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Research Article

# Comparison of the Efficiency and Safety of Oral Phenyramidol and Phenyramidol+Diclofenac Treatment in Muscle Spasms with Spinal Pain – Open-Label Study

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## Abstract

Muscle relaxants (MR) and nonsteroidal anti-inflammatory drugs (NSAID) are frequently used in the treatment of spasms and are effective combined or alone in muscle spasms. In this study, 30 patients aged 32-82 years, male and female, with moderate to severe acute spinal pain-muscle spasms due to trauma, sprain, or injury history were evaluated. Group 1 received phenyramidol 400 mg orally 3 times a day for 7 days. In the second group, phenyramidol (400 mg) three times a day + diclofenac (75 mg) once a day was given orally for 7 days. Patients were evaluated on the 0th and 7th days in terms of muscle spasm level, pain intensity, and side effects. Side effects were noted for clinical safety. Evaluation was performed at the start of treatment and after treatment. Compared with the adverse drug reactions that occurred during the study, Group 1 treated with phenyramidol alone showed a statistically significantly better safety profile than Group 2 treated with the combination of phenyramidol and diclofenac ($p<0.001$). As a result, it was observed that oral phenyramidol treatment alone and oral phenyramidol+diclofenac combination treatment did not have any difference in terms of efficacy, but when compared in terms of side effects, the use of phenyramidol alone showed a higher safety profile.

**Keywords:** phenyramidol, diclofenac, muscle spasm, spinal pain

## 1. INTRODUCTION

Muscle spasm, which is a condition that occurs with the involuntary contraction of the muscles, is also frequently encountered in spinal disorders. Although this condition is frequently seen in the low back area, it is rarely observed in the back and neck[1–4].Spasm increases pain in acute spinal diseases, and this pain causes an increase in spasm, putting the situation in a vicious pain-spasm-paincycle[5]. MR and NSAID are effective options in the treatment of these and similar conditions accompanied by muscle spasms[6].

The chemical structure of Phenyramidol is2-(beta-hydroxyphenethylamino)-pyridine hydrochloride and it is categorized in the skeletal muscle relaxant drug group. Clinical and experimental studies on phenyramidol have shown that this drug is safe in terms of side effects. It is known that this drug, which is considered safe, is also effective in the treatment of painful muscle spasms. Its mechanism of action works by blocking interneuronal and polysynaptic reflexes in the spinal cord and brainstem. It is used in oral and parenteral forms for musculoskeletal disorders and integumental pain [7–12].

Diclofenac is one of the NSAID. The anti-inflammatory activity and many of the other pharmacological effects of diclofenac are generally thought to be related to the inhibition of prostaglandin synthesis. Diclofenac inhibits the cyclooxygenase enzyme and reduces the synthesis of prostaglandin, prostacyclin, and thromboxane. It is used in conditions such as rheumatic and non-rheumatic pain, inflammation, and swelling [13].

Diclofenac is a potent COX-2 inhibitor with analgesic, anti-inflammatory, and antipyretic properties[14]. The most common side effects of diclofenac are gastrointestinal complications. Warnings regarding the use of diclofenac include cardiovascular thrombotic events, gastrointestinal bleeding, ulceration and perforation, hepatotoxicity, renal toxicity, and hyperkalemia[15].

In the light of studies showing the efficacy of diclofenac in spinal painful muscle spasms[16].In this studyit was aimed to compare the efficacy and safety of phenyramidol alone or phenyramidol+diclofenac combination treatments in spinal and painful muscle spasms.

## 2. MATERIAL AND METHODS

### 2.1 Patients

This study was conducted as a prospective, open-label, randomized, comparative study in the outpatient unit of İstanbul University Cerrahpaşa Faculty of Medicine, Department of Physical Medicine and Rehabilitation. The study protocol has been approved. The patients were evaluated according to the inclusion and exclusion criteria, and written informed consent was obtained from the patients participating in the study. The study was conducted with 30 patients aged 32-82 years, male or female, with moderate to severe acute spinal pain-muscle spasms due to a history of trauma, sprain, or injury.

The inclusion criteria of male and female patients are as follows;

1. Being 18 years old or older
2. Having a history of spinal pain and muscle spasms shorter than 7 days.

The exclusion criteria are as follows;

1. Patients with spinal pain due to infection, abnormal metabolism, malignancy, osteoarthritis, or a different disease,
2. Patients with back pain originating from other organs,
3. Patients, who are allergic to NSAIDs and skeletal muscle relaxants,
4. Patients with asthma or other allergic conditions,
5. Patients with a history of gastrointestinal bleeding, peptic ulcer, or severe dyspepsia,
6. Patients treated with NSAIDs or skeletal muscle relaxants for 3 days prior to the study,
7. Patients receiving anticoagulation therapy,
8. Patients with serious concomitant systemic disease, including bleeding diathesis,
9. Patients with liver or kidney failure, and
10. Pregnant or breastfeeding women were excluded from the study.

### 2.2 Procedure

Before starting the treatment, anamnesis including demographic information was taken from the patients participating in the study. 30 patients were randomly divided into 2 groups of 15 people. In Group 1, phenyramidol (400 mg) treatment was administered orally three times a day for 7 days. In Group 2, phenyramidol (400 mg) three times a day + diclofenac (75 mg) once a day was given orally for 7 days. Patients were evaluated on days 0 and 7 in terms of muscle spasm, pain severity, and side effects.

Pain was evaluated according to the visual analog scale (0 cm; no pain, 10 cm: excruciating pain) while the patients were at rest and in motion[17]. Muscle spasm was evaluated by measuring the finger-floor distance while standing and the chin-sternal distance while sitting [18]. The overall effectiveness rating was based on a 4-point scale marked as excellent/good/moderate/poor[19]. Side effects such as neurological and gastrointestinal complaints have been noted.

### 2.3 Statistical analysis

Data are expressed as the mean ± SEM and were analyzed using SPSS 11.0. The level of statistical significance was set at $p < 0.05$. The data for the treatment groups, including the effects of phenyramidol and phenyramidol + diclofenac combination were evaluated by Independent Student's t-test.

## 3. RESULTS

Of the 15 patients, who were administered phenyramidolalone out of a total of 30 patients, 9 were male and 6 were female; Of the 15 patients, who were administered phenyramidol + diclofenac, 8 were male and 7 were female. In Group 1, 66,6% of the patients had pain in their lower back, 20% in their neck, and 13,3% in their back. In Group 2, pain was localized at 60% in the lower back, 26,6% in the neck, and 13,3% in the back. The distribution of the groups was homogeneous (Table 1).

Table 1: Demographic characteristics and p values of the patient groups

| Characteristic | | Group 1 | Group 2 | P value |
|---|---|---|---|---|
| Age ( years) | | 36.7 ± 3.2 | 38.6 ± 2.4 | >0.05 |
| Gender | Male | 9 | 8 | |
| | Female | 6 | 7 | |
| Pain localisation | Neck | 3 | 4 | |
| | Back | 2 | 2 | |
| | Low back | 10 | 9 | |
| BMI (kg/m^2) | | 24.6 ± 1.8 | 25.3 ± 2.1 | |

In Table 2, the values of pain intensity and muscle spasm status before and after treatment are given. Their means, standard deviations, and p-values are shown in the table. Statistically, significant improvement was shown in each parameter after treatment. While the mean pain before treatment was 4.6 ± 1.2 and 7.4 ± 2.1 at rest and in motion in Group 1, respectively, these values changed to 3.0 ± 1.0 and 4.2 ± 1.8 after treatment. While the mean of pain was 4.6 ± 1.8

and 8.1 ± 1.9 at rest and in motion, in Group 2,respectively, this situation changed to 2.0 ± 0.8 and 4.6 ± 1.2 after treatment. Muscle spasm was assessed by measuring the finger-floor distance while standing and the chin-sternal distance while sitting. In Group 1, while standing, finger-floor distance was 32.1 ± 6.7, and chin-sternal distance while sitting was 8.9 ± 1.4 before treatment, these values were 20.4 ± 1.4 and 4.3 ± 2.7, respectively, after treatment. In Group 2, the finger-floor distances before and after the treatment were 36.3 ± 3.8 and 17.1 ± 2.2, and the chin-sternal distances while sitting were 7.6 ± 2.1 and 3.1 ± 0.9. According to these findings, there was a statistically significant decrease in pain intensity and muscle spasm in Group 1 receiving phenyramidol (400 mg) and Group 2 treated with phenyramidol (400 mg) + diclofenac (75 mg) (p<0.01). When the Group 1 and 2 patients were compared in terms of pain and muscle spasm, there was no statistically significant difference (p>0.05).

Table 2: Before and after treatment results of the patient groups

| Characteristic | | Group 1 | | | Group 2 | | |
|---|---|---|---|---|---|---|---|
| | | Before Treatment | After Treatment | P value | Before Treatment | After Treatment | P value |
| Pain (VAS) | Rest | 4.6 ± 1.2 | 3.0 ± 1.0 | <0.01 | 4.6 ± 1.8 | 2.0 ± 0.8 | <0.01 |
| | Movement | 7.4 ± 2.1 | 4.2 ± 1.8 | <0.01 | 8.1 ± 1.9 | 4.6 ± 1.2 | <0.01 |
| Spasm | Chin-sternum distance (cm) | 8.9 ± 1.4 | 4.3 ± 2.7 | <0.01 | 7.6 ± 2.1 | 3.1 ± 0.9 | <0.01 |
| | Finger-floor distance (cm) | 32.1 ± 6.7 | 20.4 ± 1.4 | <0.01 | 36.3 ± 3.8 | 17.1 ± 2.2 | <0.01 |
| P Value | | >0.05 | | | | | |

In Table 3, the efficiency ratio distributions are given. Evaluations made in terms of efficacy in patient groups were similar and did not show any significance (Table 3). Very good and good results were obtained in 10 of 15 patients in Group 1, and very good and good results were obtained in 12 of 15 patients in Group 2.

*Table 3: The evaluation of global assessments in patient groups*

| Efficacy | Group 1 | Group 2 |
|---|---|---|
| Excellent | 2 | 3 |
| Good | 8 | 9 |
| Average | 4 | 4 |
| Poor | 1 | 0 |
| P Value | >0.05 | |

Adverse drug reactions that occurred during the study are shown in Table 4. While 86,6% of the patients in Group 1 did not have any side effects, only 20% of the patients in Group 2 did not have any side effects. Dizziness and drowsiness were seen in 6,6% of both groups. While painful burning sensation in the chest and abdominal pain were not observed in Group 1, this value was 33,3% and 13,2% in Group 2, respectively. While the incidence of nausea was 6,6% in Group 1, it was 19,8% in Group 2. These results showed a statistically significantly better safety profile for Group 1 than for Group 2 (p<0.001) (Table-4).

*Table 4: The evaluation from the aspect of side effects in patient groups*

| Side effects | Group 1 | Group 2 |
|---|---|---|
| None | 13 | 3 |
| Dizziness | 1 | 1 |
| Drowsiness | 1 | 1 |
| Heartburn | 0 | 5 |
| Nausea | 1 | 3 |
| Abdominal pain | 0 | 2 |
| P Value | <0.001 | |

## 4. DISCUSSION

Pain, limitation of movement, and muscle spasms are common symptoms and signs of spinal disorders. Depending on these, physical disability and motor dysfunction may also develop. In the treatment of these conditions, analgesics, nonsteroidal anti-inflammatory drugs, and muscle relaxants are among the drugs that are frequently preferred[11].

Phenyramidol has been used since the 1960s as both an analgesic and a muscle relaxant. It is used both parenterally and orally. When the parenteral form is used in acute spinal muscle spasms, it causes a decrease in pain and spasm, while at the same time it provides an improvement in limitation of movement and motor function. In a study comparing patients using intravenous and intramuscular phenyramidol parenterally, it was shown that both ways were effective on pain and spasm, and it was observed that both ways were safe in terms of side effects [20]. In another study, a significant improvement was found in pain, spasms, and motor functions with the use of intramuscular phenyramidol, and side effects were observed to be negligible. At the end of the ten-day period, it was observed that once-daily parenteral administration provides an advantage for the patient [21].

In this study, we compared the efficacy and safety of phenyramidol (400 mg, orally) alone and in combination with diclofenac (75 mg, orally) in spinal painful muscle spasms. Consistent with the data in the literature, we demonstrated that phenyramidolprovided a positive and significant improvement in pain and spasm symptoms after treatment (p<0.01). It was observed that the combination of phenyramidol and diclofenac did not provide a statistically significant difference in terms of pain and muscle spasm when compared to the patients treated with phenyramidol alone (p>0.05). Group 1 treated with phenyramidol alone had a statistically significantly more successful safety profile than Group 2 treated with the combination of phenyramidol and diclofenac when compared in terms of adverse drug reactions that occurred during the study (p<0.001).

## 5-CONCLUSION

As a result, it was observed that oral phenyramidol treatment alone and oral phenyramidol+ diclofenac combination

treatment did not have any difference in terms of effectiveness, and when compared in terms of side effects, the use of phenyramidol alone showed a more successful safety profile.

## Conflicts of interest:

Fatmanur Otmar Ozcan, Kubra Saygisever-Faikoglu and Gokhan Faikoglu are medical advisors of Recordati.

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