Retrospective Study

Impact of Serum Magnesium Levels on Outcomes After Transforaminal Epidural Steroid Injections for Lumbar Radicular Pain: A Retrospective Study

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Background: Transforaminal epidural steroid injections (TFESIs) are a commonly used intervention for the management of lumbar radicular pain. While anatomical predictors of pain conditions like nerve compression severity, are well-known, the role of patient-specific metabolic factors has received comparatively less attention. Meanwhile, magnesium (Mg), a natural N-methyl-D-aspartate (NMDA) receptor antagonist, plays a major role in pain modulation and the prevention of central sensitization.

Objectives: To investigate the association between pre-procedural serum magnesium levels and the clinical success of TFESIs.

Study Design: A retrospective observational cohort study.

Setting: A tertiary referral center, Istanbul, Türkiye.

Methods: Data from 121 patients undergoing single-level TFESIs were analyzed. The severity of each patient's radiological nerve root compression was graded using magnetic resonance imaging (MRI)-based criteria. With the use of an evidence-based cutoff value of 0.85 mmol/L to identify subclinical deficiency, the patients were categorized into groups labeled Low-Mg (< 0.85 mmol/L, n = 29) and Normal-Mg (≥ 0.85 mmol/L, n = 92). Clinical progress was tracked using the Numeric Rating Scale (NRS) and Oswestry Disability Index (ODI) at baseline, one month, and 3 months. Treatment success was defined as ≥ 50% pain relief and ≥ 40% functional improvement.

Results: Despite comparable radiological nerve compression grades, patients in the low-Mg group reported significantly higher baseline pain intensity than did those in the normal-Mg group (9.65 vs. 8.15, $P < 0.001$). Post-procedural outcomes were significantly better in patients with normal Mg levels. Success rates differed significantly between the groups: 71.7% vs. 20.7% at one month ($P < 0.001$), and 66.3% vs. 34.5% at 3 months ($P = 0.002$). Correlation analysis suggested a possible threshold effect, with outcomes deteriorating below the defined Mg cutoff rather than following a linear dose–response relationship.

Limitations: Limitations include the study's retrospective design, the lack of dietary intake data, and the reliance on serum rather than ionized Mg measurements.

Conclusion: Low serum Mg levels (< 0.85 mmol/L) are associated with higher baseline pain intensity and a poor therapeutic response to TFESIs. Screening patients for their Mg levels represents a simple and potentially modifiable factor that may help improve injection outcomes, warranting consideration for supplementation in borderline cases.

Key words: Transforaminal epidural steroid injection, magnesium, lumbar radicular pain, NMDA receptor, biomarker, treatment outcome

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The transforaminal epidural steroid injection (TFESI) is a widely utilized image-guided procedure for the management of radicular pain associated with lumbar disc herniation (LDH) and spinal stenosis. The technique involves direct delivery of medication into the neural foramen, enabling the precise placement of pharmacological agents in close proximity to the affected nerve root (1). Unlike the interlaminar approach, the TFESI is considered one of the most effective techniques for accessing the ventral aspect of the thecal sac, which is often the primary site of pathology (2). The therapeutic effects of epidural injections are thought to result from disruption of nociceptive input and modulation of central neuronal activity. Corticosteroids further contribute by inhibiting the synthesis of pro-inflammatory mediators, thereby exerting anti-inflammatory effects and a reversible local anesthetic effect (3). Observational studies indicate that the TFESI provides greater than 50% pain relief in more than 70% of patients (4). Additionally, controlled trials have demonstrated the utility of TFESIs in preventing or delaying the need for surgical intervention (5). While numerous studies have investigated factors influencing the success of TFESIs, the vast majority of these studies have focused primarily on magnetic resonance imaging (MRI) findings (6).

Magnesium (Mg), the second most abundant intracellular cation and fourth most common mineral in the human body, is an essential cofactor involved in over 600 metabolic reactions (7). Rather than acting as a direct analgesic, Mg functions as a voltage-gated blocker of N-methyl-D-aspartate (NMDA) receptors. This blockade prevents calcium influx, thereby producing antinosiceptive effects and inhibiting central sensitization (8). Evidence suggests that Mg is effective in perioperative pain management and in blunting autonomic, somatic, and endocrine reflexes to noxious stimuli (9). Conversely, Mg deficiency can lead to upregulated NMDA receptor activity and Substance P release, resulting in heightened pain perception and elevated stress hormone levels (10). In a randomized controlled trial involving patients whose chronic low back pain had a neuropathic component, Mg supplementation was observed to reduce pain intensity and improve lumbar range of motion (11).

Although factors affecting TFESI outcomes and the general role of magnesium in chronic pain have been studied separately, there is, to the best of our knowledge, limited evidence evaluating the specific relationship between serum Mg levels and TFESI success. Therefore, this study aims to investigate the association between serum Mg levels and the therapeutic efficacy of TFESIs in patients with lumbar radicular pain secondary to LDH.

Methods

Study Design and Patients

This retrospective observational cohort study was carried out at a tertiary referral center between January 2021 and January 2024. The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Ethical approval was obtained from the institutional ethics committee (Ref: KAEK/2024.03.42), and the study protocol was registered at ClinicalTrials.gov (NCT06551792). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki (2013 revision), and written informed consent was obtained from all patients.

Patients who were 18 years or older and underwent a single-level TFESI were included. Inclusion criteria comprised unilateral radicular pain (Numeric Rating Scale [NRS] score $\geq$ 5) secondary to a single-level LDH at L4, L5, or S1, confirmed by physical examination and lumbar magnetic resonance imaging. To reduce interobserver variability, all MRI scans were reevaluated by a radiologist with expertise in musculoskeletal imaging. The severity of nerve root compromise was assessed using the MR-based grading system described by Pfirrmann et al (12). Using this system, nerve root compromise was classified into 4 grades: Grade 0 (normal/no contact), Grade 1 (contact without deviation), Grade 2 (deviation/displacement), and Grade 3 (compression). For statistical analysis, patients were stratified according to compression severity: Grades 0–1 were classified as low-grade compression and Grades 2–3 as high-grade compression.

Exclusion criteria included multilevel disc herniation, prior lumbar surgery, lumbar spinal stenosis, inflammatory rheumatic diseases, metabolic conditions affecting serum magnesium levels (e.g., chronic renal failure, diabetes mellitus, hypo- or hyperthyroidism), local or systemic infection, and malignancy. Additionally, patients with missing pre-procedural laboratory data or hypermagnesemia (> 1.1 mmol/L) were excluded from the analysis.

Serum Mg levels measured within 7 days prior to the procedure were recorded. Although the laboratory reference range for serum Mg at our institution

is 0.70–1.05 mmol/L, an evidence-based cutoff value of 0.85 mmol/L was used for this study, as proposed by Costello et al (13), to identify subclinical deficiency. Accordingly, the study population was stratified into 2 groups based on this cutoff: the low-Mg group (< 0.85 mmol/L) and the normal-Mg group (0.85–1.1 mmol/L).

Procedure

All procedures were performed under sterile conditions with C-arm fluoroscopic guidance. Patients were placed in the prone position with a pillow under the abdomen to minimize lumbar lordosis. The C-arm was tilted craniocaudally to align the vertebral end-plates of the target segment and then rotated 10°–30° obliquely to visualize the neural foramen. Local anesthesia (one mL of 2% lidocaine) was administered to the skin and subcutaneous tissues. A 22-gauge, 90-mm Quincke spinal needle (Egemen, Türkiye) was advanced into the subpedicular space using a coaxial (tunnel vision) technique under intermittent fluoroscopic guidance. The needle tip position was confirmed via anteroposterior and lateral fluoroscopic views. To exclude intravascular or intrathecal placement, 1–2 mL of radiopaque contrast medium (iohexol) was injected. After the confirmation of appropriate epidural spread, a total volume of 4 mL, comprising 40 mg triamcinolone acetonide, 2 mL of 2% lidocaine, and one mL of 0.9% NaCl, was administered.

Outcome Measures

To evaluate treatment efficacy, clinical scores recorded at baseline (pre-procedure) and at one month and 3 months after the procedure were obtained from routine clinical follow-up records. Pain intensity was assessed using the 11-point NRS, on which 0 represented no pain and 10 indicated the worst imaginable pain. Functional disability regarding daily living activities was measured using the Oswestry Disability Index (ODI), with scores ranging from 0 to 100 (higher scores indicating greater disability).

Treatment success was defined as a ≥ 50% reduction in NRS scores and a ≥ 40% improvement in ODI scores compared to baseline values. The primary outcome was the change in pain intensity (NRS) at one month and at 3 months after the procedure. Secondary outcome measures included functional disability levels (measured on the ODI) at one and 3 months and the presence of procedure-related complications.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics Version 27.0 (IBM Corp.). Data distribution was assessed using the Shapiro–Wilk test and visual inspection of histograms. Because the data were not normally distributed, nonparametric tests were used. Descriptive statistics were expressed as mean ± SD for continuous variables and as frequency and percentage (n, %) for categorical variables. The Mann-Whitney U test was used to compare continuous variables between the groups (low-Mg vs. normal-Mg), while the chi-square (χ^2) test was used for categorical comparisons. Additionally, Spearman's correlation analysis was conducted to evaluate the relationship between serum Mg levels and clinical outcomes. A *P*-value of < 0.05 was considered statistically significant.

Results

A total of 247 patients who underwent single-level TFESIs during the study period were screened for eligibility. One hundred twenty-six patients were excluded, most commonly because of prior lumbar surgery, spinal stenosis, or relevant comorbidities. Accordingly, 121 patients were included in the final analysis (Fig. 1). Based on the 0.85 mmol/L cutoff, 29 patients (24.0%) were assigned to the low-Mg group, and 92 patients (76.0%) to the normal-Mg group. Baseline demographic and clinical characteristics were comparable between the groups (Table 1). There were no significant differences between the groups in age, gender distribution, BMI, symptom

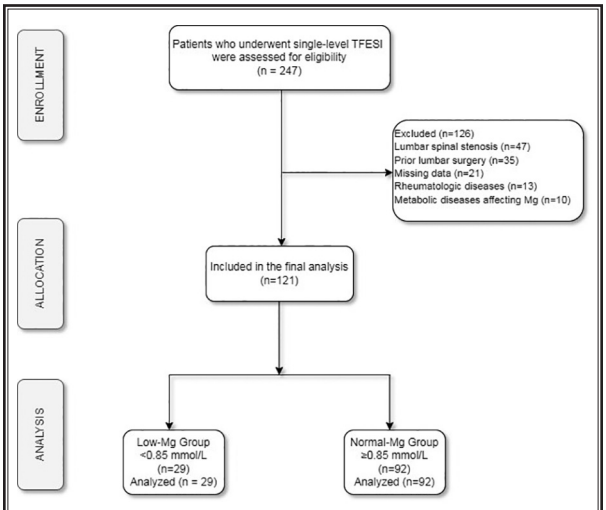


Fig. 1. *Flow diagram of the study population.*
TFESI: transforaminal epidural steroid injection, Mg: Magnesium.

duration, or disc herniation grade ($P > 0.05$). While baseline functional disability scores on the ODI were similar ($P = 0.864$), the low-Mg group presented with significantly higher baseline pain intensity than did the normal-Mg group (mean NRS: 9.65 vs. 8.15, $P < 0.001$).

Clinical Outcomes

After the TFESI procedure, both groups showed improvements in pain and functional status from baseline. However, intergroup comparisons demonstrated better clinical outcomes in patients with normal Mg levels (Table 2). The normal-Mg group had significantly lower mean NRS scores at both the first (T1) and third (T3) months than did the low-Mg group ($P < 0.001$). Similar findings were observed for functional recovery; ODI scores at T1 and T3 were significantly lower in the normal-Mg group ($P = 0.002$ and $P = 0.003$, respectively). In addition, the magnitude of improvement was greater in the normal-Mg group, which also saw larger percentage reductions in NRS and ODI scores at all follow-up points.

Correlation analysis revealed a weak but statistically significant positive correlation between serum Mg levels and the percentage of NRS reduction at the first month ($r = 0.179$, $P < 0.05$). However, no significant linear correlation was observed at the third month. The absence of a linear correlation at 3 months, despite significant group differences, indicates a possible threshold effect rather than a linear dose–response relationship.

Treatment Success

When treatment efficacy was evaluated based on the predefined success criteria, a clear difference was observed between the groups (Table 3). At the first month, the treatment success rate in the normal-Mg group was 71.7%, whereas the success rate was limited to 20.7% in the low-Mg group ($P < 0.001$). This significant difference persisted at the third-month follow-up (66.3% vs. 34.5%, $P = 0.002$), indicating that lower serum Mg levels were associated with poorer therapeutic responses (Fig. 2).

The procedure was tolerated without major adverse events. No major complications, including infection, hematoma, dural puncture, or permanent neurological deficits, were observed during the procedure or follow-up.

Discussion

This retrospective observational cohort study examined the association between serum Mg levels and the efficacy of TFESIs. It was hypothesized that patients with normal serum Mg levels (the normal-Mg group) would exhibit higher procedural success. The results showed that while TFESIs were associated with significant improvements in pain and functional disability scores (as measured on the NRS and ODI, respectively) relative to baseline in both groups, the magnitude of clinical improvement was distinct between the cohorts. Consistent with this hypothesis, the treatment success rate in the normal-Mg group was significantly higher than that of the low-Mg group at both the first and third months. These findings indicate that serum Mg level may represent a modifiable biological factor that influences TFESI outcomes.

Another notable observation of our study was that patients in the low-Mg group presented with significantly higher baseline pain scores (NRS), despite having comparable grades of nerve root compression to the normal-Mg group. This discrepancy can be attributed to the inhibitory role of Mg in pain modulation. Mg is known to function as a natural antagonist of NMDA receptors and prevents neuronal hyperexcitability by blocking voltage-gated

Table 1. *Demographic characteristics of the study groups.*

Variables	Low-Mg Group (< 0.85 mmol/L) (n = 29)	Normal-Mg Group (≥ 0.85 mmol/L) (n = 92)	*P*-value
Age (years), mean ± SD	49.00 ± 10.03	46.64 ± 10.71	0.466
Gender, n (%)			0.311
Female	12 (41.4%)	48 (52.2%)	
Male	17 (58.6%)	44 (47.8%)	
BMI (kg/m^2), mean ± SD	27.86 ± 3.64	28.94 ± 3.99	0.205
Duration of Pain (years)	7.44 ± 5.08	8.20 ± 5.95	0.550
Side, n (%)			0.597
Left	11 (37.9%)	30 (32.6%)	
Right	18 (62.1%)	62 (67.4%)	
Disc Herniation Grade, n (%)			0.374
Low-Grade	20 (69.0%)	55 (59.8%)	
High-Grade	9 (31.0%)	37 (40.2%)	

BMI: body mass index, NRS: Numeric Rating Scale, ODI: Oswestry Disability Index

calcium channels. Consequently, low serum Mg levels may compromise this blockade mechanism, thereby facilitating central sensitization (8). The similarity in baseline ODI scores between the groups reinforces the hypothesis that Mg deficiency exerts a direct influence on pain perception and threshold, rather than on the mechanical functional impairment caused by the disc herniation.

Research predicting the success of TFESIs has focused predominantly on anatomical or demographic variables, such as the degree of nerve root compression, symptom duration, age, and spinal stenosis (2,14-16). By comparison, patient-specific biochemical and metabolic factors that may influence pain modulation have received limited attention. For instance, a recent study had reported that vitamin D deficiency was associated with inadequate pain control following a TFESI (17). While the immunomodulatory effects of vitamin D are valuable, Mg may play a more central role in pain modulation due to the mineral's direct regulation of neuronal excitability via NMDA receptor antagonism and calcium channel blockade. Although literature exists regarding the use of Mg (specifically, $MgSO_4$) as an adjuvant in epidural steroid mixtures to prolong analgesic duration and reduce postoperative analgesic requirements (18,19), data regarding the influence of preexisting serum Mg levels on treatment outcomes remain very limited. In this context, our study adds to the existing literature by demonstrating that serum Mg level may serve as an independent and, crucially, a modifiable biomarker for injection success.

Interpretation of these findings should consider the complex physiology of Mg homeostasis. Approximately 99% of total body Mg is stored in bone and soft tissues, with only ~0.3% present in the serum. The body regulates serum concentrations strictly by mobilizing stores from bones and soft tissues; consequently, serum levels may appear normal even in the presence of significant intracellular depletion ("chronic latent deficiency"). Although measurements of ionized or red blood cell Mg reflect physiological status more accurately, their cost and limited availability restrict routine clinical use. Therefore, total serum Mg remains the most feasible and widely applicable screening tool. Costello et al have suggested that serum Mg levels at the lower end of the reference range (< 0.85 mmol/L) likely indicate that body reserves (bone and soft tissue) are significantly depleted and that a functional deficit exists in neural tissues where NMDA receptors are located (13). The poorer outcomes observed in

Table 2. *Comparison of pain (NRS) and disability (ODI) scores over time.*

Outcome Measures	Low-Mg Group (n = 29)	Normal-Mg Group (n = 92)	*P*-value
NRS Score (Mean ± SD)			
T0	9.65 ± 0.55	8.15 ± 0.78	< 0.001
T1	4.75 ± 1.24	3.11 ± 0.98	< 0.001
T3	4.79 ± 1.82	3.02 ± 1.16	< 0.001
ODI Score (Mean ± SD)			
T0	56.03 ± 3.52	56.48 ± 2.55	0.864
T1	31.93 ± 8.67	26.94 ± 8.13	0.002
T3	32.06 ± 10.45	25.57 ± 9.29	0.003
Reduction Rates (%)			
NRS (T0→T1)	50.7 ± 12.8%	61.6 ± 12.6%	< 0.001
NRS (T0→T3)	50.3 ± 18.5%	62.9 ± 14.4%	0.001
ODI (T0→T1)	42.9 ± 15.3%	52.0 ± 15.1%	0.004
ODI (T0→T3)	42.5 ± 19.1%	54.7 ± 16.4%	0.003

NRS: Numeric Rating Scale, ODI: Oswestry Disability Index.
T0: pre-procedure (baseline), T1: first month post-procedure, T3: third month post-procedure.

Table 3. *Evaluation of treatment success rates.*

Time Interval	Success Status	Low-Mg Group (n = 29)	Normal-Mg Group (n = 92)	*P*-value
T0 →T1	Successful	6 (20.7%)	66 (71.7%)	< 0.001
	Unsuccessful	23 (79.3%)	26 (28.3%)	
T0 →T3	Successful	10 (34.5%)	61 (66.3%)	0.002
	Unsuccessful	19 (65.5%)	31 (33.7%)	

Treatment success was defined as ≥ 50% reduction in NRS score and ≥ 40% reduction in ODI score.
T0: pre-procedure (baseline), T1: first month post-procedure, T3: third month post-procedure.

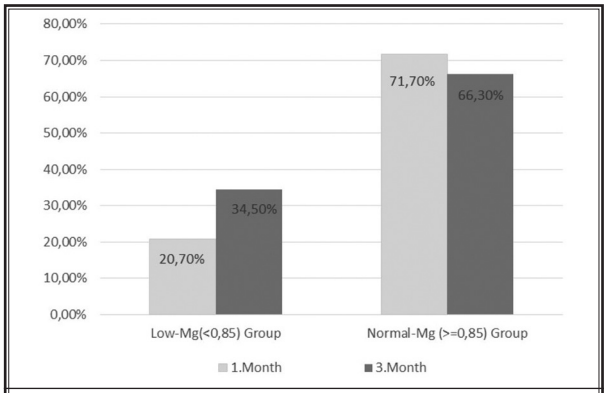


Fig. 2. *Comparison of treatment success rates between low-Mg (< 0.85 mmol/L) and normal-Mg (≥ 0.85 mmol/L) groups at first- and third-month follow-up.*

patients below this threshold in our study support this hypothesis. Moreover, our analysis revealed a positive correlation between serum Mg levels and pain reduction in the early period (the first month), whereas this relationship did not persist at the third month. However, the persistence of the difference between the low and normal Mg groups at the third month suggests that the clinical determinant is falling below a "critical threshold" rather than a linear principle in which higher scores are better. These findings suggest that the 0.85 mmol/L cutoff value used in this study may represent a clinically meaningful threshold.

It has been reported that approximately 60% of adults in Western populations do not consume adequate amounts of Mg in their diet, making "subclinical deficiency" far more common than estimated (20). This situation is even more critical in chronic pain patients. Mg deficiency weakens NMDA receptor blockade, increasing pain sensitivity, while the physiological stress caused by chronic pain consumes the body's Mg reserves, potentially creating a vicious cycle (21). From a clinical perspective, assessing serum Mg levels prior to a TFESI may represent a simple approach to patient stratification. For patients with low or borderline levels, Mg supplementation could be considered; however, its impact on procedural success should be confirmed in future prospective trials. To our knowledge, limited data are available regarding the predictive role of serum Mg levels in TFESI outcomes.

This study had several limitations, which should be acknowledged. The retrospective design precludes causal inference. In addition, Mg levels were measured at a single preprocedural time point; potential fluctuations in serum levels due to dietary changes or unreported supplementation during the follow-up period could not be monitored. Finally, measurements of ionized or red blood cell Mg are more accurate than those of the level of serum Mg, although the last parameter remains the most accessible in clinical practice.

Conclusions

In conclusion, this study shows that serum Mg level is associated with treatment success in patients undergoing TFESIs for lumbar radicular pain. Low serum Mg levels were observed to be linked to poorer pain control and limited functional recovery. Therefore, preprocedural assessment of Mg levels and supplementation when necessary may serve as a simple and beneficial strategy to enhance therapeutic efficacy.

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