Clinical Study

Detection of Intravascular Injection During Cervical Transforaminal Epidural Injection: A Comparison of Digital Subtraction Angiography and Real Time Fluoroscopy

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Background: Transforaminal epidural injection (TFEI) with local anesthetics and steroids are effective in treating spinal radicular pain. However, inadvertent intravascular injection can lead to severe neurologic complications. To reduce complications of intravascular injection, use of imaging modality, such as real-time fluoroscopy (RTF) or digital subtraction angiography (DSA), has been recommended. DSA is an imaging technique that can clearly visualize the blood vessels from surrounding bones or dense soft tissues by subtracting the pre-contrast image from the image after injecting contrast medium.

Objective: In this study, we investigated whether there is a difference between RTF and DSA in the detection of intravascular injection during cervical TFEI.

Study Design: Clinical study.

Setting: Pain clinic in South Korea.

Methods: We prospectively examined 137 cervical TFEIs on 128 patients who have a radiating pain from spinal stenosis and herniated nucleus pulposus. The needle position was confirmed using biplanar fluoroscopy and 2 mL of nonionic contrast medium was injected at the rate of 0.5 mL/sec under RTF. Thirty seconds later, 2 mL of nonionic contrast medium was injected at the rate of 0.5 mL/sec under DSA. Intravascular injection was defined as contrast medium spreading throughout the vascular channel during injection of contrast medium under RTF and DSA. This study is registered in the ClinicalTrials.gov (NCT03040648).

Results: The detection rate of intravascular injection in RTF was not statistically different compared to that in DSA (30.7 % vs. 34.3%, $P > 0.05$).

Limitations: We injected 2 mL of contrast medium at the rate of 0.5 mL/sec. Further studies about the ideal injection speed and volume of contrast medium for improvement of detection of intravascular injection during TFEI are needed. This study was a single center study. Therefore, multi-center studies are needed to obtain the high level of evidence. Additionally, the procedural pain physician was not blinded to the type of imaging modality, such as RTF and DSA, to detect intravascular injection. To minimize this confirmation bias and provide homogenous procedural conditions for TFEI, the same procedural physician performed all 137 injections.

Conclusions: In this study, there is no significant difference in detection rate of intravascular injection between RTF and DSA during cervical TFEI.

Key words: Analgesia, bleeding, clinical trials, complications, diagnostic equipment, epidural, radiculopathy, spine

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Transforaminal epidural injections (TFEI) with local anesthetics and steroids are an effective treatment option for cervical and/or lumbar spinal radicular pain (1,2). Schellhas et al (3) demonstrated that cervical selective nerve root injection is useful for cervical radicular pain in a retrospective study including 4612 patients who underwent fluoroscopic guided cervical selective root injection. However, during TFEI intravascular injection should be avoided, which can cause fatal neurologic deficits, such as spinal infarction and cerebral infarction (4-7). To avoid intravascular injection, use of imaging modality, such as real-time fluoroscopy (RTF) or digital subtraction angiography (DSA), has been recommended (7-11). In a recent meta-analysis in 2015, DSA had a 32% improvement for detection of intravascular injection during lumbosacral TFEI, compared to RTF (10). However, Kim et al (11) failed to find any benefit of DSA during lumbosacral TFEI, compared to RTF.

The incidence of intravascular injection during TFEI with RTF guidance depends on spinal level. The previous studies using RTF demonstrated that the incidence of intravascular injection of cervical TFEI is higher than that of lumbosacral TFEI (12-14). Until now, there is no study comparing DSA and RTF for the same patients during cervical TFEI prospectively. The present study, therefore, was designed to investigate whether there is a difference between RTF and DSA in the detection of intravascular injection during cervical TFEI. Methods

Patients

The present study was approved by the institutional review board of our hospital and informed written consent was obtained from all patients. This study is registered in the ClinicalTrials.gov (NCT03040648).

We prospectively examined 137 cervical TFEIs. Inclusion criteria of this study were patients over 18 years of age, patients with radiating pain from spinal stenosis, and herniated nucleus pulposus. Exclusion criteria were pregnancy, allergic to contrast medium, patient refusal, and patients with persistent contraindication to nerve block, such as coagulopathy and infection of the injection site.

Study Designs

Two pain physicians were involved in this study. They had more than 10 years of experience in the department of pain medicine. TFEI was performed by the same physician and were simultaneously observed by the other pain physician.

Before the procedure, all patients were monitored using an electrocardiogram, pulse oximetry, and non-invasive blood pressure. A 22-gauge cannula needle was inserted in the patient's hand. The patients did not receive any sedation. Under fluoroscopic guidance, TFEI was performed using a Quincke type, 25-gauge, 9 cm spinal needle (Taechang Industrial Co., Kongju, Korea). For TFEI, the patient is placed in a supine position on a fluoroscopic table with their head slightly extended. The fluoroscope (Ziehm vision, Ziehm imaging, Nuremberg, Germany) is rotated obliquely to the ipsilateral side to supply the view of the neural foramen with maximum transverse width. At the skin entry site 1% lidocaine was infiltrated. The spinal needle was advanced toward the posterior aspect of the intervertebral foramen until the tip reached the superior articular process at the division between the caudal and middle thirds. Then the needle was advanced 2–3 mm into the foramen, no further than halfway across the facet column, on the anteroposterior fluoroscopic view. After the confirmation of final needle position using biplanar fluoroscopy, 2 mL of nonionic contrast medium (Omnipaque 300, GE Healthcare, Little Chalfont, Buckinghamshire, UK) was injected at the rate of 0.5mL/sec under RTF. Thirty seconds later, 2 mL of nonionic contrast medium was injected at the rate of 0.5mL/sec under DSA. Intravascular injection was defined as contrast medium spreading throughout the vascular channel during the injection of contrast medium under RTF and DSA. If intravascular injection was observed, the needle position was changed.

Sample Size

Based on the previous study, the incidence of intravascular injection during cervical TFEI was 20.6 % (14). We considered a 50% increment in the incidence of intravascular injection to be clinically important. Therefore, to detect such difference, a minimum size of 137 of TFEI were calculated with Type I and II errors < 0.05 and < 0.2, respectively.

Statistical Analysis

The patient's age, gender, diagnosis, and spinal level of the procedure were collected. The data was analyzed with a McNemar test, using SAS software version 9.3 (Cary, NC), A *P* value under 0.05 was considered statistically significant.

Results

A total of 137 cervical TFEIs were performed on 128 patients (Fig. 1). There were no complications dur-

ing cervical TFEI. The mean age of patients was 51.7 years (range, 28–84 years). The characteristics of study patients are presented in Table 1. TFEIs were performed from C3 to C8 spinal levels; 3 injections at C3, 6 at C4, 16 at C5, 46 at C6, 49 at C7, and 15 at C8. The incidence of intravascular injection on each level using RTF or DSA is presented in Table 2. Forty-two intravascular injections were detected in an overall intravascular injection rate of 30.7% using RTF. Forty-seven intravascular injections were detected in an overall intravascular injection rate of 34.7% using DSA. Intravascular injection detected by RTF were also observed using DSA. However, the detection rate of intravascular injection in RTF was not statistically different compared to that in DSA (P = 0.064).

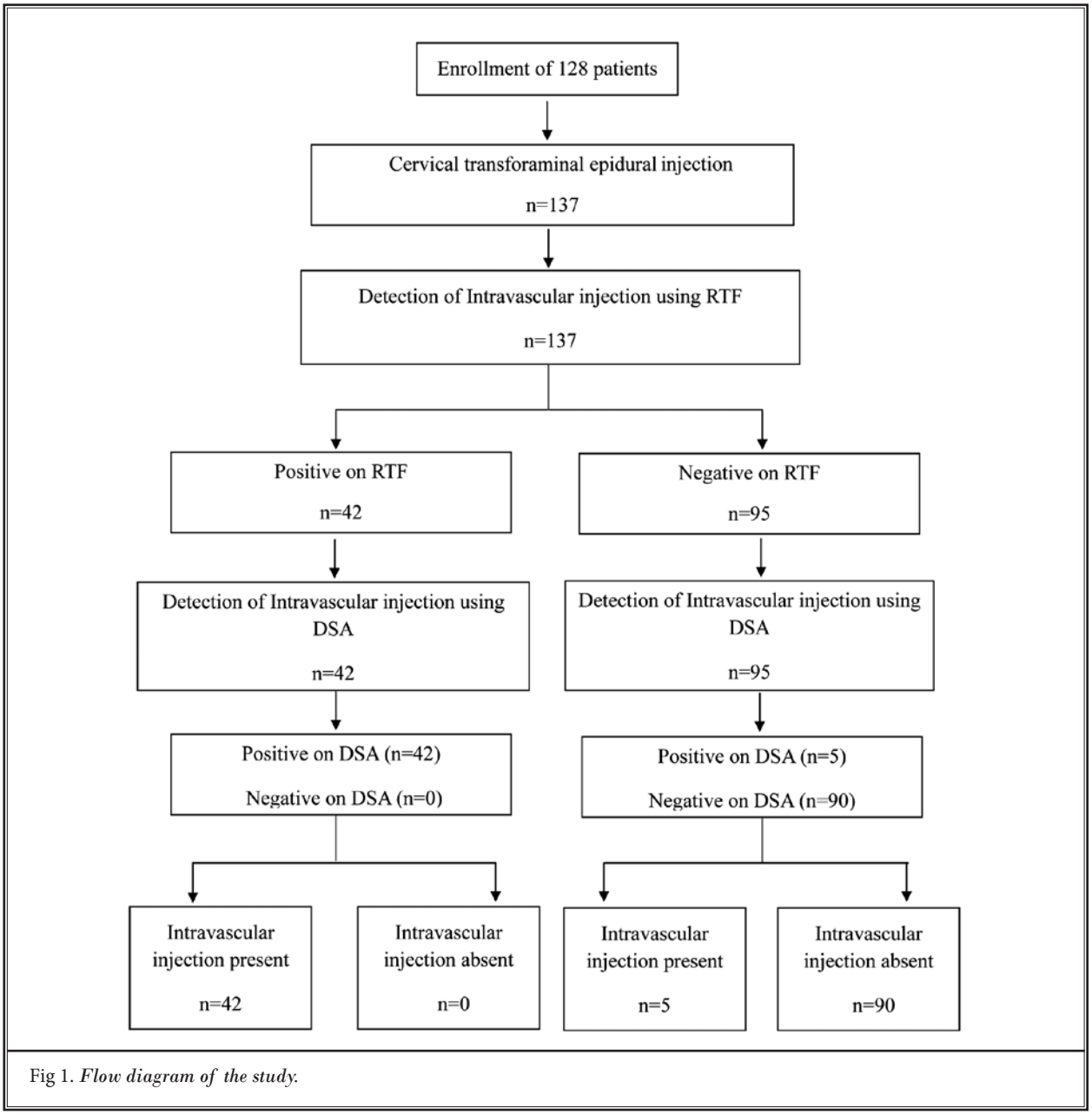

Fig 1. *Flow diagram of the study.*

Discussion

From our findings, there is no significant difference in detecting intravascular injection during cervical TFEI between RTF and DSA.

The incidence of intravascular injection during TFEI with RTF guidance depends on the region of the spine. Cervical TFEI is associated with higher incidence of intravascular injection compared to thoracic and lumbosacral TFEI (14). In the cervical spine, it was reported that the incidence of intravascular injection with RTF was 26% to 32.8% (8,13). In the present study, the incidence of intravascular injection with RTF was 30.7%, which is compatible with the previous studies (8,13).

DSA is an imaging technique that can clearly visualize the blood vessels from surrounding bones or dense soft tissues by subtracting the pre-contrast image from the image after injecting contrast medium (15). In a recent meta-analysis in 2015, it was suggested that DSA guidance was more effective to detect intravascular penetration than RTF during lumbosacral TFEI. In the retrospective study by McLean et al (9), 177 cervical TFEIs were performed with RTF or DSA guidance in the different patients with different machine. They found that the incidence was 32.8% in the group with DSA guidance, and 17.9% in the group with RTF guidance ($P = 0.041$).

In the present study, during cervical TFEI the intravascular injection of contrast medium was measured by RTF and DSA sequentially. The incidence of intravascular injection using DSA was 34.4%, which is similar to the previous study by McLean et al (9). However, DSA did not improve the detection rate of intravascular injection, compared to RTF alone.

El Abd et al (16) compared the detection rate of intravascular injection with DSA and other safety precautions, such as aspiration and RTF in the 150 consecutive patients who received TFEI. A total of 222 TFEIs in the cervical (18.47%), lumbar (50.9%), and sacral levels (30.36%) was performed, and in the sacral region an additional 5.26% intravascular injection was found using DSA. Kim et al (11) conducted a large prospective study to compare DSA with RTF for detection of intravascular injection in the same patients who receive lumbosacral TFEI. They evaluated 732 injections performed on 348 patients and found that there were no significant difference in the detection rate between DSA (8.1 %) and RTF alone (10.5%).

In this study, DSA did not improve the detection rate of intravascular injection during cervical TFEI, compared to RTF. Several possible reasons can be considered. First, 2 mL of contrast medium was injected at the rate of 0.5 mL/sec in the present study. In previous studies, it was found that DSA is more effective than RTF to detect intravascular injection with a small volume of contrast medium such as 1 mL (10,16,17). However, it demonstrated that a small volume of contrast medium is not sufficient to detect the intravascular injection

Table 1. *Demographic and clinical characteristics of the study patients (n = 128).*

Variables	Value
Age (year)	51.7 ± 12.0
Height (cm)	166.2 ± 7.6
Weight (kg)	64.5 ± 11.0
Men	66 (51.6%)
Diagnosis	
HNP	109
SS	17

HNP = herniated nucleus pulposus; SS = spinal stenosis; DSA = digital subtraction angiography; RTF = real-time fluoroscopy.

Table 2. *Incidence of intravascular injection during cervical transforaminal epidural block by level.*

Level	Number of injections	Number of intravascular injection on RTF (%)	Number of intravascular injection on DSA (%)	*P* value
C3	3	2 (66.7%)	2 (66.7%)	
C4	6	1 (16.7%)	1 (16.7%)	
C5	16	5 (31.3%)	5 (31.3%)	
C6	46	20 (43.5%)	23 (50.0%)	
C7	49	11 (22.4%)	13 (26.5%)	
C8	15	3 (20.0%)	3 (20.0%)	
Total	137	42 (30.7%)	47 (34.3%)	0.064

DSA = digital subtraction angiography; RTF = real-time fluoroscopy

during transforaminal epidural injections using RTF (12). Therefore, 2 mL of contrast medium was used in the present study. Kim et al (11) did not find any beneficial effect of DSA on the detection of the intravascular injection TFEI in the lumbosacral region using 1~2 mL of contrast medium. In addition, we prospectively investigated the incidence of intravascular injection in the same patients using RTF and DSA. In the study by El Abd et al (16), RTF and DSA was successively applied in the same patients, but DSA did not additionally detect intravascular injection in the cervical and lumbar region. Mclean et al (9) conducted a retrospective study to evaluate the detection rate of intravascular injection during cervical TFEI. They compared the patients monitored by RTF with the patients monitored by DSA. We think that many factors, including volume of contrast medium and the type of study, might have contributed to discrepancies with previous studies.

In the cervical spine, the arterial branches come from the vertebral artery. The risk of arterial injection is more devastating than that of venous injection. Unintentional intraarterial injection during TFEI can induce dissection, vasospasm, or occlusion, which can result in insufficient blood supply in the distal area (4-6). In addition, accidental intraarticular injection of particulate steroids during TFEI can occlude the artery, resulting in infarction of brain or spine (7). In the previous studies, it could be impossible to define the vascular contrast spreading pattern as venous or arterial during epidural TFEI because the patterns were ambiguous despite using RTF (12,14,18) and DSA (19,20). We could not differentiate between the 2 types of vascular pattern, which was compatible with previous studies. Chang Chien et al (21) suggested that DSA was not reliable to identify intravascular injection of contrast medium during nerve block. Therefore, to reduce the complications of intravascular injection during cervical TFEI, use of test dose of short acting local anesthetic, and use of only nonparticulate corticosteroids were recommended (22).

In addition, DSA has disadvantages, such as additional radiation exposure to physicians and patients and the high cost of the new and upgraded fluoroscopic equipment (15). DSA was reported to increase the effective radiation dose incurred by 2.3 ~ 4.3 fold for TFEI compared to conventional fluoroscopy (23).

In the present study, intravascular injection was detected using RTF and DSA guidance sequentially. There were some limitations of the present study. First, in the present study, 2 mL of contrast medium was injected at the rate of 0.5 mL/sec. Until now, there are no studies about the association between the injection speed and volume of the contrast medium and the detection of intravascular injection during TFEI. Therefore, further studies about the ideal injection speed and volume of contrast medium for improvement of detection of intravascular injection during TFEI are needed. Second, in the present study, the procedural pain physician was not blinded to the type of imaging modality, such as RTF and DSA, to detect intravascular injection. To minimize this confirmation bias and provide homogenous procedural conditions for TFEI, the same procedural physician performed all 137 injections.

Conclusion

In conclusion, DSA did not improve the detection rate of intravascular injection during cervical TFEI, compared to RTF in the present study. DSA increases the radiation exposure to physicians and patients and the cost for new and upgraded fluoroscopic equipment. Therefore, further studies to evaluate whether employment of DSA can be ideal for cervical TFEI are needed.

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Author Contributions

All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors designed the study protocol. Dr. Jeon managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. Dr. Kim provided revision for intellectual content and final approval of the manuscript.

Conflict of Interest

All authors have no conflicts of interest to report. None of the authors of the manuscript received any remuneration. Further, the authors have not received any reimbursement or honorarium in any other manner.

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Role of Sponsor

The financial sponsor of this work had no role in

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References

1. Manchikanti L, Singh V, Pampati V, Falco FJ, Hirsch JA. Comparison of the efficacy of caudal, interlaminar, and transforaminal epidural injections in managing lumbar disc herniation: Is one method superior to the other? *Korean J Pain* 2015; 28:11-21.
2. Pobiel RS, Schellhas KP, Eklund JA, Golden MJ, Johnson BA, Chopra S, Broadbent P, Myers ME, Shrack K. Selective cervical nerve root blockade: Prospective study of immediate and longer term complications. *AJNR Am J Neuroradiol* 2009; 30:507-511.
3. Schellhas KP, Pollei SR, Johnson BA, Golden MJ, Eklund JA, Pobiel RS. Selective cervical nerve root blockade: Experience with a safe and reliable technique using an anterolateral approach for needle placement. *AJNR Am J Neuroradiol* 2007; 28:1909-1914.
4. 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.
5. Heckmann JG, Maihofner C, Lanz S, Rauch C, Neundorfer B. Transient tetraplegia after cervical facet joint injection for chronic neck pain administered without imaging guidance. *Clin Neurol Neurosurg* 2006; 108:709-711.
6. Karasek M, Bogduk N. Temporary neurologic deficit after cervical transforaminal injection of local anesthetic. *Pain Med* 2004; 5:202-205.
7. 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.
8. Smuck M, Fuller BJ, Chiodo A, Benny B, Singaracharlu B, Tong H, Ho S. Accuracy of intermittent fluoroscopy to detect intravascular injection during transforaminal epidural injections. *Spine (Phila Pa 1976)* 2008; 33:E205-E210.
9. McLean JP, Sigler JD, Plastaras CT, Garvan CW, Rittenberg JD. The rate of detection of intravascular injection in cervical transforaminal epidural steroid injections with and without digital subtraction angiography. *PM R* 2009; 1:636-642.
10. Visnjevac O, Kim P, Farid-Davari S, Johnson P, Nader ND. Digital subtraction angiography versus real-time fluoroscopy for detection of intravascular penetration prior to epidural steroid injections: Meta-analysis of prospective studies. *Pain Physician* 2015; 18:29-36.
11. Kim YH, Park HJ, Moon DE. Rates of lumbosacral transforaminal injections interpreted as intravascular: Fluoroscopy alone or with digital subtraction. *Anaesthesia* 2013; 68:1120-1123.
12. Kim DW, Han KR, Kim C, Chae YJ. Intravascular flow patterns in transforaminal epidural injections: A comparative study of the cervical and lumbar vertebral segments. *Anesth Analg* 2009; 109:233-239.
13. Furman MB, Giovanniello MT, O'Brien EM. Incidence of intravascular penetration in transforaminal cervical epidural steroid injections. *Spine (Phila Pa 1976)* 2003; 28:21-25.
14. Nahm FS, Lee CJ, Lee SH, Kim TH, Sim WS, Cho HS, Park SY, Kim YC, Lee SC. Risk of intravascular injection in transforaminal epidural injections. *Anaesthesia* 2010; 65:917-921.
15. Jasper JF. Role of digital subtraction fluoroscopic imaging in detecting intravascular injections. *Pain Physician* 2003; 6:369-372.
16. 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.
17. Lee MH, Yang KS, Kim YH, Jung HD, Lim SJ, Moon DE. Accuracy of live fluoroscopy to detect intravascular injection during lumbar transforaminal epidural injections. *Korean J Pain* 2010; 23:18-23.
18. Hong JH, Kim SY, Huh B, Shin HH. Analysis of inadvertent intradiscal and intravascular injection during lumbar transforaminal epidural steroid injections: A prospective study. *Reg Anesth Pain Med* 2013; 38:520-525.
19. Nagpal AS, Chang-Chien GC, Benfield JA, Candido KD, Rana MV, Eckmann M. Digital subtraction angiography use during epidural steroid injections does not reliably distinguish artery from vein. *Pain Physician* 2016; 19:255-266.
20. Hong JH, Huh B, Shin HH. Comparison between digital subtraction angiography and real-time fluoroscopy to detect intravascular injection during lumbar transforaminal epidural injections. *Reg Anesth Pain Med* 2014; 39:329-332.
21. Chang Chien GC, Candido KD, Knezevic NN. Digital subtraction angiography does not reliably prevent paraplegia associated with lumbar transforaminal epidural steroid injection. *Pain Physician* 2012; 15:515-523.
22. Candido KD, Knezevic N. Cervical epidural steroid injections for the treatment of cervical spinal (neck) pain. *Curr Pain Headache Rep* 2013; 17:314.
23. Maus T, Schueler BA, Leng S, Magnuson D, Magnuson DJ, Diehn FE. Radiation dose incurred in the exclusion of vascular filling in transforaminal epidural steroid injections: fluoroscopy, digital subtraction angiography, and CT/fluoroscopy. *Pain Med* 2014; 15:1328-1333.