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Real-world data on the effectiveness of the meloxicam and pridinol combination for musculoskeletal pain

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Abstract

Musculoskeletal pain includes several types of discomfort associated with the skeletal system. Pharmaceutically, pridinol was developed in order to relax muscles. No empirical data exist to support the effectiveness of using meloxicam in combination therapy for the treatment of musculoskeletal pain. This study compared pridinol and meloxicam for musculoskeletal pain. The current observational study assessed a total of 82 patients. The study's participants were divided into three groups: the "meloxicam" group, the "pridinol" group, and the "meloxicam + pridinol" group. Pain levels were measured before and four weeks after giving the drug, by using a visual analogue scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). We employed a Kruskal-Wallis test in order to evaluate the variations in pain measurement among the groups. The three groups' VAS and WOMAC scores did not differ before the drug administration. The "meloxicam + pridinol" treatment resulted in significant pain relief based on VAS and WOMAC scores at 1, 2, and 4 weeks (as compared to other groups; $p<0.05$). At 4 weeks, the VAS and WOMAC ratings exhibited no significant pain relief in the "meloxicam" group when compared to the "pridinol" group. The meloxicam-pridinol combination proved efficacious for musculoskeletal pain, and is recommended for its therapy.

KEYWORDS
muscle cramps, spasm, meloxicam, pridinol, combination therapy

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1. INTRODUCTION

The International Association for the Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience related to tissue damage or described as such [1]. Chronic musculoskeletal pain (CMP) is pain in bones, joints, and tissues that lasts more than three months. CMP affects a large portion of Western adults, with prevalence rates reaching up to 20% [2], and projections showing that it will rise by more than 50% by 2050 [3]. CMP includes many diseases, including osteoarthritis, discogenic back pain, spinal pain, fi-

bromyalgia, and chronic widespread pain.

Skeletal muscle relaxants treat central muscle spasms (like those after a stroke) and peripheral musculoskeletal spasms (like those associated with low back pain) [4]. Anticholinergic pridinol, a central nervous system muscle relaxant, weakens polysynaptic reflexes [5]. This molecule has long been used to relax skeletal muscles, and it is available as a standalone therapeutic drug in Germany and Italy. In January 2016, Strathmann's Hamburg-made "Myoson direct" tablets were pulled from the market. This decision was regulatory-compliant. The current study shows that Germany reauthorized pridinol-containing tablets in December 2017. Strathmann in Hamburg, Germany, manufactures "Myopridin" (3-mg tablets) to treat central and peripheral muscle spasms, torticollis, lumbago, and general muscle discomfort in adults. The user's text doesn't need rewriting [5]. Moreover, UK, Poland, and Spain approved pridinol tablets in 2020, using "Myopridin" as the reference product [5]. In Germany, pridinol is one of two muscle relaxants approved for peripheral muscle spasms linked to low back pain. Since re-approval, its prescriptions have increased: Germany prescribed 5.5 million daily defined doses in 2020; up 96.4% when compared to 2019 [6].

High doses of muscle relaxants and nonsteroidal anti-inflammatory drugs (NSAIDs) are needed for optimal efficacy. The European Medicines Agency (EMA) Committee on Medicinal Products for Human Use recommends administering selective and non-selective NSAIDs at the lowest effective doses, and for the shortest time needed to relieve disease symptoms. This strategy aims to lower cardiovascular disease risk [7]. Thus, choosing the right analgesic and muscle relaxant combination reduces the time needed for the analgesic and anti-inflammatory treatment to be effective [8]. One option is to give 500 mg of chlorzoxazone and 400 mg of ibuprofen. Indian authorities have approved this combination for short-term musculoskeletal pain treatment in 2010, as it reduces musculoskeletal disorder pain and spasms synergistically. Combining a skeletal muscle relaxant with an NSAID or paracetamol relieves pain better than giving the analgesic alone [9,10]. A clinical trial examined how well meloxicam and baclofen worked together and how well they were tolerated by 50 patients with a worsening CMP syndrome. The study found that by combining these medicines one can improve therapeutic outcomes and reduce pain intensity by over 50% in the first week. Moreover, meloxicam for chronic muscle and joint pain was found to be safe and effective [10].

This study examined the benefits of combining meloxicam and pridinol into one dose. In order to treat musculoskeletal disorders, a strong analgesic effect was accelerated this way, while in order to reduce nonsteroidal anti-inflammatory drug side-effects, the former is crucial. Recently named as "the best spasticity treatment", pridinol works centrally.

2. PATIENTS AND METHODS

The study protocol of this investigation has been approved by the ethical committee of our institution prior to study's start. Informed consent was diligently collected from each participant. The study sample consisted of individuals who were selected from a pool of outpatients who sought medical care at an orthopaedic clinic within the community. A total of 82 patients were chosen from a total of 120 individuals who had experienced various forms of musculoskeletal pain. These patients were selected based on the following inclusion criteria: (i) the existence of knee pain lasting for a duration exceeding one month, and (ii) the observation of muscle spasms during the testing process. The exclusion criteria included a documented medical history of knee pain, Parkinson disease, infection, or rheumatoid arthritis. The participants in the study were asked to complete a questionnaire that collected information on sociodemographic parameters (such as age and sex) as well as on the duration of their pain.

All participants underwent a visual analogue scale (VAS) assessment to evaluate pain during movement at various time points (before treatment as well as 1, 2, and 4 weeks after treatment initiation). Additionally, they completed the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire before the study and at the 4-week mark. Prior to the study, participants also underwent a painDETECT screening. The study also recorded every adverse event, including its level (mild, moderate, or severe) and the investigator's assessment of its relationship to each medicine. Patients received no antiemetics.

Data were analysed using statistical tests so as to compare pain values between the three classified groups. Specifically, a Kruskal-Wallis test was employed for this purpose. Additionally, a one-way ANOVA with *post hoc* comparisons was conducted in order to examine the relationship between age, symptom duration, and follow-up. Furthermore, a Fisher's test was utilised so as to assess the association between dichotomous or categorical variables. A significance level of $p<0.05$ was deemed to indicate statistical significance.

3. RESULTS

Our study included 82 patients (59 women and 23 men). Participants had an average age of 54.0 ± 4.0 years. The mean symptom duration was 23.7 ± 4.0 months. Osteoarthritis caused knee pain for at least a month. The VAS and WOMAC pain levels were found to be similar between groups (p>0.05). Table 1 presents the painDETECT score before and during the medication administration, indicating neuropathic pain likelihood as follows: "likely" (≥19), "possibly" (≥13 to ≤18), and "unlikely" (≤12). The study found 8 (9.8%) cases of "likely" neuropathic pain, while 57 participants (69.5% of the cohort) did not suspect any neuropathic pain, and 17 (20.7%) did. The three groups exhibited similar neuropathic pain scores (p>0.05). All three groups' pain scores improved during medication when compared to those before the treatment. The "meloxicam + pridinol" combination achieved significant pain reduction (VAS score at 1, 2, and 4 weeks; WOMAC score at 4 weeks) when compared to "meloxicam" or "pridinol" alone (p<0.05; Table 1).

Table 1. Overview of the assessment of the painDETECT score without and during medication. The painDETECT score had a distribution ranging from 0 to 38. The participants were categorised into three distinct categories based on their likelihood of experiencing neuropathic pain: "highly likely" (score of 19 or above), "somewhat likely" (scoring between 13 and 18), and "unlikely" (score of 12 or lower). Note: unless otherwise stated, values represent a mean ± SEM. Abbreviations used: VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Assessment of painDETECT score without medication					
Score	**Number of patients (%)** (n=82)	**Meloxicam (%)** (n=28)	**Pridinol (%)** (n=25)	**Meloxicam + Pridinol (%)** (n=29)	***p*-value**
0-12	57 (69.5%)	20 (71.4%)	17 (68%)	20 (69%)	0.52
13-18	17 (20.7%)	4 (14.3%)	5 (20%)	8 (27.6%)	0.44
19-38	8 (9.8%)	4 (14.3%)	3 (12%)	1 (3.4%)	0.61
Assessment of painDETECT score while receiving medication					
Pain score; VAS		**Meloxicam**	**Pridinol**	**Meloxicam + Pridinol**	***p*-value**
1 week		4.4 ± 2.1	4.2 ± 2.0	3.2 ± 2.0	0.024
2 weeks		3.7 ± 2.0	3.4 ± 1.9	2.4 ± 1.4	0.042
4 weeks		2.3 ± 1.5	2.1 ± 1.2	1.0 ± 1.1	0.02
WOMAC score (4 weeks)		**Meloxicam**	**Pridinol**	**Meloxicam + Pridinol**	***p*-value**
Pain		5.6 ± 2.2	5.8 ± 2.1	2.9 ± 1.5	0.41
Stiffness		4.6 ± 2.3	4.5 ± 2.1	4.6 ± 2.3	0.03
Physical function		32.0 ± 10.0	30.0 ± 11.0	19.2 ± 7.5	0.02
Total		42.2 ± 10.1	40.3 ± 10.5	26.7 ± 7.1	0.02

4. DISCUSSION

This study is a preliminary observational study aiming to evaluate the nonbenzodiazepine antispasmodic pridinol and the NSAID meloxicam in adults with acute muscle pain and osteoarthritis. Musculoskeletal pain can be relieved by combining skeletal muscle relaxants with NSAIDs or paracetamol. In this study, meloxicam and pridinol had significant analgesic effects at 1, 2, and 4 weeks, and increased the WOMAC score after 4 weeks.

Pridinol's efficacy and tolerability are examined using de-identified German Pain e-Registry data. The largest non-interventional pridinol study in the world involves 1,133 patients with acute musculoskeletal pain. Despite receiving mostly NSAIDs and non-opioid analgesics, these patients reported moderate-to-severe pain intensity and significant pain limitations in various life activities. In this group of patients, pridinol for 4 to 64 days was well received and improved pain intensity, pain-related impairments, and overall wellbeing in most cases. Only 6.4% of pridinol-receiving patients reported global treatment failures, which can be attributed to insufficient analgesic response or drug-related adverse events. A remarkable 58.8% of patients had a complete global response without drug-related adverse events, while 34.9% had a partial global response. Our study has found that the patients' real-world efficacy contradicts current antispasmodic guidelines.

5. CONCLUSION

Acute muscular pain often resolves without treatment, but many patients may need temporary medication to reduce pain and physical limitations. Current guidelines recommend starting with NSAIDs; however, their efficacy in noninflammatory muscular pain is limited, and their use is associated with serious side-effects. Our study has found that by combining meloxicam with pridinol, one can treat musculoskeletal pain well.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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