

## Prospective Study

## The Effects of Gastroretentive Gabapentin (Gralise®) on Spinal Stenosis Patients with Radicular Pain

Alan David Kaye, MD, PhD<sup>1,2</sup>, Franklin Rivera Bueno, MS, MS<sup>1</sup>, Bonnie Katalenich, MPG<sup>3</sup>, Carol Stell, RN<sup>3</sup>, Henry Liu, MD<sup>2</sup>, Frank A. Rosinia, MD<sup>2</sup>, Eric Luk, MD<sup>1</sup>, Ken Ehrhardt, BS<sup>1</sup>, and Charles J. Fox, MD<sup>4</sup>

From: <sup>1</sup>Department of Anesthesiology, Tulane School of Medicine, New Orleans, LA; <sup>2</sup>Department of Anesthesiology, Tulane School of Medicine, New Orleans, LA; <sup>3</sup>Tulane Medical School Clinical Research at the Clinical Translational Unit, New Orleans, LA; <sup>4</sup>LSU School of Medicine, Shreveport, LA

Dr. Kaye is Professor and Chairman, Department of Anesthesiology, LSU School of Medicine, New Orleans, LA and Professor, Department of Anesthesiology, Tulane School of Medicine, New Orleans, LA. Mr. Bueno is a Research Associate, Department of Anesthesiology, LSU School of Medicine, New Orleans, LA. Ms. Katalenich, MPH, is with the Tulane Medical School Clinical Research at the Clinical Translational Unit, New Orleans, LA. Ms. Stell, is an RN at Tulane Medical School Clinical Research at the Clinical Translational Unit, New Orleans, LA. Dr. Liu is an Associate Professor, Department of Anesthesiology, Tulane School of Medicine, New Orleans, LA. Dr. Luk and Mr. Ehrhardt are both are Research Associate, Department of Anesthesiology, LSU School of Medicine, New Orleans, LA. Dr. Fox is a Professor and Chairman, Department of Anesthesiology, LSU School of Medicine, Shreveport, LA.

Address Correspondence:  
Alan David Kaye, MD, PhD  
Department of Pharmacology  
LSU School of Medicine T6M5  
1542 Tulane Ave., Room 656  
New Orleans, Louisiana 70112  
E-mail: alankaye44@hotmail.com

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**Background:** The health and efficacy profiles of Gralise® in the treatment of pain from spinal stenosis and radicular symptomatology have not been measured. A review of the current literature indicates that no studies exist that evaluate the safety and efficacy profiles of Gralise® in the treatment of pain from spinal stenosis and radicular symptomatology.

**Objective:** Our study is aimed at determining whether Gralise is a safe and effective pharmacotherapy for the pain from spinal stenosis and radicular symptomatology.

**Study Design:** A 4-week prospective open label single arm and single center study of patients with MRI diagnosis of spinal stenosis with radicular pain.

**Methods:** The primary measure of efficacy was a change in average daily pain (ADP) score from baseline to completion of Gralise therapy for 4 weeks. The secondary efficacy endpoints were the patients' Patients Global Impression of Change Scale (PGIC), the clinician's Clinical Global Impression of Change Scale (CGI) reports, and the Medical Outcomes Study (MOS) sleep scale of improvement from baseline to completing 4 weeks of Gralise therapy. The safety and tolerability were evaluated by the incidence of adverse events reported while on Gralise therapy.

**Setting:** The study was performed at the Clinical Research Facilities at Tulane Medical Center, New Orleans, Louisiana, in the period from December 1, 2012, to August 30, 2013.

**Results:** Thirty-five patients achieved an efficacy point of one-week Gralise medication treatment. Twenty-seven of 35 (77.2%) patients completed all 5 visits. The PGIC noted a significant positive change in: (1) activity limitations; (2) symptoms; (3) emotions and overall quality of life when related to their condition from first visit as well as improved degree of change when related to their condition from first to last visit. The MOS sleep scale and sleep diaries noted a significant increase of hours slept on average (an increase in over one hour per night — 5.8 hours versus 6.86 hours) from the beginning of the study to the end. The CGI noted a majority of 10 out of 27 with marked significant therapeutic effect with no side effects. The ADP rating from pain intensity scale and pain diaries noted significant improvement of lesser levels of pain experienced ( $P=.5907$  and  $P=.8547$  respectively). No significant adverse effects were noted in the study.

**Limitations:** Variation in degree of spinal stenosis, small sample size.

**Conclusions:** Gralise demonstrated moderate efficacy with reduced pain intensity and increased sleep and was well tolerated in spinal stenosis patients with radicular symptoms.

**Key words:** Spinal stenosis, gabapentin, Gralise®, radicular pain, neuropathic pain

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**S**pinal stenosis has been identified as a cause of pain and functional limitation for 100 years (1). Spinal stenosis is the diagnosis that clinicians often use in order to characterize patients who have symptoms that may relate to reduction of the lumbar spinal size (2). The condition of developmental spinal stenosis is characterized by the narrowing of the spinal canal and spinal stenosis itself may be described as the “narrowing of the spinal canal with encroachment on neural structures by the surrounding soft tissues and bones” (1,3). The actual anatomical reduction of spinal size is necessary for the diagnosis of spinal stenosis (2). Pain from spinal stenosis often includes, but is not limited to, the lower back, buttocks, and legs (4). Often these particular pain sensations result from lateral recess stenosis (4).

The incidence of the diagnosis of spinal stenosis has increased (2). This increase in diagnosis may result from both improved and increased imaging radiology and an aging population (2). It has been reported that the annual incidence of lumbar spinal stenosis is 5 cases per 100,000 individuals (5). This incidence is 4 times the incidence of cervical spinal stenosis (5).

Spinal stenosis often results from degenerative phenomena, such as spondylolisthesis and age-related changes (e.g. loss of intervertebral disc height, disc bulging, infolding of ligamentum flavum, facet joint osteoarthritis/ hypertrophy/ osteophyte/ cystic formation) (1). The development of spinal stenosis may also stem from degenerative changes in the aging and elderly or may develop due to genetics (1,2). The severity of symptoms and the range of functional impairment differ in patients with spinal stenosis (2). Patients with congenital spinal stenosis usually suffer from pain early in life (3). Many people may have spinal stenosis without being aware of the condition (2).

Many patients undergo back surgery because of spinal stenosis and the cost of these procedures exceeds one billion dollars per year (1,6-8). However, surgery offers many risks to patients with failure rates reported as high as 45% (1,7). The availability of other nonsurgical options, especially pharmacotherapy, is growing in importance for the treatment of spinal stenosis, especially for the elderly population (1,9).

Radicular pain can, and in many cases does, originate from spinal stenosis (10). Cervical radicular pain is characterized as “pain perceived in the upper limb, shooting or electric in quality, caused by irritation and or injury of a cervical spinal nerve” (11). Approximately one person in 1,000 suffers from cervical radicular pain

(11). The International Association for the Study of Pain holds a slightly different definition for cervical radicular pain (11). According to this association, cervical radicular pain is “pain perceived as arising in the upper limb caused by ectopic activation of nociceptive afferent fibers in a spinal nerve or its roots or other neuropathic mechanisms” (11). Lumbosacral radicular pain has a similar mechanism and is only distinct in that it radiates in one or more lumbar or sacral dermatomes. Lumbosacral radicular pain may occur with other radicular irritation symptoms (12).

Radicular pain distinguishes itself from somatic referred pain (13). The physiological basis of radicular pain stems from “ectopic discharges emanating from a dorsal root or its ganglion” (13). It is held that disc herniation is the most common cause of radicular pain (13). The inflammation of the affected nerve from the disc herniation is so far identified as the “critical pathophysiological process” in the generation of this pain (13).

Gabapentin has been identified as a possible pharmacotherapy for spinal stenosis and accompanying radicular pain (1). In a study by Yaksi et al (14), with a 4-month regimen in patients treated with gabapentin combined with conservative management or conservative management alone, the group with conservative management (e.g. including physical therapy with lumbar flexion, pelvic traction, and strengthening of abdominal muscles), those patients who were administered gabapentin were able to walk a greater distance. In addition, it was found after 4 months that the group with gabapentin had lower pain scores and a more drastic reduction in sensory deficits compared with conservative management (decrease of 28.6% vs. 7.4%, respectively;  $P = 0.04$ ) (14).

Gabapentin has a short elimination half-life and limited absorption due to a saturable L-amino acid transport system, which is expressed predominantly in the proximal small intestine. Hence, gabapentin must usually be taken 3 times a day for optimal efficacy. Gabapentin taken 3 times a day is also associated with a high incidence of dizziness and somnolence and some patients are unable to tolerate the doses required for maximum pain relief (15). A once-daily, gastroretentive formulation of gabapentin (Gralise) was approved by the FDA for the management of postherpetic neuralgia. This formulation provides gradual release of gabapentin to the optimal site of absorption in the proximal small intestine and reduces the chance of saturating intestinal uptake, thus enabling once-daily dosing of ga-

bapentin. This novel preparation may increase patient compliance and provide relief from the pain generated by spinal stenosis and radicular symptomatology.

The pain alleviation properties of Gralise pharmacotherapy have been documented and approved by the FDA. Therefore, Gralise is currently available for patients with postherpetic neuralgia. However, the safety and efficacy profiles of Gralise in the treatment of pain from spinal stenosis and radicular symptomatology have not been measured, observed, or established. A review of the current literature indicates that no studies exist that evaluate the health and efficacy profiles of Gralise in the treatment of pain from spinal stenosis and radicular symptomatology. Therefore, this study was undertaken to establish whether Gralise is a safe and effective pharmacotherapy for the pain from spinal stenosis and radicular symptomatology and if Gralise will ultimately find an extra indication for the treatment of pain from spinal stenosis and radicular symptomatology.

## **METHODS**

Both Tulane and Louisiana State University Health Sciences Center (LSUHSC) Institutional Review Board (IRB) approvals were obtained for the study. It was a prospective, open label, single arm, 4 week single center study, performed at the Clinical Research Facilities at Tulane University School of Medicine, New Orleans, Louisiana. The primary objective of the study was to evaluate the efficacy and safety of Gralise, the novel preparation of gabapentin, in spinal stenosis patients with radicular symptomatology. The study drug was supplied in a pre-packaged form by Depomed, Inc., Gralise, and stored according to the Depomed, Inc. guidelines: 25 degrees Celsius (77 degrees Fahrenheit) and managed by a research pharmacist. The dosing regimen in this study was as follows: subjects were dispensed a one week supply of Gralise at Visit 1, 2, 3, and 4. Treatment was started at a dose of 300 mg/day and increased over 2 weeks to a total daily dose of 1800 mg/day. This was followed by stable dosing at 1800 mg/day for an additional 2 weeks. At the end of the study, Gralise was discontinued gradually over one week.

The study population included patients 18 years or older with a diagnosis of cervical or lumbar stenosis documented by a magnetic resonance imaging (MRI) or computed tomography (CT) scan within the last 5 years and accompanied by radicular pain. Any patients currently on gabapentin or pregabalin had a 15 day washout period before the start of the study. Other exclusion criteria included immunocompromised patients,

currently pregnant or breastfeeding, with creatinine clearance < 50 mL/min and with any known allergy or intolerance to gabapentin. Patients were allowed to be on other concomitant neuropathic pain medications, including opiates, but were required to keep their medicine regimen stable during the study and to have been on these agents for at least 3 weeks before enrollment. A total of 50 subjects with either cervical or lumbar stenosis were recruited from the Tulane and LSU University Departments of Anesthesiology where they were actively being evaluated and treated for spinal stenosis. Out of the 50 enrolled patients, 35 met the efficacy point of completing treatment for one week, while 27 subjects completed all 6 study visits.

The mean age of the 50 patients was 48.6 (SD = 10.85) years old at the first visit, while for those who achieved the efficacy point the mean age was 49.2 (SD = 10.21) years old. The distribution of gender for all 50 patients was 28 (56%) men and 22 (44%) women and for those who completed a full week of treatment were 23 (65.71%) men and 12 (34.29%) women. Racial demographics for all 50 patients were 26 (52%) Caucasian, 23 (46%) African-American, and one (2%) Hispanic. For those 35 that completed one full week of treatment, 19 (54.29%) were Caucasian, 15 (42.86%) were African-American, and one (2.86%) was Hispanic. Lastly from concomitant medications and pain diaries assessment for other opioid use during the study, there were 26 patients out of 50 (52%) who used opioids during the study period. Out of the 35 who achieved the efficacy point of one week of treatment, 25 (71.43%) patients used opioids at some point during their time in the study. These demographics have been summarized in Table 1.

The pain and sleep diaries given to the patients were given for the week between visits. Each day the patient filled in the sleep diary, entering information about what time they fell asleep, how long it took to fall asleep, when they woke up, how long they slept, if they woke up during the night, and if they got out of bed. There were also questions regarding activities during the day which may have disturbed their sleep, like drinking caffeine or alcohol or eating a large meal. The patient also noted if they took any medications that day and what medication. As for the pain diary, the patient was instructed to record an entry whenever they were in pain or took medication. They were to rate their pain on a 0 to 10 pain intensity scale, state what they were doing when the pain started, and if they took any medication or other methods to relieve

Table 1. Demographics of the study population.

Variable	Unadjusted (n = 50)	Adjusted (n = 35)
Age in years, mean (SD)	48.60 (10.85)	49.20 (10.21)
BMI at Visit 0, mean (SD)	29.73 (6.12)	29.90 (6.02)
Race, n (%)		
White	26 (52.00)	19 (54.29)
Black	23 (46.00)	15 (42.86)
Hispanic	1 (2.00)	1 (2.86)
Sex, n (%)		
Male	28 (56.00)	23 (65.71)
Female	22 (44.00)	12 (34.29)
Use of Opioids During the Study, n (%)		
Yes	26 (52.00)	25 (86.21)
No	24 (48.00)	4 (13.79)

the pain. Then they were to rate their pain one hour after initial reporting.

### Statistical Analysis

Means and standard deviations (SD) were calculated for all continuous variables, which were normally distributed. To compare week 4 of treatment to week 1 of treatment, means were compared using 2 sample t-tests. Results were considered statistically significant if  $P < .05$ . For all categorical variables frequencies were counted and compared. All analysis was done using SAS 9.2 (Tulane University, New Orleans, Louisiana).

### RESULTS

There were a total of 6 clinic visits and one telephone visit to confirm the first treatment dose was taken. At the first clinic visit, informed consent and eligibility confirmation was completed. Confirmation of eligibility was determined through documented medical records of MRI or CT scan and radicular symptoms and serum creatinine levels were obtained through local labs. Once eligibility was confirmed the patient returned for visit one at the clinic for a physical examination and completion of the study questionnaires: Patients' Global Impression of Change (PGIC), intensity pain scale, and medical outcomes study (MOS) sleep scale. In addition, training on how to complete the pain and sleep diary was done by the study coordinator and the clinician completed the Clinician Global Impression of Change (CGIC) questionnaire. The patient was then given a week's worth of medication and an appointment for the next visit. A telephone call was made by

the study coordinator the next business day to confirm the first dose was taken.

For the next 4 weeks the patient returned weekly for a clinic study visit, at each visit the patient completed the PGIC and the pain intensity scale questionnaires, as well as returning the sleep and pain diaries and receiving new diaries and medication. At the last visit, at the end of 4 weeks of treatment, the subject also completed the MOS sleep scale and the clinician completed the CGIC questionnaire in addition to the 2 other questionnaires. Patients, who wished to continue Gralise therapy upon the conclusion of the 4 week study, were able to do so through a prescription by the principal investigator or their regular physician.

All patient questionnaires, PGIC, pain intensity scale and MOS sleep scale were self-administered. The PGIC assessed the change in the patient's condition through 2 questions. The first question evaluated the change in activity, limitations, symptoms, and overall quality of life, while the second question measured the amount of change experience since the beginning of treatment. The pain intensity scale is a 3 question survey to assess current level of pain, level of pain at its worst and best, and an acceptable level of pain. The MOS sleep scale is a 12 question survey to assess sleep quality and quantity over the last 4 weeks. One question asks the average number of hours slept, the rest of the questions are scored on a 0 to 100 index, where higher numbers equate to lower levels of sleep quality. The CGIC was completed by the physician at the baseline to assess the mental state of the patient, then again completed at the end of the study to assess mental state, global improvement of the patient's condition and efficacy of Gralise in relation to therapeutic effect and side effects.

The primary measure of efficacy was a change in average daily pain score from baseline to completion of Gralise therapy for 4 weeks. The secondary efficacy endpoints were the patients' PGIC and the clinician's CGIC which reports improvement in condition from baseline to the completion of the study. The safety and tolerability were evaluated by the incidence of adverse events reported while on Gralise therapy. All results have been adjusted for those patients who achieved efficacy by completing a full week of Gralise therapy.

The average daily pain score was evaluated from the pain intensity scale and the daily pain diary entries. The pain intensity scale showed a decrease of pain level at the time of the questionnaire starting at a mean level of 6.41 (SD = 2.11) before treatment started to

5.11 (SD = 2.86) on a 0 to10 scale at the end of 4 weeks of treatment. The mean difference of current pain ratings between the end of the study and at the beginning of the study was .23 ( $P = 0.5907$ ).

Another way to evaluate daily pain levels was through the pain entries in the diary. Each entry was examined from each patient. From the initial week of treatment, the mean level of pain at the time of the entry was 7.04 (SD = 1.81) to the fourth week of treatment the mean pain level at the time of entry was 6.84 (SD = 2.49), for all patients who completed a full week of treatment. However, the mean difference between the pain ratings at the time of the diary entry at the last week compared to the first week was .06 ( $P = 0.8547$ ). For both the current level of pain from the pain intensity scale and the pain diaries there was a decrease in the overall mean pain level, but not a statistically significant difference in the means between the last week of treatment and the first week of treatment. The results from both the pain intensity scale and the pain diaries are displayed in Fig. 1 and included in Table 2.

The secondary efficacy endpoint used the PGIC and the CGIC questionnaires to assess if the treatment improved the patient's condition. Patients were asked to rate their change in activity, limitations, symptoms, and overall quality of life among a scale from no change to a great deal of change. Out of 28 completed PGICs 10 (35.71%) patients rated their change was about the same or no change, while 18 out of 28 (64.29%) rated their change was at least a little better to a great deal better. Six out of 28 (21.43%) rated their change as better or a great deal better. The PGIC results are summarized in Fig. 2.

The CGIC questionnaire that was completed by

the physician to assess efficacy noted 21 out of 25 (84%) had minimally or more global improvement in the patient's condition. The physician noted 10 out of 25 (40%) patient's global improvement as being very much improved. When assessing for treatment efficacy 10 out of 27 (37.04%) were rated as having a marked therapeutic effect and no side effects. And only 3 out of 27 (11.11%) were rated as having no therapeutic effect or worsening effect, and 2 of those 3 had no side effects while the other one had no significant side effects. None of the patients were noted to have significant side effect ratings on the CGIC questionnaire. These results are also summarized in Fig. 3 with the PGIC.

Out of the total 50 patients only 9 patients reported adverse events. There were a total of 18 adverse events, from these events only 3 of the events were found to be related to the study drug. Those 3 adverse events were lethargy/sleepiness, disorientation, and dizziness, and

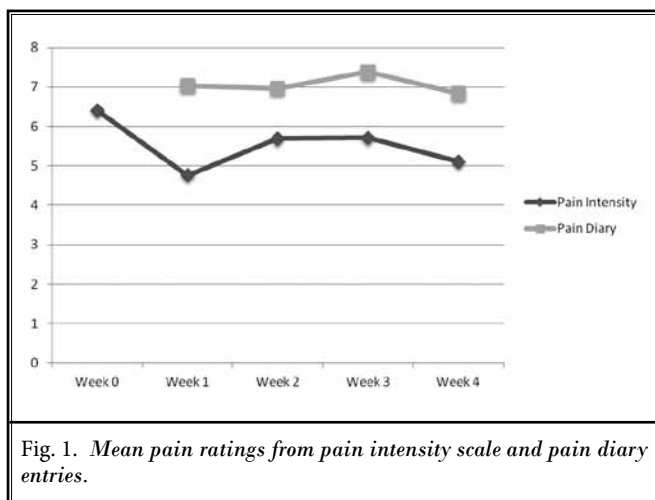
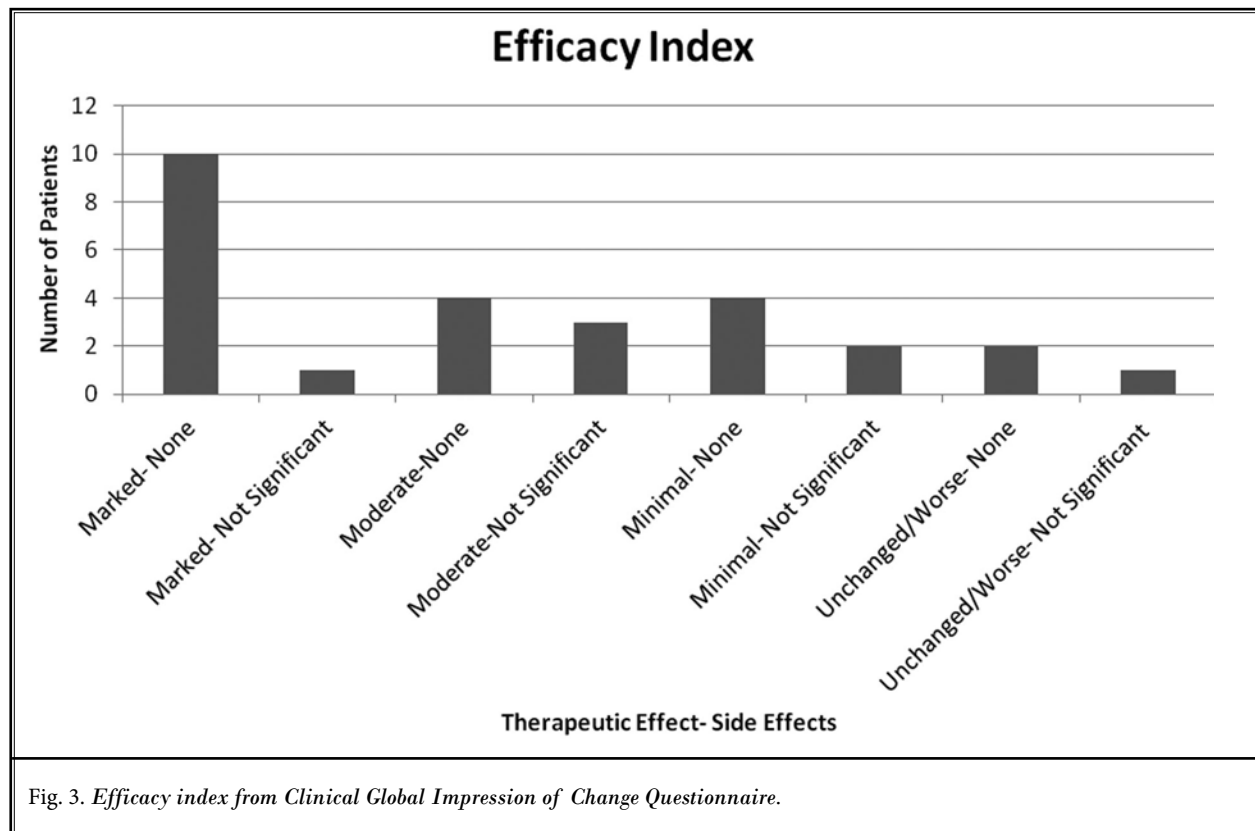
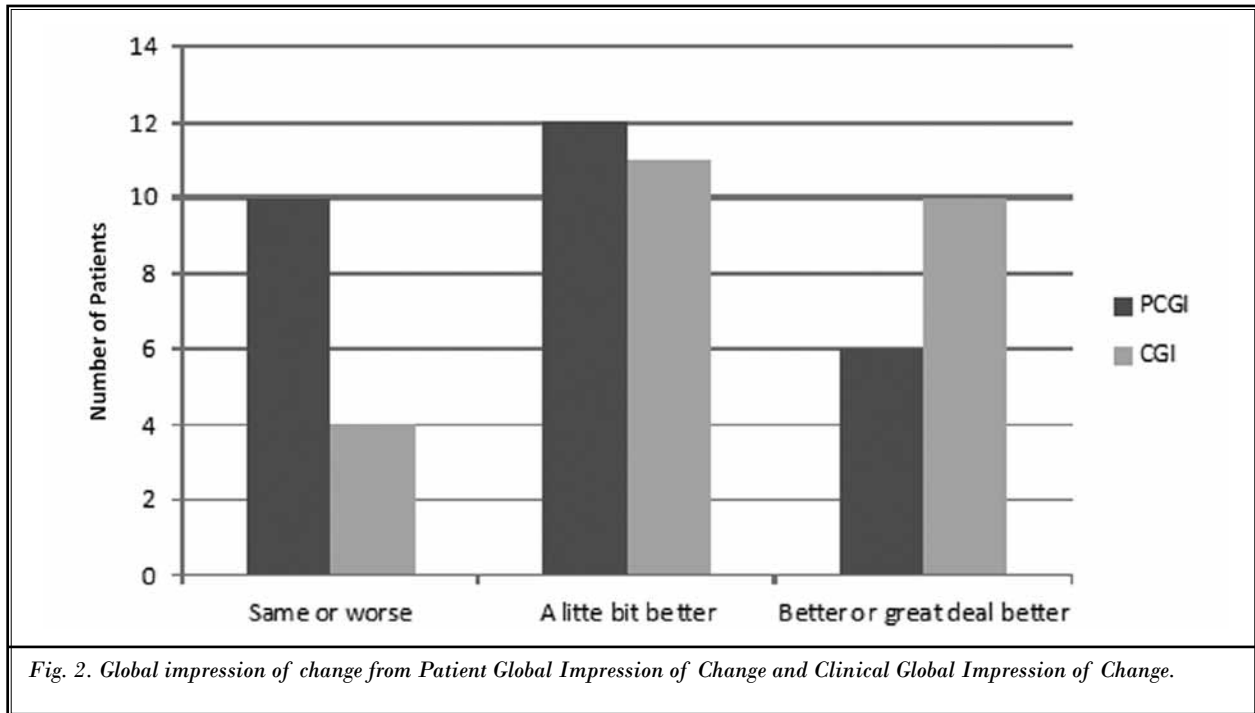


Fig. 1. Mean pain ratings from pain intensity scale and pain diary entries.

Table 2. Mean differences between week 1 of treatment and week 4 of treatment.

Variable	Mean (SD) Week 1	Mean (SD) Week 4	Mean difference	P value
Current pain ratings from Pain Intensity Scale	6.41 (2.11)	5.11 (2.86)	.23	.5907
Pain level at time of pain diary entry	7.04 (1.81)	6.84 (2.49)	-.06	.8547
Average numbers of hours slept over the past 4 weeks	4.91 (1.38)	6.07 (.34)	1.25	.0006
Sleep Adequacy Index from MOS Sleep Scale	71.71 (21.07)	53.21 (32.67)	-19.64	.0013
Sleep Disturbance Index from MOS Sleep Scale	68.61 (24.72)	45.48 (20.07)	-23.18	.0007
Sleep Somnolence Index from MOS Sleep Scale	40.76 (26.85)	32.36 (25.39)	-7.74	.1507
Sleep Problems Index from MOS Sleep Scale	58.80 (16.06)	41.91 (24.31)	-16.76	.0007
Total Opioid Use during the week from pain diaries	10.90 (8.36)	17.08 (10.20)	4.67	.1152
Percentage of Opioid use when any medication was taken	74.88% (31.05)	69.54% (32.07)	-.06%	.3024





were solved at the time the patient left or completed the study.

Other objectives for this study were to assess if there were any changes to sleep patterns and opioid use. Through the MOS sleep scale we are able to analyze various problems with sleep patterns. First we looked at sleep quantity. The mean hours slept for the past 4 weeks at the baseline visit was 4.91 (SD = 1.38), at the last visit, 4 weeks later, the mean hours slept for the past 4 weeks increased to 6.07 (SD = .34). The mean difference from the baseline visit to the end of 4 weeks of treatment with Gralise patients slept on average 1.25 hours more per night ( $P = .0006$ ). Quantity of sleep result is evaluated and included in Table 2.

We also used several combinations of questions from the questionnaire to assess sleep adequacy, disturbance, somnolence, and general sleep problems (MOS sleep scale). The evaluation of the scale is based on an index from 0 to 100, with higher numbers correlating to more problems with sleep. At the baseline visit sleep adequacy was measured at 71.71 (SD = 21.07) but at the end of 4 weeks of treatment it decreased to 53.21 (SD = 32.67). The mean difference between the 2 visits was also statistically significant, the mean difference was -19.64 ( $P = 0.0013$ ), meaning after 4 weeks of treatment patients were experiencing more adequate sleep. Sleep disturbance also had significant

improvement after 4 weeks of treatment. At baseline the mean was 68.61 (SD = 24.72) and at the end of the study it was 45.48 (SD = 20.07) with a mean difference of -23.18 ( $P = 0.0007$ ). Patients had fewer disturbances to their sleep after 4 weeks of Gralise treatment than initially at baseline. Sleep somnolence was the only measurement that was not statistically significant. At baseline somnolence was measured at 40.76 (SD = 26.85) and 32.26 (SD = 25.39) at baseline and the end for 4 weeks of treatment respectively. The mean was -7.74 ( $P = 0.1507$ ), indicating that there was essentially no difference in drowsiness or somnolence at the end of treatment when compared to at baseline. Lastly, overall the mean sleep problems index at baseline for patients was 58.80 (SD = 16.06) and at the end of 4 weeks of treatment the mean index was 41.91 (SD = 24.31) and the mean difference between the 2 time points was statistically significant as a difference of -16.76 ( $P = 0.0007$ ). Overall, after 4 weeks of treatment with Gralise patients showed a significant decrease in the level of sleep problems. All of the sleep pattern results, adequacy, disturbance, somnolence, and sleep problems index, have been displayed and summarized in Fig. 4 and Table 2.

The last measurement of interest is additional opioid use. The use of opioids was collected from the pain diaries, when patients recorded if they took medication

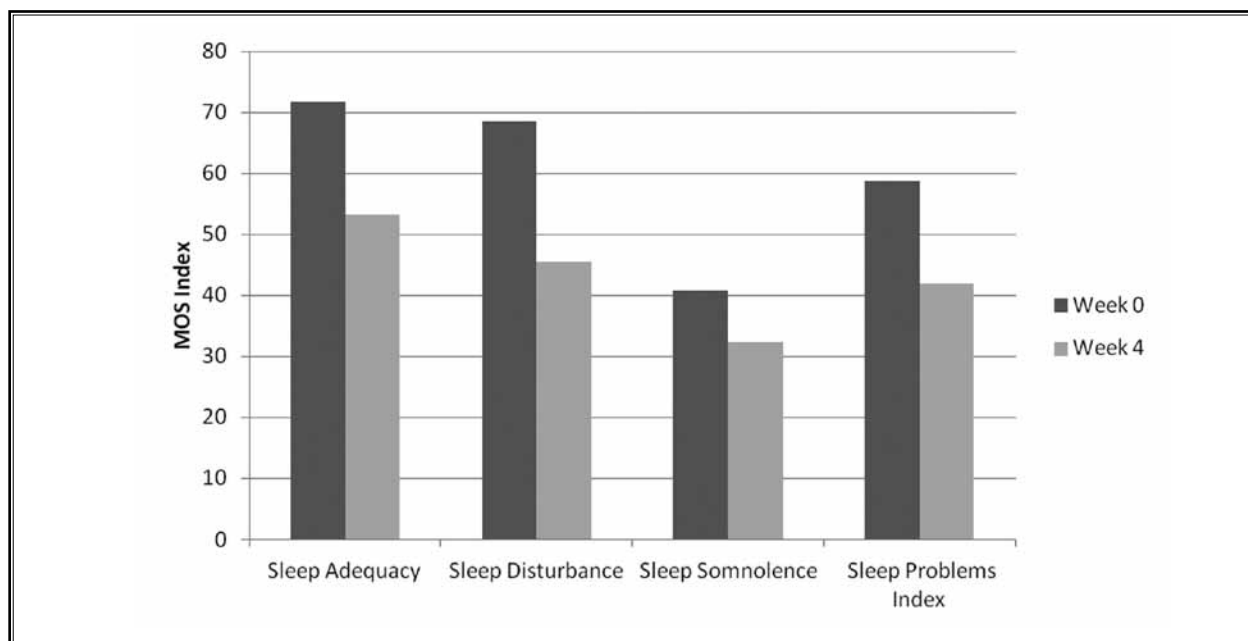
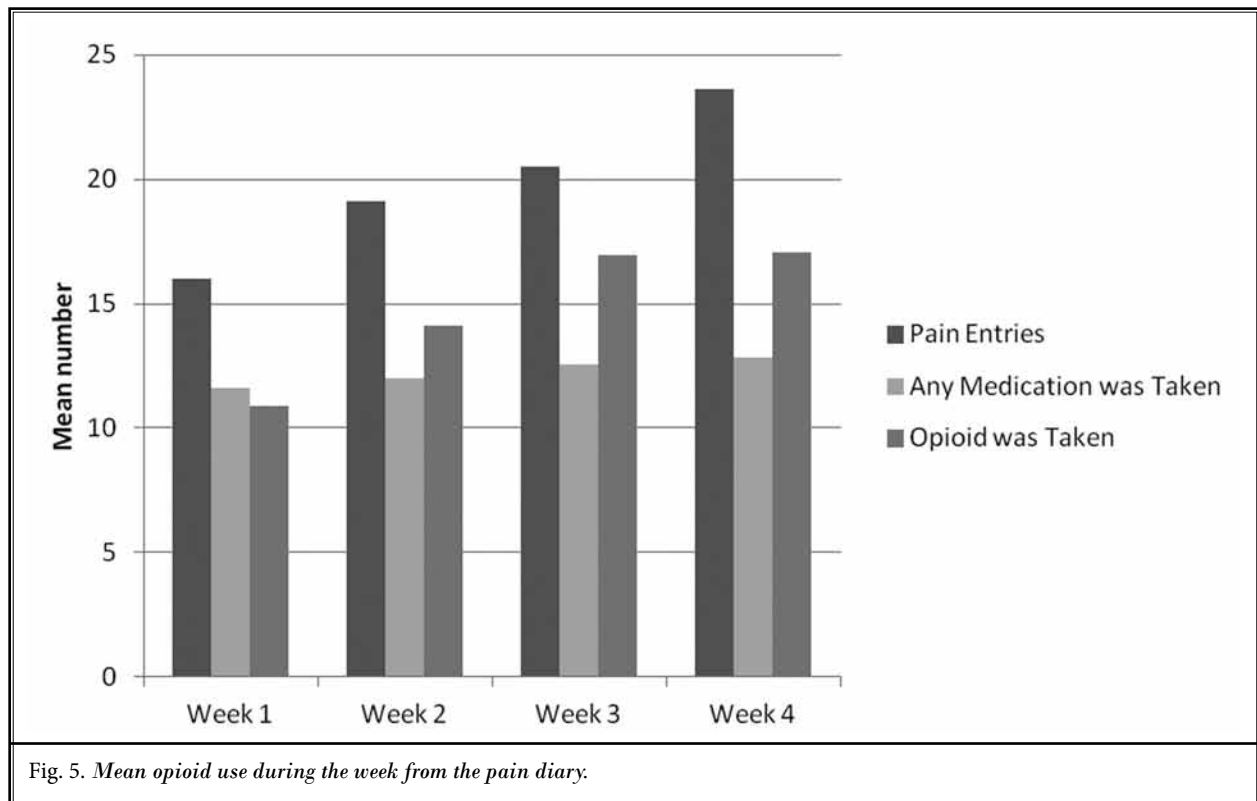


Fig. 4. Sleep problems measured from the Medical Outcomes Study Sleep Scale.



at the time of entry and what medication they took. To analyze this data, opioid use was analyzed as a count and a percentage of how many times an opioid was taken in comparison to how many times any medication was taken. The actual count of the average times an opioid was taken during the week increased from week 1 of treatment to week 4 of treatment, from 10.90 (SD = 8.36) to 17.08 (SD = 10.20), respectively. Results from the number of times opioids were used have been displayed in Fig. 5. However, the percentage of opioid use in comparison to pain entries where any medication was taken decreased over the 4 weeks. At week one, opioids were taken at 74.88% (SD = 31.05%) of the times when any medication was taken, but at week 4 opioids were taken at 69.54% (SD = 32.07%) of the pain entries when any medication was taken. These results are shown in Fig. 6. Neither of the mean differences between week 4 of treatment and week one of treatment was statistically significant. For the total number of times opioids were taken in a week, the mean difference was 4.67 ( $P = 0.1152$ ) and the percentage of entries where opioids were taken was .06% ( $P = 0.3024$ ). Therefore, percentage of opioid use when any medication was taken was reduced during the study period. All results from the number of times opioids were

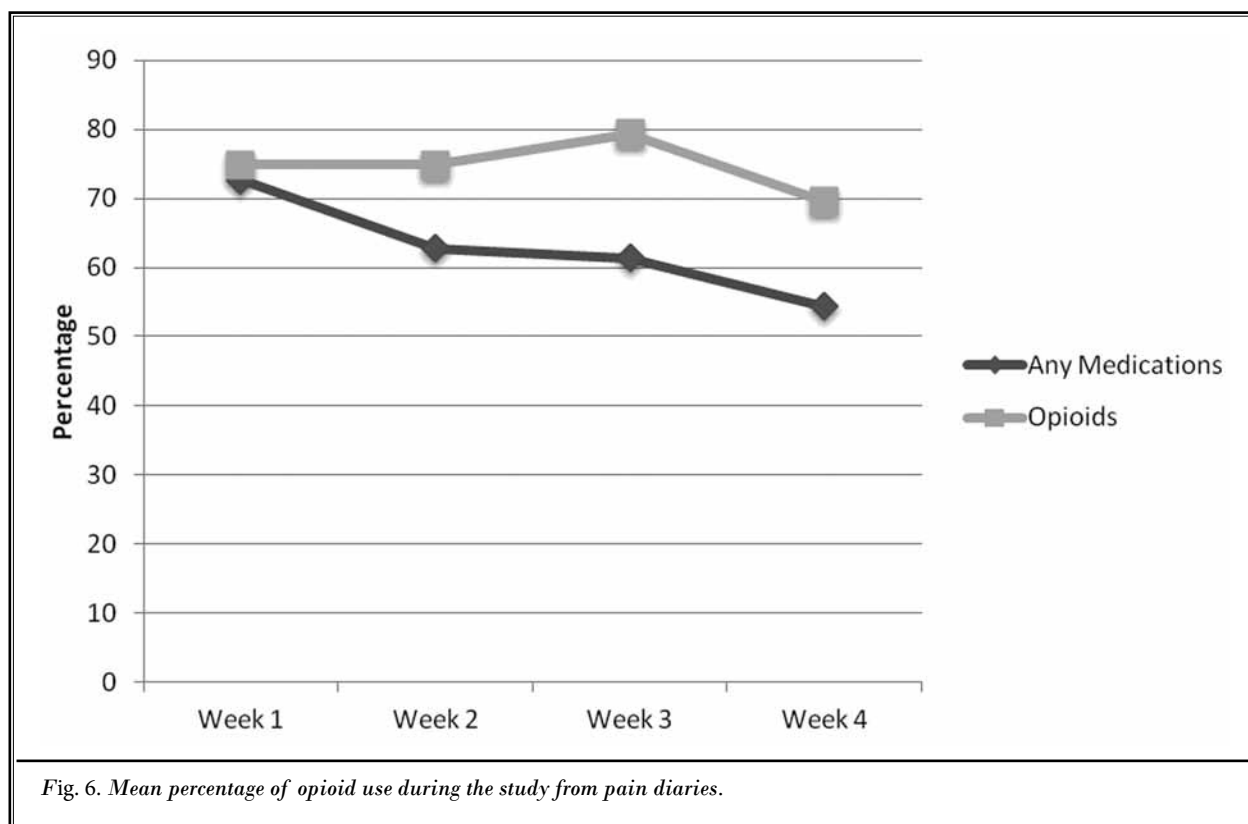
used and average number of times opioids were used are summarized in Table 2.

## DISCUSSION

The results of the present study indicate that Gralise demonstrated moderate efficacy with reduced pain intensity and increased sleep and was well tolerated in spinal stenosis patients with radicular symptoms. The PGIC noted a significant positive change in: (1) activity limitations, (2) symptoms, (3) emotions, and overall quality of life when related to their condition from first visit to last visit. Additionally, PGIC also noted an improved degree of change since their care began with the study. The MOS sleep scale and sleep diaries noted a significant increase in hours slept on average with an increase in over one hour per night from the beginning of the study to the end (5.8 hours vs. 6.86 hours). The CGIC noted a majority of marked significant therapeutic effect with no side effects. Average pain rating from pain intensity scale and pain diaries noted significant improvement of lesser levels of pain experienced.

Gabapentin preparations have been used for neuropathic states including post herpetic neuralgia for many years. Off label usage of these agents for other neuropathic states is commonplace. Though there is





limited, if any, clinical data beyond post herpetic neuralgia, numerous gabapentin preparations have been delivered to ease pain associated with the low back, diabetic peripheral neuropathy, cancer-associated neuropathic pain states, spinal cord injuries, causalgia and reflex sympathetic dystrophy, multiple sclerosis, phantom pain, post-stroke pain, HIV-associated neuropathic pain states, and trigeminal neuralgia.

Gralise is a pharmacologically unique gastroretentive preparation of gabapentin that affords efficacy with increased tolerability. Gastroretentive gabapentin is thus an extended-release formulation of gabapentin. When administered with a meal, the tablet swells and resides in the stomach for up to 15 hours, releasing the drug gradually for absorption by the small intestine. Starting dose is typically 300 mg/day once daily and increased over 2 weeks to a target dose of 1800 mg/day. When administered with an evening meal, peak dose occurs in the early morning (approximately 3 AM), when patients are sleeping. This may account for the improved tolerability of gastroretentive gabapentin with lower rate of dizziness and sedation relative to immediate release gabapentin and pregabalin (16).

Our data in the present study clearly demonstrate moderate efficacy and tolerability of Gralise in spinal stenosis patients with radicular symptoms. Our data also demonstrated a reduction in the percentage of opioid usage when any medication was taken by patients. This is concordant with a recent meta-analysis in which over 100 clinical trials were reviewed examining the use of gabapentin perioperatively to reduce postoperative pain and a smaller number examining the efficacy of pregabalin. The authors concluded that perioperative use of gabapentinoid agents reduced early postoperative pain and opioid use (17).

Spinal stenosis can have a wide range of debilitating symptoms and the role for a drug such as Gralise will require future studies. These studies should stratify in a reproducible manner mild, moderate and severe lesions and relative efficacy and tolerability in each pain state. One of the potential benefits of Gralise is that a larger proportion of the population of these patients will be likely to reach the target dose of 1800 mg/day owing to its unique gastroretentive preparation.

## CONCLUSIONS

In summary, the results of the present investiga-

tion demonstrate efficacy and tolerability of Gralise in the patients with spinal stenosis and radicular symptoms. The study demonstrated a reduction in opioid medication usage over the course of the one month treatment period and improved nightly sleep. Larger studies emphasizing degree of stenosis relative to symptoms should better identify patients who will

have success using this agent. Though there are many options for patients with spinal stenosis including many different types of medications and interventional pain procedures, Gralise appears to be a safe and effective treatment option for patients with radicular symptoms associated with spinal stenosis.

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