# The Efficacy Of Calcitonin Treatment In Patients With Lumbar Spinal Stenosis

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## ÖZET

***Lomber Spinal Stenozlu Hastalarda Kalsitonin Tedavisinin Etkinliği***

***Amaç:*** *Bu çalışmada, lomber kanal stenozu olan hastalarda kalsitoninin klinik semptom ve bulgulara etkisi araştırıldı.*

***Materyal ve Metod:*** *Çalışmamıza nörojenik intermittan klodikasyo şikayeti ön planda olan lomber spinal stenozlu 26 hasta alındı.Bütün hastalardan L3-S1 kesitlerinden çekilen lomber kolon bilgisayarlı tomografi ile santral kanal çapı ve lateral reses çapı ölçümü yapıldı. Hastalara 6 ay boyunca nasal salmon kalsitonin 200 İÜ/gün verildi. Hareketle olan ağrı, lomber ekstansiyon açısı, yürüme mesafesi, nörolojik defisit açısından hastalar takip edildi.*

***Sonuç:*** *Kalsitonin tedavisi ile;nörojenik klodikasyo mesafesinde artış,hareketle oluşan ağrının şiddetinde azalma,duyu kusurunda düzelme ve lomber ekstansiyon derecesinde artış saptandı. Bu bulgular istatistiksel olarak anlamlı idi. Derin tendon reflekslerinde ve motor kayıpta düzelme saptanmış olup,istatistiksel olarak anlamlı değildi. Lomber spinal stenozda kalsitonin kullanımı tedavi seçeneği olarak düşünülmelidir.*

***Anahtar Kelimeler:*** *Kalsitonin, Lumbar Spinal Stenoz, Nörojenik Kladikasyo*

## SUMMARY

***Aim:*** *Lumbar spinal stenosis is characterized with neurogenic claudication secondary to the compression of cauda equina. The most common cause of spinal stenosis is spinal spondylosis. There are studies indicating calcitonin as an effective treatment for this condition.*

***Materials and Method:*** *This study was performed to evaluate the clinical effects of calcitonin in patients with lumbar spinal stenosis. For this purpose, we studied 26 patients with lumbar spinal stenosis. Diameters of lumbar central canal and lateral recess were measured with lumbar computerized tomography in order to diagnose spinal canal stenosis. Patients were treated with nasal calcitonin (200 IU / day) for six months. The clinical assessments of patients included pain on movement, lumbar extension angle, walking distance, and neurological deficit.*

***Results:*** *An increase in neurogenic claudication distance and lumbar extension angle, and decrease in pain were observed with calcitonin therapy. These findings were statistically significant.*

*Consequently, it can be concluded that calcitonin should be considered as an option in the treatment of lumbar spinal stenosis.*

***Key words:*** *Calcitonin,Lumbar spinal stenosis,Neurogenic claudication*


## INTRODUCTION

Lumbar spinal stenosis (LSS) is a neurologic syndrome resulting from the narrowing either of the spinal canal, the lumbar nerve root canals, or the intervertebral foramina. According to a classification based on anatomical location, narrowing of the spinal canal in its sagittal and/or coronal diameter is called central canal stenosis, whereas narrowing of nerve roots in the lateral canal is called lateral nerve canal stenosis (lateral recess syndrome). The narrowing beyond a critical level compresses the neural and neurovascular elements, and histopathologic changes such as edema, fibrosis, demyelination, and axonal degeneration develop in the affected nerves. Clinically, pain, numbness, weakness, and/or cramps may develop in one or both legs. These symptoms typically occur when standing or walking beyond a threshold distance and subside when sitting, stooping, or bending forward. This constellation of symptoms is aptly referred to as neurologic intermittent claudication (NIC).

The initial management of LSS entails non-surgical (conservative) approaches, such as analgesia with nonsteroidal anti-inflammatory drugs (NSAIDs) and physical therapy exercises. (3) Surgery (decompressive laminectomy) is offered to many patients who are severely affected or who are not adequately managed with conservative measures alone. (1) In fact, LSS has become the

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most common reason for spinal surgery in individuals over 65 years of age. (4) The superiority of surgical methods over non-surgical treatment methods has not been established, and the role of various treatment strategies remains an active field of investigation.

Exercise is one of the key components of the conservative management of LSS. (2, 4) Flexion exercises are especially beneficial because lumbar flexion not only widens the intervertebral foramina but also stretches the spinal nerves, reducing their diameter. The end result is a reduction in the level of compression of the spinal nerves. Lumbar flexion also reduces the lumbar lordosis; increases the volume of the spinal canal; stretches the tight hip flexors and the back extensors, and strengthens abdominal and gluteal muscles.

Calcitonin, a polypeptide hormone synthesized by the parafollicular cells of the thyroid gland, has important roles in calcium homeostasis in the body. Because it promotes mineralization in the bones, it has been used as a therapeutic adjunct in the treatment of osteoporosis and Paget's disease. The discovery of its analgesic properties has led to its adjunctive use in diseases associated with bone pain. Earlier studies have shown that parenterally administered calcitonin is effective in the treatment of LSS. An intranasal formulation of salmon calcitonin is now available and is frequently prescribed for the treatment of various skeletal disorders.

In this study, we tested the effectiveness of a combination of exercise and nasal salmon calcitonin therapy in the conservative management of LSS.

## MATERIALS AND METHODS

The study was open to recruitment during the first four months of 2005 and was conducted at the outpatient clinics of the department of Physical Medicine and Rehabilitation of the Istanbul and Vakif Gureba (Ministry of Health Training and Research) Hospitals. The study was approved by the institutional ethics committee and all study participants provided informed consent. Subjects were recruited from patients with newly diagnosed LSS, all referred because of symptoms of NIC. The diagnosis of LSS was established in the presence of narrowing of < 11.5 mm in the central canal or in the presence of narrowing < 3 mm in the lateral recess, as detected

**Table 1:** Improvement in the walking distance with treatment

| | Walking Distance | | | | | | |
|---|---|---|---|---|---|---|---|
| | Mean ± SD | >1000m n (%) | 501-1000m n (%) | 201-500m n (%) | 101-200m | 51-100m n (%) | 0-50m n (%) |
| Pre-treatment | | | 2 (7 7) | 5 (19.2) | 5 (19.2) | 5 (19.2) | 9 (34.6) |
| 1st month | | 2 (7 7) | 2 (7.7) | 4 (15.4) | 8 (30.8) | 3 (11.5) | 7 (26.9) |
| 3rd month | | 5 (19.2) | 2 (7 7) | 5 (19.2) | 8 (30 8) | 5 (19.2) | 1 (3.8) |
| 6th month | | 10 (38 5) | 5 (19.2) | 6 (23.1) | 2 (7.7) | 2 (7.7) | 1 (3.8) |

SD: Standard deviation

*P= 0 000

**Table 2:** Distribution of patients according to lumbar extension angle at baseline and sixth month after the treatment

| | Lumbar extension angle 25 degrees or less n (%) | Mean Change in Lumbar extension angle Mean ± SD |
|---|---|---|
| Pre-treatment | 25 (96) | 18.12 ± 6.00 |
| | | |
| | | |
| 6th month of treatment | 7 (27) | 28.88 ± 5.58* |

SD: Standard deviation

*P= 0.014

**Table 3:** Distribution of patients with pain during movement score 5 or more(measured with VAS) before and after the treatment

| | Presence of pain during movement 5 or more according to VAS n (%) | VAS (Mean ± SD) |
|---|---|---|
| Pre-treatment | 26 (100) | 7.73 ± 1.87 |
| 6th month of the treatment | 8 (31) | 3.92 ± 2.48* |

SD: Standard deviation; VAS. visual analogue scale

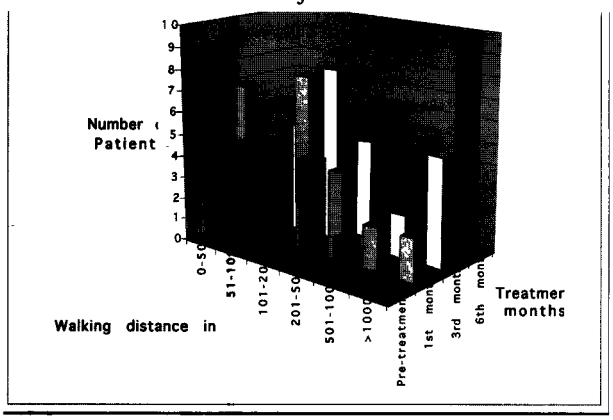
*P= 0 018

**Table 4:** Improvements in sensory deficits with treatment

| Sensory deficit | Pre-treatment | 6th month |
|---|---|---|
| | n (%) | n (%) |
| Absent | | 12 (46.2) |
| Present | 26 (100.0)*†‡ | 14 (53.8)* |

*P= 0.125

**Figure 1.** Improvement in the walking distance of the subjects.




with computerized tomography (CT) of the lumbar spine. The same radiologist took CT measurements for all subjects. Patients with peripheral vascular disease, osteoarthritis of the hip or knee joint, history of lumbar herniation were excluded.

The therapeutic interventions included salmon calcitonin (Miacalcic, Novartis Pharma AG Huningue, France) 200 IU administered as a spray intranasally once daily; vitamin B supplementation (vitamin B1 500 mg/day orally and vitamin B6 500 mg/day orally); and active flexion exercise for all subjects. Patients did not take NSAIDs during the study period. The exercise therapy consisted of pelvic tilt manoevre (supine and standing); stretching of hip and back muscles; modified and lateral straightening; hamstring stretching. Exercises were prescribed in sets of ten repetitions, 2 sets per day.

Demographic data (age and sex) were obtained at the first visit. Patients were seen monthly for six months. Measurements obtained prior to the study and at each visit included the walking distance (measured on a flat, constant surface), presence or absence of motor and/or sensory deficits (paresthesia, hypoesthesia, hyperesthesia, or dysesthesia of the L4, L5, or S1 dermatomes), degrees of lumbar extension movement (patient lying in prone position) and pain. A score of 1 was given for the presence and a score of 0 for the absence of the sensory or motor deficits. The intensity of the low back and leg pain during movement was measured using the visual analog pain scale (VAS), where the score ranges from 0 (no pain) to 10 (the worst pain).

Statistical evaluation: Changes in the walking distance were analyzed using Wilcoxon and Friedman tests. Lumbar extension angles were compared using paired t-test. Variance analysis, paired t test, Friedman, Wilcoxon and McNemar tests were used on repeated measurements. p value of $<0.05$ was considered as statistically significant.

## RESULTS

Thirty-three patients were recruited during the study period; however, seven withdrew from the study prior to analysis. Three withdrew because of high treatment costs, two withdrew because they believed the study did not provide therapeutic benefit, and the remaining two did not show up for follow-up visits without stating any reason.

Patients included in the final analysis consisted of 20 females (77%) and 6 males (23%), with a mean age of 52.4 years (range 35-65 years). Seventeen (65%) were 50 years or older. Fifteen patients (58%) had central stenosis; while 2 (7%) had lateral recess stenosis and 9 (35%) had both types of (central and lateral recess) stenosis.

History of severe lumbar trauma was present in two (8%) patients, while one had a history of myelography following a trauma. Lower back and leg pain were present in all patients. Eighteen (69%) patients had both lower back and leg pain, whereas 8 (31%) had only lower back pain. Computerized tomography revealed articular facet hypertrophy in 22 (85%) patients, ligamentum flavum hypertrophy in 16 (61.5%) and posterior osteophyte formation in 4 (15%). One patient had ligamentum flavum calcification .

Changes in the walking distance: Walking distances of the patients had increased significantly by the end of the study period ($p<0.001$). While none of the patients tolerated a walking distance greater than 1000 meters at the beginning of the study period, 10 (38.5%) patients were able to tolerate walking beyond 1000 m at the 6th month of the treatment. Whereas 9 patients (34.6%) had a walking distance range of 0-50 meters prior to the treatment, only one (3.8%) had remained in this category at the 6th month of the treatment (Table 1,Figure 1).

Evaluation of the lumbar extension movement: Twenty-five patients (96%) had a lumbar extension angle of 25 degrees or lower, while this number was reduced

to 7 (27%) at the 6th month. The increase in the lumbar extension angle between periods was statistically significant (p=0.014) (Table 2).

Evaluation of the low back and leg pain during movement: While pre-treatment VAS score for pain during movement was 5 or above for all (100%) patients, at the 6th month treatment 8 patients (31%) had a VAS score of 5 or above. VAS values were reduced in a statistically significant fashion (p=0.018) (Table 3).

Evaluation of motor deficit: Motor strength was reduced in 2 (7.7%) patients before the treatment. At the 6th month of the treatment, no motor deficits were detected in any of the patients. However this was not found to be statistically significant.

Evaluation of the sensory deficit: Before the treatment, sensory deficits (paresthesia, hypo-hyperesthesia) were present in 26 (100%) of the patients at the L4, L5 or S1 levels. The number of patients with sensory deficits had reduced to 14 (53.8%) at the 6th month of the treatment. There was a significant improvement in sensory deficits after the treatment (p=0.125) (Table 4).

Adverse effects: One patient reported facial flushing that subsided as therapy was continued. All patients continued the treatment to completion, and none of the patients experienced side effects severe enough to stop the drug.

## DISCUSSION

Lumbar spinal stenosis is a disease that can easily be diagnosed through clinical, radiological and other methods. The narrowing of the bony canal alone is not enough for the LSS (Lumbar Spinal Stenosis) symptoms to appear. NIC (Neurogenic Intermittent Claudication) develops when the adequate perfusion of the soft tissues, especially that of the nerve tissue, is inhibited (1-5).

Decompression with extensive laminectomy surgery, which is the only established method of treatment, has a success rate of 66-85%. Many LSS patients are elderly people and this causes a high surgical risk (6,11).

In our study, we investigated the responses of NIC, limitation of lumbar extension, sensory deficit, motor strength loss and deep tendon reflex abnormalities to calcitonin treatment.

Use of calcitonin treatment in NIC, has previously been reported by Eskola, and this is one of the most specific findings in NIC. Calcitonin provides an adequate blood supply for the nerve roots. Calcitonin has vasoactive properties in addition to its analgesic, anti-inflammatory and anti-edema effects. (7,8).

A marked increase was observed in the NIC distances of the LSS patients in our study. There are also other studies reporting a similar increase in the walking distance with calcitonin treatment (6-8,11,12).

In the randomized, placebo-controlled, double-blind study of Eskola et al. which included 40 LSS patients, the effect of calcitonin was observed to be weak in patients whose baseline walking distance was 200-300 meters or less (7). In our study, upon treatment with calcitonin, a significant increase was observed in the walking distances of the patients that had a walking distance of 200 meters or less. This might be due to the higher dose of calcitonin and longer duration of treatment. The placebo effect of calcitonin should also be considered.

There are studies reporting that calcitonin treatment leads to a decrease in the pain experienced by LSS patients during movement (6,11,12). Such a significant decrease was also detected in our study. Calcitonin's strong central analgesic effect on hypothalamic receptors, increase in the amount of circulating endogenous opioids, and the inhibition of prostaglandin E2 synthesis and its anti-depressant actions may be responsible for this outcome (9,10).

Improvements in flexion and extension movements following the treatment have been detected in previous studies (11,12). Our study also demonstrated an increase in the degree of lumbar extension of the patients. Appropriate combination of flexion exercises improves the posture of the lower back, increases the strength of the abdominal and lower back muscles, decreases the excessive strain on spinal structures and protects the mobile structures. The increases in the lumbar extension degrees might be due to the performance of therapeutic exercises. The analgesic effect of calcitonin can also decrease the restriction caused by pain.

In our study, a significant improvement was detected in the sensory deficits of the patients. The results in the literature concerning the improvements in sensory deficits vary.

Sarı H et al. applied active physical therapy modali-

ties, active lower back and abdominal muscle strengthening exercises together with salmon calcitonin to patients with osteoporosis and LSS, and although the number of patients experiencing sensory deficits decreased with treatment, no statistically significant improvements were detected (6).

In another study, Oner et al. administered salmon calcitonin, calcium salts, and applied physical therapy modalities in addition to active flexion and extension exercises. This study also demonstrated that the treatment provides a significant improvement in sensory deficits (14).

The improvements recorded in the sensory deficits in our study might be due to the effect exerted by calcitonin via vasoactive mechanisms, correcting the venous pooling and ischemia that occur in LSS and consequently preventing the myelin loss due to compression and ischemia in addition to assisting re-myelinization. The Vitamin B complex administered to the patients can also display a positive effect on the treatment of sensory deficits. Calcitonin's effect on sensory deficits may become more prominent with longer duration of administration. Besides, the greater number of patients with sensory deficits in our study might have accounted for these statistically significant results. In this study, sensory deficit was classified as paresthesia, hyperesthesia and/or hypoesthesia. Studies in the literature do not provide a clear definition for sensory deficits. In those studies of the literature, sensory deficit might have been used to define hypoesthesia.

Our study demonstrated an improvement in motor deficit with treatment, but this improvement was not statistically significant. There is a one study in the literature reporting an improvement in motor deficit (12). In another study, no improvement was detected (6).

The sensory improvement observed with treatment could also have been anticipated in motor deficits. Although no motor deficit had been detected in the follow-up at 6 months, this finding is not statistically significant (6). This, might be explained by the presence of low number of patients with motor deficits in our study. The persistence of the canal narrowing could be responsible for the persisting motor deficit.

Some of the patients in our study with deep tendon reflex abnormalities were found to improve in that aspect. However, this improvement was not statistically significant, compatibly with the literature findings (6,12).

The mechanism of deep tendon reflex abnormalities in LSS is probably the same as that of neurological deficits. Loss of myelin secondary to venous pooling and arterial ischemia could also be responsible. The persistence of canal narrowing could cause the deep tendon reflex abnormality to persist, which might be corrected with a treatment of longer duration.

## CONCLUSION

As a result, the use of nasal calcitonin for 6 months is effective in reducing the pain that restricts daily activities of the patients and in increasing the NIC distance. In addition, it has positive effects on sensory deficits and restriction of Lumbar extension movements. Although there is a decrease in the number of patients with motor deficit and deep tendon reflex abnormalities, this is not statistically significant. There are a few disadvantages of our study:in order to investigate the efficacy of calcitonin in neurological deficits, a controlled study should be performed with a larger patient group.Walking distance shold be measured in standard platform such as treadmill.Double-blinded placebo controlled studies should be made and long term effects of calcitonin shoud be evaluated. Calcitonin should be considered as the treatment of choice in symptomatic LSS. Calcitonin treatment for LSS must be considered before surgical treatment, particularly in the elderly, in whom LSS is more common and surgical risk is involved.

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