perineal irritation. N Engl J Med 1986; 314:1643-1644.
- Andrews D, Grunau VJ. An uncommon adverse effect following bolus administration of intravenous dexamethasone. J Can Dent Assoc 1986; 52:309-311.
- Zaglama NE, Rosenblum SL, Sartiano GP, Brady M, Gonzalez MF, Valdivieso JG. Single, high-dose intravenous dexamethasone as an antiemetic in cancer chemotherapy. Oncology 1986; 43:27-32.
- Taleb N, Geahchan N, Ghosn M, Brihi E, Sacre P. Vulvar pruritus after high-dose dexamethasone. Eur J Cancer Clin Oncol 1988; 24:495.
- Perron G, Dolbec P, Germain J, Bechard P. Perineal pruritus after i.v. dexamethasone administration. Can J Anaesth 2003; 50:749-750.
- El Abd O, Amadera JED, Pimentel DC. General pruritus as an unusual adverse effect after transforaminal epidural injection with dexamethasone: A case report. PM&R 2011; 3:S296.
- 54. McAllister RK, McDavid AJ, Meyer TA, Bittenbinder TM. Recurrent persistent

hiccups after epidural steroid injection and analgesia with bupivacaine. *Anesth Analg* 2005; 100:1834-1836.

- 55. Slipman CW, Shin CH, Patel RK, Braverman DL, Lenrow DA, Ellen MI, Nematbakhsh MA. Persistent hiccup associated with thoracic epidural injection. Am J Phys Med Rehabil 2001; 80:618-621.
- Abbasi A, Roque-Dang CM, Malhotra G. Persistent hiccups after interventional pain procedures: A case series and review. PM R 2012; 4:144-151.
- 57. Gilbar P, McPherson I. Severe hiccups during chemotherapy: corticosteroids the likely culprit. J Oncol Pharm Pract

2009; 15:233-236.

- Zaman FM, Wong M, Slipman CW, Ellen MI. Dysphonia associated with shoulder steroid injection. Am J Phys Med Rehabil 2005; 84:307-309.
- 59. Bhat AL, Chow DW, DePalma MJ, Garvan C, Chou L, Lenrow D, Slipman CW. Incidence of vocal cord dysfunction after fluoroscopically guided steroid injections in the axial skeleton. Arch Phys Med Rehabil 2005; 86:1330-1332.
- 60. Slipman CW, Chow DW, Lenrow DA, Blaugrund JE, Chou LH. Dysphonia associated with epidural steroid injection: A case report. Arch Phys Med Rehabil

2002; 83:1309-1310.

- Botwin KP, Gruber RD, Bouchlas CG, Torres-Ramos FM, Freeman TL, Slaten WK. Complications of fluoroscopically guided transforaminal lumbar epidural injections. Arch Phys Med Rehabil. 2000; 81:1045-1050.
- 62. Cicala RS, Westbrook L, Angel JJ. Side effects and complications of cervical epidural steroid injections. J Pain Symptom Manage 1989; 4:64-66.
- 63. DeSio JM, Kahn CH, Warfield CA. Facial flushing and/or generalized erythema after epidural steroid injection. *Anesth Analg* 1995; 80:617-619.