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Original Contribution

Tizanidine Is Effective in the Treatment of Myofascial Pain Syndrome

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Myofascial pain syndrome (MPS) is difficult to treat. The efficacy and safety of tizanidine, an alpha$_2$-adrenergic agent with effects on spasticity and pain, in treating MPS was evaluated. Female subjects (n = 29) with MPS of 9 to > 52 weeks' duration and mean age 37.5 (range 20–51) years, who also had reduced pressure thresholds, were enrolled. Subjects were titrated up to 12 mg of tizanidine over 3 weeks and maintained for 2 weeks. Sleep was assessed via visual analog scale (VAS), pain intensity via short form McGill questionnaire including VAS, disability/level of function, and pressure threshold (tested by algometry) at baseline, weeks 3 and 5, and 1 week after tizanidine was discontinued. Patient and physician global assessments of treatment were reported at week 5. Twenty-four subjects completed the study. Pain intensity and disability decreased significantly from baseline at weeks 3 and 5 and after washout ($P < .001$). Pressure threshold and sleep improved for all study periods ($P < .001$). Tizanidine was rated as good to excellent in relieving pain by 89% of subjects and 79% of physicians. No serious adverse events occurred. Tizanidine was effective in the treatment of MPS.

Key words: Tizanidine, adrenergic, myofascial pain syndrome

Myofascial pain syndrome (MPS) is an extremely common problem in the general population; its prevalence has been estimated at 12% (1). Skootsky et al (2) reported that 30% of patients in a general medical clinic satisfied the criteria for MPS. MPS is characterized by trigger points, which cause a local taut band of muscle, a distant referral pattern of pain, and a local twitching or "jump" response. These trigger points can be latent—remaining non-painful—or active—inducing a painful focus of muscle irritability. The underlying etiology is multifactorial; however, postural stresses secondary to poor ergonomic design, improper body mechanics, and repetitive overuse are the causes most frequently encountered in clinical practice (3). Sustained muscle contraction may overload the muscle and perpetuate the myofascial trigger points (4). The trapezius is commonly involved in myofascial pain because of the significance of its role in supporting the arm and the fact that it provides postural stabilization during movements of the arm and hand (5, 68).

Many pharmacologic agents have been used to treat myofascial pain, including tricyclic antidepressants, muscle relaxants, and non-steroidal anti-inflammatory agents (NSAIDS). None have provided complete resolution of this disabling problem, and research into new strategies to treat this problem is ongoing. Tizanidine is a centrally acting alpha$_2$-adrenergic agonist, which presumably reduces spasticity by increasing pre-synaptic inhibition of motor neurons, with effects at the levels of both the brain and the spinal cord. It has been used in Europe to provide effective treatment of spasticity, without affecting muscle strength, for more than 20 years (7). Tizanidine is also successful in the treatment of painful muscle spasm working via polysynaptic pathways within both the brain and spinal cord. In a clinical therapeutic trial of tizanidine hydrochloride for acute painful muscle spasm, patients receiving 2 mg 3 times a day achieved significant decreases in painful muscle spasms of the neck and shoulder as soon as 3 days after starting the drug (8). In a multinational study involving 2251 patients, Hutchinson et al (9) showed that the effectiveness of tizanidine hydrochloride in treating painful muscle spasms was good or very good in 89% of the patients.

The purpose of the this open-label, dose-titration, pilot

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study described here was to evaluate the efficacy and safety of tizanidine in treating patients with subacute and chronic cervical myofascial pain in the form of upper trapezius muscle spasm and pain.

METHODS

Participants

Female patients were included in the study if they were between 20 and 51 years' of age, presented with a documented diagnosis of subacute or chronic cervical MPS based on the presence of upper trapezius muscle spasm of the dominant side for > 2 weeks, and provided written consent to participate in the study. The study was approved by the Institutional Review Board at Kessler Medical Rehabilitation Research and Education Corporation and Western Institutional Review Board®. Subjects also needed to have a maximum pressure threshold (as determined by algometry to the dominant trapezius) ≤ 13.4 lb/cm^2; this value was based on the result from previous research on pressure thresholds in patients with MPS of the upper trapezius (10-12). Subjects were required to discontinue pain medications, including NSAIDS, corticosteroids, antidepressants, and muscle relaxants, for 1 week before the baseline visit and to be willing to remain off these medications for the duration of the study. Occasional use of acetaminophen (iei.e., Tylenol) for pain other than myofascial pain (eg, headache) was allowed. Patients were allowed to continue using antidepressants provided their dose remained stable, otherwise they were to be withdrawn from the study. Subjects were informed that the study medication, Zanaflex tizanidine would be started at 2 mg (1/2 tablet) at bedtime and would be gradually increased over three weeks. Depending on how well the study medication was tolerated, subjects were informed that they would receive up to 12 mg (3 tablets) per day, given in up to three daily doses. At the discretion of the principal investigators, the dosing schedule and final study dose could be modified.

Exclusions

Subjects were excluded if they had evidence of cervical radiculopathy based on history and physical examination, were unable to stop existing prescription alpha$_2$- adrenergic agonists or receptor-blocking medications, were unable to discontinue sleep medications, or had received botulinum toxin in the dominant upper trapezius muscle within 6 months of the start of the study. Others excluded were those with with pending worker's compensation claims or legal claims relating to their current medical condition condition.and those who had any Subjects with a severe debilitating concurrent medical condition, including severe coronary artery disease, azotemia, hepatic failure, systemic cancer or similar severe conditions, or any systemic disease, such as renal insufficiency, impaired liver function (serum glutamic-oxaloacetic transaminase (SGOT) or serum glutamic-pyruvic transaminase (SGPT) more than twice the upper normal limit), and severe, uncontrolled systemic hypertension (systolic blood pressure > 180 mmHg, diastolic blood pressure > 100 mmHg), were excluded.

Patients with spasticity secondary to multiple sclerosis, spinal cord injury, or upper motor neuron involvement or those with any medical disorder or previous surgery that might interfere with absorption, metabolism, or excretion of tizanidine were also excluded. In addition, patients with a history of drug or alcohol abuse within the past two years, lactating or pregnant women or women of childbearing potential without appropriate mechanical/barrier or oral contraceptive treatment, and those who had received an investigational drug or device in the 30 days before the screening visit were excluded.

The study protocol included a screening visit; visits at baseline, weeks 1 (telephone contact), 3, and 5; and a washout visit (1 week after discontinuation of the medication; week 6). History, physical examination, and laboratory testing (including serum pregnancy, complete blood count, and blood chemistry) were performed at screening. Physical examination was repeated at washout, and liver enzymes (SGOT/SGPT) were retested at week 5.

Participants completed various evaluation tools, including the short form McGill questionnaire, disability/level of functioning scale (0 = no disability/no effect on daily activities, 4 = complete disability/need to stay in bed), visual analog scale for sleep, and numerical rating scale for pain (0 = no pain, 10 = pain as bad as you can imagine), at baseline, weeks 3 and 5, and week 6. Pressure threshold (PT) was also measured at screening, baseline, weeks 3 and 5, and week 6. PT was defined as the minimum pressure (in lb/cm^2) that induced pain or discomfort. The maximum pressure threshold (MPT) was defined as the highest pressure (in lb/cm^2) tolerated by the patient. PT and MPT were measured with a pressure threshold meter (PTM) or algometer—a force gauge fitted with a rubber disk with a surface area of 1 cm^2. The rubber tip of the PTM was placed on the dominant upper trapezius muscle, 9 cm lateral to the C7 spinous process

Table 1. *Mean values and mean changes from baseline for sensory pain level—short form McGill pain questionnaire*

Time Point	n	MV(SD)	Mean Change From Baseline MV (SD)	P value
Baseline	29	15.6 (10.02)		
Week 3	25	10.0 (7.70)	-7.2 (9.39)	< .001
Week 5	25	3.3 (3.58)	-13.6 (10.48)	< .001
Endpoint	29	3.7 (4.48)	-11.9 (10.82)	< .001
Week 6	24	7.4 (7.56)	-10.0 (10.01)	< .001

n = number MV = Mean Value SD = Standard Deviation P value generated from paired t-test comparing baseline and post-baseline values.

(consistent with the motor point of the upper trapezius, with the shaft vertical to the examined surface (13). Pressure was then increased continuously by approximately 0.2 lb/second until the PT and MPT were obtained. At week 5, patient and investigator global assessments of the response to tizanidine were obtained with a 5-point categorical scale (poor, fair, good, very good, excellent).

Statistical analysis

The study aimed to evaluate and estimate the efficacy of tizanidine in decreasing muscle spasm and pain in patients with subacute and or chronic cervical myofascial pain. A previous study determined that 25 patients were needed to provide adequate power to detect moderate or greater pain relief in patients with multiple sclerosis treated with gabapentin (14). In addition, the computer program SPSS Sample Power determined that 25 patients would allow detection of a mean maximum pressure threshold difference as small as 2 lb/cm^2 (which is considered clinically significant) by algometry.

Measurements used to assess efficacy—ie scores from the short form McGill questionnaire, pressure algometry scores, VAS for sleep, disability/level of functioning scale, and daily 10-point pain assessment—were summarized using descriptive statistics for continuous variables (n, mean, median, standard deviation, and range). Change in response between baseline and each time point on the various evaluation tools was evaluated using paired *t*-tests. Study end-point corresponds to the last observation carried forward for the active-treatment period. Frequency analysis was used to evaluate categorical variables encountered on the patient and investigator global assessment scales, concomitant medication usage and treatment-emergent adverse events.

Demographics, dose titration information (eg daily dose and maximum tolerated dose), vital signs, and laboratory test results were summarized using descriptive statistics.

RESULTS

Overall, 43 female patients were screened for enrollment into this study—19 at one site and 24 at a second site. Seven patients from each site were screening failures—they did not meet the inclusion/exclusion criteria at the screening or baseline visit—and were not eligible for participation. The remaining 29 patients received at least one dose of study medication, and they were included in the efficacy (intent-to-treat) and safety populations. Twenty-four (82.8%) patients completed the study.

Short Form McGill Pain Questionnaire

Sensory pain levels

The mean baseline sensory pain level was 15.6 (out of a maximum of 33). The mean scores decreased progressively while the participants were taking tizanidine, reaching a value of 3.7 at study endpoint. During the off-drug week, the scores began to increase. The difference from baseline was statistically significant at every evaluation point (Table 1). A greater proportion of participants had sensory pain levels ≤5 by study endpoint than at baseline; this proportion began to fall once patients were taken off the study medication.

The distribution of patients by sensory pain level category through the study is summarized in Table 2.

Table 2. *Sensory pain level categories—short form McGill pain questionnaire*

Time Point	n	Category (Total Score)	Number (%)
Baseline	29	(<=5)	6 (20.7)
		Mild (6-15)	10 (34.5)
		Moderate (16-25)	7 (24.1)
		Severe (> 25)	6 (20.7)
Week 3	25	(<= 5)	9 (36.0)
		Mild (6-15)	10 (40.0)
		Moderate (16-25)	5 (20.0)
		Severe (> 25)	1 (4.0)
Week 5	25	(<= 5)	20 (80.0)
		Mild (6-15)	4 (16.0)
		Moderate (16-25)	1 (4.0)
		Severe (> 25)	0 (0.0)
Endpoint	29	(<= 5)	23 (79.3)
		Mild (6-15)	4 (13.8)
		Moderate (16-25)	2 (6.9)
		Severe (> 25)	0 (0.0)
Week 6	24	(<= 5)	11 (45.8)
		Mild (6-15)	11 (45.8)
		Moderate (16-25)	1 (4.2)
		Severe (> 25)	1 (4.2)

n=number

Table 3. *Mean values and changes from baseline for affective pain level—short form McGill pain questionnaire*

Time Point	n	MV(SD)	Mean Change From Baseline MV(SD)	P value
Baseline	29	4.9 (4.41)		
Week 3	25	3.3 (2.87)	-2.0 (3.50)	.009
Week 5	25	0.4 (0.70)	-4.6 (4.67)	< .001
Endpoint	29	0.6 (1.57)	-4.3 (4.48)	< .001
Week 6	24	1.8 (2.76)	-3.3 (4.11)	< .001

n = number MV = Mean Value SD = Standard Deviation *P* value generated from paired *t*-test comparing baseline and post-baseline values.

Table 4. *Affective pain level categories—short form McGill pain questionnaire*

Time Point	n	Total Score	Number (%)
Baseline	29	<= 8	21 (72.4)
		> 8	8 (27.6)
Week 3	25	<= 8	25 (100)
		> 8	0 (0)
Week 5	25	<= 8	25 (100)
		> 8	0 (0)
Endpoint	29	<= 8	29 (100)
		> 8	0 (0)
Week 6	24	<= 8	23 (95.8)
		> 8	1 (4.2)

n=number

Affective Pain levels

The mean baseline affective pain level was 4.9 (out of a maximum of 12). The mean scores decreased progressively while the patients were taking tizanidine, reaching a value of 0.6 at study endpoint. The difference from baseline was statistically significant at every evaluation point (Table 3).

The distribution of patients by affective pain level category through the study is summarized in Table 4.

PAIN INTTENSITY (VAS)

The mean score on the 10-cm pain intensity VAS was 6.0 at baseline. The mean score decreased progressively while the patients were taking tizanidine, reaching a value of 2.5 at study endpoint. The difference from baseline was statistically significant at every evaluation point (Table 5).

Pain Intensity Description

The mean baseline value for pain intensity, measured on a 6-point scale (0 = no pain, 5 = excruciating pain), was 2.8. The mean value decreased while the patients were taking tizanidine, reaching a value of 1.1 at study endpoint. The difference from baseline was statistically significant at every evaluation point (Table 6).

The distribution of patients by pain intensity through the study is summarized in Figure 1.

Pressure Algometry Measurements

Mean values for PT and MPT increased progressively while the patients were taking tizanidine (Table 7). Changes from baseline were statistically significant at every active-treatment evaluation point.

Disability/Level of Functioning Scale

The mean baseline value for the disability/level of functioning scale (a 5-point scale in which 0 = no disability and no effect on daily activities and 4 = complete disability and the need to stay in bed) was 1.8. The mean value decreased while the patients were taking tizanidine, reaching a value of 0.5 at study endpoint. The difference from baseline was statistically significant at every evaluation point (Table 8).

Sleep VAS

On the sleep VAS, a score of 0 indicated that pain had not interfered at all with sleep during the preceding week and

Table 5. *Mean values and changes from baseline for pain intensity (VAS)—short form McGill pain questionnaire*

Time Point	n	MV(SD)	Mean Change From Baseline MV(SD)	P value
Baseline	29	6.0 (2.33)	——	——
Week 3	25	3.6 (2.06)	-2.8 (1.87)	< .001
Week 5	25	2.5 (2.49)	-3.8 (3.00)	< .001
Endpoint	29	2.5 (2.55)	-3.5 (2.93)	< .001
Week 6	24	3.1 (2.90)	-3.3 (3.22)	< .001

n = number MV = Mean Value SD = Standard Deviation *P* value generated from paired *t*-test comparing baseline and post-baseline values.

Table 6. *Mean values and changes from baseline for pain intensity description—short form McGill pain questionnaire*

Time Point	n	MV(SD)	Mean Change From Baseline MV (SD)	P value
Baseline	29	2.8 (1.02)		
Week 3	25	1.6 (1.08)	-1.3 (1.31)	< .001
Week 5	25	1.0 (1.10)	-1.8 (1.58)	< .001
Endpoint	29	1.1 (1.29)	-1.7 (1.59)	< .001
Week 6	24	1.7 (1.17)	-1.2 (1.63)	.002

n = number MV = Mean Value SD = Standard Deviation *P* value generated from paired *t*-test comparing baseline and post-baseline values.

a score of 10 indicated the worst possible interference with sleep. The mean value, which was 5.55 at baseline, decreased to 1.73 at study endpoint. The difference from baseline was statistically significant at every evaluation point (Table 9).

Global Assessments

Both the patients and the investigators provided an assessment of tizanidine at study endpoint (week 5 or early termination visit). Figure 2 shows 89% of patients

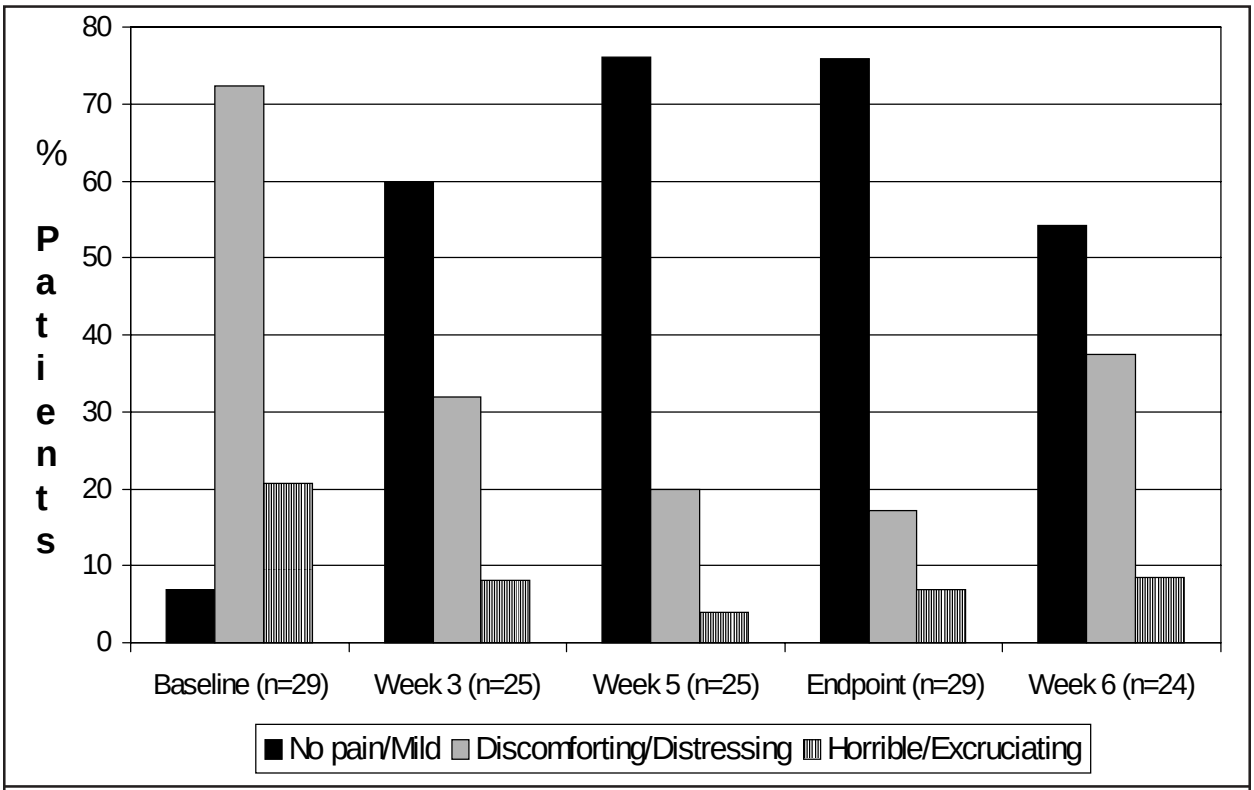

Fig. 1. Pain Intensity Description - Short Form McGill Pain Questionnaire
P value generated from paired *t*-test comparing baseline and post-baseline values.

Table 7. *Pressure algometry measurements*

Time Point	n	MV(SD)	Mean Change From Baseline MV (SD)	P value
Pressure Threshold (lb/cm2)				
Baseline	29	5.7 (1.93)	—	—
Week 3	25	6.8 (2.70)	1.3 (1.44)	< .001
Week 5	25	7.0 (2.31)	1.5 (1.40)	< .001
Endpoint	29	7.1 (2.21)	1.4 (1.69)	< .001
Week 6	24	6.3 (3.71)	0.8 (2.20)	.099
Maximum Pressure Threshold (lb/cm2)				
Baseline	29	7.8 (2.95)		
Week 3	25	9.7 (4.03)	2.3 (2.55)	< .001
Week 5	25	10.6 (3.77)	3.1 (3.15)	< .001
Endpoint	29	10.7 (3.65)	3.0 (2.96)	< .001
Week 6	24	9.2 (4.23)	1.9 (2.86)	.004

n = number MV = Mean Value SD = Standard Deviation *P* value generated from paired *t*-test comparing baseline and post-baseline values.

rated study medication as good, very good or excellent for pain. Seventy-eight percent of investigators rated tizanidine as good, very good, or excellent.

Adverse Events

Overall, 19 (66%) of the 29 patients experienced at least one adverse event at some time during the study (Table 10). The most commonly reported adverse events were somnolence (28%), headache (24%), and dizziness (24%). Most adverse events were judged by the investigator to be at least possibly related to tizanidine. One (3%) patient was withdrawn from the study because of an adverse event (rash). There were no deaths and no serious adverse events.

Evaluation of Liver Enzymes

Concentrations of SGOT/aspartate aminotransferase (AST) levels decreased significantly between baseline and the end of study ($P = .030$); there was no significant change in SGPT/alanine aminotransferase (ALT) (Table 11). Twenty-two patients had normal values for SGPT/ALT at baseline and the end of the study. Four patients had

Table 8. *Mean values and changes from baseline for disability/level of functioning scale*

Time Point	n	MV(SD)	Mean Change From Baseline MV (SD)	P value
Baseline	29	1.8 (0.85)		
Week 3	25	1.1 (0.49)	-0.9 (0.64)	< .001
Week 5	25	0.5 (0.65)	-1.5 (0.92)	< .001
Endpoint	29	0.5 (0.69)	-1.3 (1.00)	< .001
Week 6	24	1.2 (0.88)	-0.8 (0.90)	< .001

n = number MV = Mean Value SD = Standard Deviation *P* value generated from paired *t*-test comparing baseline and post-baseline values.

Table 9. *Mean values and changes from baseline for sleep VAS*

Time Point	n	MV(SD)	Mean Change From Baseline MV (SD)	P value
Baseline	29	5.55 (2.996)		
Week 3	25	2.92 (2.375)	-3.06 (2.246)	< .001
Week 5	25	1.74 (2.035)	-4.14 (2.934)	< .001
Endpoint	29	1.73 (2.096)	-3.82 (2.946)	< .001
Week 6	24	2.94 (2.956)	-3.03 (2.955)	< .001

n = number MV = Mean Value SD = Standard Deviation *P* value generated from paired *t*-test comparing baseline and post-baseline values.

baseline values outside the normal range, but these had returned to normal by the end of the study. One patient had values above the upper limit of normal at baseline (49 IU/L) and the end of the study (53 IU/L); the investigator did not consider either elevation to be clinically significant. One patient had normal values for SGPT/ALT at baseline (36 IU/L) and values above the normal range at the end of the study (43 IU/L); the investigator did not consider the increase to be clinically significant. No patient had any treatment-emergent adverse event related to these laboratory tests.

DISCUSSION

Myofascial pain syndrome is difficult to treat because it may be initiated by peripheral and central mechanisms that appear to be inter-related. Central sensitization refers to an increased excitability of spinal and supraspinal regions resulting from injury or inflammation-induced activation of peripheral nociceptors (15). Central sensitization leads to nociceptive nerve impulses being perceived as painful (hyperalgesia) and non-nociceptive nerve impulses being perceived as painful (allodynia). The phenomenon of non-nociceptive pain correlates very strongly with myofascial pain; they have many similar characteristics: the description of pain seems inappropriate compared with the tissue pathology (or lack of discernible tissue pathology), noxious stimuli result in a pain experience greater than is normally expected, normally non-noxious stimuli result in pain, and the extent of the pain boundary is greater than would normally be expected based on the site of the original tissue injury (15). The

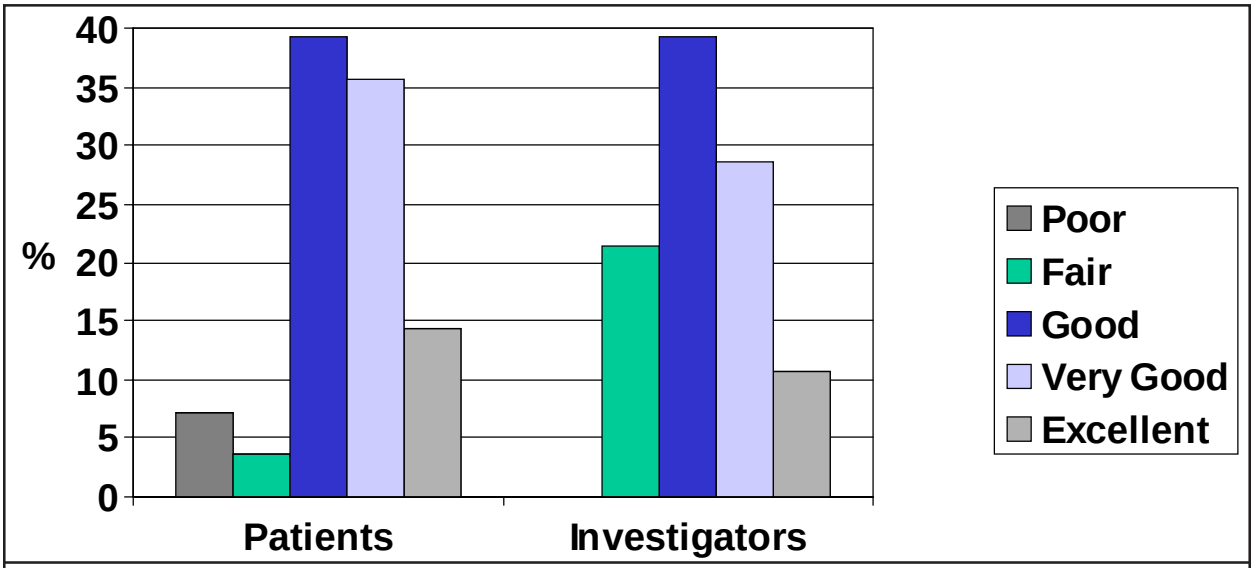

Fig. 2. Patient and Investigator Global Assessment of Study Medication
Question: How would you rate the study medication you (the patient) received for pain?

Table 10. *Treatment-emergent adverse events*

	All Patients (n = 29)		
Body System Preferred Term	**Total Events n[a] (%)**	**Severe Events[b] n (%)**	**Related Events[c] n (%)**
Any adverse event	19 (65.5)	9 (31.0)	16 (55.2)
Body as a Whole	11 (37.9)	7 (24.1)	4 (13.8)
Abdominal pain	2 (6.9)	1 (3.4)	1 (3.4)
Asthenia	3 (10.3)	1 (3.4)	2 (6.9)
Back pain	3 (10.3)	2 (6.9)	1 (3.4)
Headache	7 (24.1)	2 (6.9)[d]	1 (3.4)
Infection	2 (6.9)	0 (0)	0 (0)
Pain	5 (17.2)	1 (3.4)	0 (0)
Cardiovascular System[e]	1 (3.4)	1 (3.4)	0 (0)
Digestive System	8 (27.6)	3 (10.3)	7 (24.1)
Dry mouth	3 (10.3)	2 (6.9)	3 (10.3)
Nausea	5 (17.2)	0 (0.0)	4 (13.8)
Musculoskeletal System[e]	1 (3.4)	1 (3.4)	0 (0)
Nervous System	13 (44.8)	5 (17.2)	13 (44.8)
Anxiety	2 (6.9)	0 (0)	1 (3.4)
Depression	2 (6.9)	1 (3.4)	1 (3.4)
Dizziness	7 (24.1)	1 (3.4)	7 (24.1)
Somnolence	8 (27.6)	3 (10.3)	8 (27.6)
Respiratory System	4 (13.8)	2 (6.9)	0 (0)
Bronchitis	2 (6.9)	1 (3.4)	0 (0)
Rhinitis	2 (6.9)	1 (3.4)	0 (0)
Skin and Appendages[e]	2 (6.9)	0 (0)	1 (3.4)

a n = number
b Within each body system, a patient was counted once if she had at least one severe event within that body system. For specific events, a patient was counted once if she had at least one severe episode of the event.
c Within each body system, a patient was counted once if she had at least one event that was considered related to treatment within that body system. For specific events, a patient was counted once if she had at least one episode of the event that was considered related to treatment.
d Intensity of headache was unknown for one patient.
e No specific adverse event (by preferred term) within this body system occurred in > 1 patient.

use of agents that address both central and peripheral components of pain therefore make good clinical sense in light of the impact of the central sensitization phenomena in MPS.

Tizanidine, an alpha-$_2$-adrenergic agonist, exerts effects in both the brain and spinal cord, with effects at the second order dorsal horn neurons and wide dynamic range neurons—the same location implicated in the central sensitization process (16). Tizanidine decreases spasticity by reinforcing presynaptic inhibition and reinforcing Ia reciprocal and Ib nonreciprocal postsynaptic inhibition (17). The exact mechanism by which the alpha$_2$-adrenergic agonists reduce pain is unknown; however, it may occur

Table 11. *Mean values and mean changes from baseline for SGOT/AST and SGPT/ALT*

Laboratory Test Time Point	N	MV (SD)	Mean Change From Baseline (SD)	P value
SGOT/AST (IU/L)				
Baseline	29	19.0 (4.54)		
End of study	28	17.6 (3.86)	-1.5 (3.55)	.030
SGPT/ALT (IU/L)				
Baseline	28	23.8 (12.54)		
End of study	28	24.1 (11.99)	0.4 (4.53)	.644

n = number MV = Mean Value SD = Standard Deviation *P* value generated from paired *t*-test comparing baseline and post-baseline values.

via modulation of the excitatory amino acids glutamate and aspartate along with substance P (18,19). Tizanidine's mechanism of action therefore shows promise for the treatment of myofascial pain, by reducing both pain and associated muscle tone.

Efficacy

In this study, significant reductions in pain, tissue tenderness, and disability along with improved sleep properties were associated with the use of tizanidine in subjects with MPS. These results may be consistent with effects previously noted in the central nervous system and with theorized peripheral effects on substance P and excitatory neurotransmitters.

Various pharmacologic agents have been used in the treatment of myofascial pain, including tricyclic antidepressants, serotonin agonists, serotonin reuptake inhibitors, NSAIDS, and capsaicin cream (20-23). Amitriptyline was shown to be somewhat effective in reducing pain, without changing the patient's pain or pressure threshold (20). Injectable diclofenac was also shown to provide significantly better pain relief, as measured on the VAS, than injections of lidocaine in the treatment of MPS (22). Significant risks associated with prolonged use of NSAIDS, including gastrointestinal bleeding and renal toxicity, make diclofenac a less favorable treatment strategy for patients who may require chronic treatment (24,25). Capsaicin decreased chronic neck pain, as measured on a VAS, but no significant improvement in affective pain levels, as measured by the McGill pain questionnaire, was shown (23). Serotonin agonists and serotonin reuptake inhibitors have met with limited success in studies on myofascial pain (21,22). In light of the variable results with other pharmacologic agents and our study results, tizanidine has a role as a first-line medication in the treatment of MPS.

Adverse events

No deaths or serious adverse events occurred in this study. The most common adverse events with tizanidine are dry mouth, somnolence/sedation, asthenia, and dizziness (26). The rates of dry mouth, somnolence, and asthenia in this study, which had a lower maximum allowable dose than some of the spasticity trials, were considerably lower than previously reported, but the rate of dizziness was somewhat higher. None of the patients in this study experienced hypotension or bradycardia, which are more commonly encountered in subjects being treated for spasticity. Other less common adverse events reported in this study were similar in type and incidence to those that occurred in clinical trials in patients with spasticity. The safety profile of tizanidine demonstrated in this study was similar to the known safety profile.

CONCLUSION

Tizanidine is effective in the treatment of subacute and chronic myofascial pain syndrome. Pain, disability, and muscle tenderness were significantly reduced, and sleep was significantly improved. No serious adverse events occurred in this study, in which one patient discontinued secondary to a rash. Tizanidine should be considered as a first-line pharmacologic agent for the treatment of myofascial pain.

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