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Effect of statin use on pain relief by transforaminal epidural steroid injection

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Abstract

Aim: To investigate the impact of statin use on response to fluoroscopy-assisted transforaminal anterior epidural steroid injection (TAESI).

Methods: Patients undergoing TAESI for low back pain were recruited and stratified according to statin use. Pain was evaluated with a visual analogue scale (VAS) before and at 1, 3, and 6 months after TAESI. Health-related quality-of-life was evaluated using the Short Form 36 (SF-36) questionnaire 6 months after TAESI.

Results: There were no significant differences in VAS scores after TAESI between statin users ($n = 40$) and statin nonusers ($n = 253$). The SF-36 subgroup: role limitations due to emotional problems score was significantly lower in statin users than statin nonusers. There were no significant between-group differences in any other SF-36 parameter.

Conclusion: Statin use had no effect on pain scores after TAESI.

Keywords

Statin, transforaminal epidural steroid injection, pain

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Introduction

Low back painis the leading cause of activity limitation and work absence throughout much of the world, and places a large economic burden on individuals, families, communities, industry and governments.[1] Low back pain is classified as nonspecific pain without radiculopathy, pain with radicular symptoms, or secondary pain with a spinal cause.[2] The pathophysiology of low back pain with radicular symptoms is complex, and its association with elevated

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plasma and local concentrations of inflammatory cytokines suggests an inflammatory component.

Steroid injection therapy has been commonly and increasingly used in the treatment of lumbosacral radiculopathies.[3,4] Of the various methods of epidural steroid injection (caudal, interlaminar, or transforaminal injection[5]), fluoroscopy-assisted transforaminal anterior epidural steroid injection (TAESI) is the preferred technique as it allows direct guidance into the targeted area and requires a smaller steroid dose.[6,7] The transforaminal approach targets the ventral lateral epidural space, which is the primary pathological site.[8] Epidural steroid injections are usually supplemented with analgesic drugs, due to insufficient analgesic effects of the steroid itself.

Statins are selective inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme of cholesterol biosynthesis. As well as their broad use as lipid-lowering drugs, studies have found immunomodulatory and anti-inflammatory activities for statins, both in vivo and in vitro, which may be relevant to their therapeutic effects in neuroinflammatory conditions.[9,10–13] Furthermore, statins have been shown to alleviate neuropathic pain in a rat model.[14] The impact of statin use on response to epidural steroid injections remains unknown, however.

The aim of the present study was to test the hypothesis that statin use results in lower pain scores (assessed using a visual analogue scale [VAS]) both before and after TAESI in patients with low back pain, compared with those patients not taking statins. The effect of statin use health-related on quality-of-life (evaluated with Short Form 36 [SF36][15]) was also assessed.

Patients and methods

Study population

This prospective, single blind study included all patients aged ≥18 years scheduled to undergo TAESI for low back pain at the Department of Algology, Adnan Menderes University, Aydin, Turkey, between April 2012 and December 2013. Indications for TAESI included radicular pain, lumbar disc hernia, lumbar canal stenosis or failed back surgery. Treatment was prescribed by a pain physician who was blinded to the patient's statin use (O.N.A.). Exclusion criteria were: prior TAESI; known allergy to steroids; indication for surgery; ongoing workers' compensation claims; unstable opioid use; psychiatric disorders; drug or alcohol abuse within the previous 6 months; severe medical illness that could interfere with the interpretation of study outcomes; myocardial infarction within the previous 6 months; pregnancy. Patients were stratified between two groups: statin users (20 mg atorvastatin for ≥3 months) or statin nonusers. Morphometric and demographic data (age, sex, weight and height), statin type and dosage, duration of symptoms, surgical history and a detailed history of low back pain were recorded. A detailed pain history was obtained.

The study was approved by the Institutional Review Board of Adnan Menderes University, Aydin, Turkey, and all patients provided written informed consent prior to enrolment.

TAESI

Before TAESI, all patients provided a VAS score (0 = no pain, 10 = most severe pain possible). Vascular access was established and a 0.9% isotonic sodium chloride drip was set up. Patients were premedicated with midazolam 0.02 mg/kg and fentanyl 1 μg/kg, placed in the prone position on the fluoroscopy table, and monitored for heart rate, blood pressure and oxygen saturation. The skin was cleaned with iodine-based antiseptic solution and then covered, in line with the intstitute's standard sterilization protocol. All procedures were carried out under local

anaesthesia using C-arm fluoroscopic guidance.

The TAESI procedure was initiated by placing the C-arm scope in anteroposterior position to determine the intervention level. The scope was then brought into an ~15–20° oblique position to obtain an image of the intervertebral foramina. The skin and subcutaneous region was infiltrated with 1 ml of 1% lidocaine, and a 100 mm 21 G stimulation needle (Stimuplex A 100, B Braun, Melsungen, Germany) was guided into the intervertebral foramen. When frontal, anterior and lateral images indicated that the point of the needle was in the correct position, 0.5–1 ml of contrast agent was injected to verify the typical anterior epidural spread. The image was further verified with anteroposterior and lateral projections. Subsequently, a mix of 80 mg triamcinolonacetonide (Sinokort A ampoule, 40 mg/ml, İ.e.ulagay ilaç sanayi, İstanbul) and 3 ml of 0.5% bupivacaine (Bustesin, Vem ilaç sanayi, İstanbul) was injected accompanied by negative aspiration. The total injection volume was 4 ml if the procedure involved a single level, or 3 ml/level if more than one level was involved. The same pain physician, who was blinded to the patient's statin use (O.N.A.) performed all the procedures.

After the procedure, all patients were monitored in the recovery room for 2 h before returning to the ward. Patients with no complications were discharged after 6 h and were followed-up after 2 weeks (routine postprocedure assessment). Pain scores (VAS) were assessed 1, 3 and 6 months after TAESI. Health-related quality-of-life was evaluated using Short Form 36 (SF-36) 6 months after TAESI.

Statistical analyses

Data were presented as mean ± SD. Between-group comparisons were made using Student's *t*-test with Bonferroni's correction for multiple comparisons. *P*-values <0.05 were considered statistically significant. Statistical analyses were performed using JMP Pro version 9.0.00 (SAS Institute, Cary, NC, USA).

Results

The study evaluated 676 patients for eligibility. Of these, 273 patients were excluded, 403 were enrolled, and 110 were lost to follow up. The final analysis included 293 patients (131 male/162 female; mean age 58.4 ± 14.6 years; age range 20–89 years). Patients were classified as statin users ($n = 40$; 19 male/21 female; mean age 63.1 ± 12.4 years; age range 35–89 years) or statin nonusers ($n = 253$; 112 male/141 female; mean age 52.5 ± 14.2; age range 20–86 years). Demographic and clinical parameters are shown in Table 1. There were no significant between-group differences in demographic characteristics except age and duration of pain. None of the patients experienced any side-effects of TAESI.

Data regarding VAS and SF-36 scores are shown in Table 2. There were no significant between-group differences in VAS score. Role limitations due to emotional problems SF-36 scores were significantly lower in statin users than statin nonusers ($P < 0.05$; Table 2). There were no statistically significant between-group differences in any other SF-36 parameter.

Discussion

There was no between-group difference in pain score after TAESI in the present study. With the exception of the role limitations due to emotional problems subcategory, there were no between-group differences in health-related quality-of-life.

Low back pain with radicular symptoms is characterized by a combination of neuropathic and nociceptive mechanisms, and inflammation with neuronal injury has been shown to contribute to neuropathic pain.[16,17]

Table 1. Demographic and clinical characteristics of patients undergoing fluoroscopy-assisted transforaminal anterior epidural steroid injection for low back pain, stratified according to statin use.

Characteristic	Statin users $n = 40$	Statin non-users $n = 253$
Age, years	63.1 ± 12.4	52.5 ± 14.2*
Sex, male/female	19/21 (47.5/52.5)	112/141 (44.2/55.8)
Weight, kg	78.5 ± 10.6	76.1 ± 11.3
Height, cm	161.4 ± 7.8	160.4 ± 14.2
Duration of pain		
≥1 month – <6 months	2 (5.0)	19 (7.5)
≥6 months – <2 years	1 (2.5)	58 (22.9)
≥2 years – <5 years	18 (45.0)	101 (39.9)
≥5 years – <10 years	19 (47.5)	75 (29.7)

Data presented as mean ± SD or *n* (%) of patients.
*$P < 0.05$ vs statin users; Student's *t*-test with Bonferroni's correction.

Table 2. Pain (visual analogue scale) and health-related quality-of-life scores in patients undergoing fluoroscopy-assisted transforaminal anterior epidural steroid injection (TAESI) for low back pain, stratified according to statin use.

Parameter	Statin users $n = 40$	Statin non-users $n = 253$
Pain score		
Pre TAESI	7.5 ± 1.1	7.2 ± 1.3
Post TAESI		
1 month	2.9 ± 2.2	2.7 ± 2.3
3 months	2.9 ± 2.3	2.9 ± 2.4
6 months	3.4 ± 2.3	3.1 ± 2.6
Health-related quality-of-life score[a]		
Physical functioning	58.7 ± 21.6	65.7 ± 25.2
Role limitations due to physical health	35.7 ± 43.9	50.3 ± 45.3
Role limitations due to emotional problems	40.1 ± 12.3	46.3 ± 15.7*
Energy	78.3 ± 41.0	76.3 ± 42.1
Emotional well being	64.9 ± 13.4	62.8 ± 15.1
Social functioning	69.7 ± 25.7	66.5 ± 30.0
Pain	54.2 ± 22.6	64.4 ± 26.2
General health	43.6 ± 16.3	52.3 ± 17.4

Data presented as mean ± SD.
*$P < 0.05$ vs statin users; Student's *t*-test with Bonferroni's correction.
[a]Assessed via Short Form 36.[15]

The main treatment modality for chronic low back pain with radicular symptoms is epidural steroid injection.[18] Statins have significant anti-inflammatory effects, and systemic administration of statins was shown to alleviate mechanical allodynia and thermal hyperalgesia in neuropathic pain models.[9,19] Additionally, statins significantly reduced

spinal microglial and astrocyte activation produced by sciatic nerve injury in rodents.[9,19] Atorvastatin protects rats from neuropathic pain inflicted through chronic constriction injury via inhibition of a nuclear factor κB and inducible nitric oxide synthase-mediated injury pathway.[20] Few studies have evaluated the effects of statin use on pain in humans, although a single case report demonstrated a significant decrease in stump pain with initiation of statin treatment.[21] There was no between group difference in pain scores after TAESI in the present study. This may be due to the small number of patients in the statin group or the significant between-group difference in age.

Long-term statin use is associated with peripheral neuropathy and myotoxicity.[22,23] Muscle symptoms are a principal reason for nonadherence and/or discontinuation, contributing to adverse cardiovascular outcomes.[24] These side-effects can also result in pain, and may be a possible explanation of the lower then expected pain relief effect seen in statin users in the present study. Statin-associated myopathy with elevated serum creatinine kinase (CK) is a rare but serious side-effect, affecting between 0.01 and 0.1% of people taking standard statin doses.[24] Statin-associated muscle symptoms cover a broader range of clinical presentations, usually with normal or minimally elevated CK levels, with a prevalence of 7–29% in registries and observational studies.[24] Preclinical studies indicate that statins decrease mitochondrial function, attenuate energy production, and alter muscle protein degradation, thereby providing a potential link between statins and muscle symptoms.[24] Controlled mechanistic and genetic studies are necessary to further elucidate this effect, although none of the patients in the present study experienced any side-effects.

Neuropathic pain adversely affects health-related quality-of-life, and reduces physical and emotional function. The lack of a between group difference in health-related quality-of-life in our study may be related to the absence of long-term decreases in pain score. Alternatively, there may be unresolved secondary gains or other unknown factors.

Our study has several limitations. The sample size was small and patients were not randomized. Larger, randomized studies are therefore required to confirm our findings. In addition, the duration of statin use may affect the outcome, but this parameter was not included in our study design. Furthermore, chronic pain has variable emotional and affective consequences that should be addressed. Including SF-36 assessment at the beginning of the study period as well as 6 months after TAESI would have provided valuable additional information regarding the effect of the procedure on health-related quality-of-life.

In conclusion, we found no significant effect of statin use on the efficacy of TAESI for chronic low back pain. Randomized, double-blind, longitudinal studies with larger sample sizes are required to confirm this finding.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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