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Research Article

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Real World Effectiveness of Orphenadrine citrate 50 mg + Paracetamol 650 mg (Norgesic ® Forte) on Low Back Pain of Filipino Patients

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Abstract

Introduction: *Low back pain is a common musculoskeletal disorder, estimated to affect up to 84% of adults at some point in their lives. It is one of the leading causes of activity limitation, work absenteeism, and lost productivity, inflicting substantial costs on health, social, and economic systems. Globally, back pain causes more disability than any other condition. The study aimed to determine the effectiveness of a combination drug: Orphenadrine citrate 50 mg + paracetamol 650 mg (Norgesic ® Forte) in alleviating low back pain of adult Filipino patients who are presenting with acute non-specific moderate to severe low back pain.*

Methods: *This is a real-world, uncontrolled, longitudinal, observational study on the effectiveness of a combination drug: Orphenadrine citrate 50 mg + paracetamol 650 mg (Norgesic ® Forte). Patients with acute low back pain were prescribed by participating physicians with said drugs according to local prescribing information and routine clinical practice. The pain was assessed using the Visual Analogue Scale (VAS), and the Roland-Morris Disability Questionnaire (RMDQ) was used to evaluate for self-rated physical disability. Patients were followed up until the total resolution of the low back pain or up to a maximum of ten (10) days. The study also documented any adverse effects for ten (10) days.*

Results: *In the 181 participants, the median onset of pain relief occurred an hour after the first dose; the fastest occurred at 5 minutes, and the slowest at 8 hours. At baseline, the median VAS score was 7, the lowest was 2, and the highest was 10. Generally, a decreasing trend was observed on subsequent time points compared to baseline ($p<0.0001$). By day 5, VAS scores dropped to 0 until day 10. The mean duration of symptoms before total resolution of low back pain was 4.3 SD ± 2.0 days. As much as 72.4% of the participants' VAS scores decreased by 2 points from baseline as early as day 1. The highest observed proportion of respondents with at least two 2-point decreases from baseline VAS scores was on day 3. Using the RMDQ with scores ranging from 0 (no disability) to 24 (severe disability), the median physical disability score on day 1 was 9, with a minimum value of 1 and a maximum of 23. On day 11, this significantly decreased to 1, with values ranging from 0 to 11 ($p<0.0001$). Thirteen participants developed adverse events, which were generally mild.*

Conclusion: *Results indicate that Orphenadrine citrate 50 mg + Paracetamol 650 mg (Norgesic ® Forte) provides pain relief compared to the baseline. In addition to its analgesic effects, there is an improvement in physical function, as evidenced by the significant decrease in the physical disability scores and, subsequently, an improvement in the quality of life (QoL) of these patients.*

Keywords: Orphenadrine citrate, paracetamol, acute low back pain

Introduction

Low back pain is a common musculoskeletal disorder, estimated to affect up to 84 percent of adults at some point in their lives [1-3]. It is one of the leading causes of activity limitation, work absenteeism, and lost productivity, inflicting substantial costs on health, social, and economic systems [1,4-6]. Globally, back pain causes more disability than any other condition. According to the 2019 Global Burden of Disease Study, low back pain ranked ninth in the top ten conditions with increasing burden from 1990 to 2019 across all ages. It had one of the largest absolute increases in disability-adjusted life years [7]. In the Global Pain Index 2017 report, the Philippines was among the countries reported to have 56% of its population experiencing body pain every week. Among those who experienced weekly pain, 28 % experienced lower back pain [8].

Low back pain can be acute (less than four weeks), sub-acute (between 4 to 12 weeks), or chronic, depending on the duration of symptoms [9]. Among the several etiologies (spine diseases or infection, neoplasms, autoimmune inflammatory arthritis, and minor trauma), more than 85 %of the patients seen in primary care have nonspecific back pain, primarily musculoskeletal [10]. The general approach to care includes nonpharmacologic and pharmacologic therapies. Nonpharmacologic therapies include heat, massage, acupuncture, spinal manipulation, and exercise and physical therapy [11]. If the patient prefers a pharmacologic approach, the initial drug prescribed would be an analgesic such as paracetamol or a nonsteroidal anti-inflammatory drug (NSAID) such as ibuprofen or naproxen. Nonbenzodiazepines may be added when there is refractory pain after initial pharmacotherapy, or if there is still inadequate relief of pain, then opioids may be given. However, there is limited evidence to support its use.

It has been common practice in emergency departments and outpatient clinics to give multiple concurrent medications. Common medication combinations include NSAIDs with benzodiazepines, opioids, or skeletal muscle relaxants (SMRs). A systematic review showed moderate-quality evidence of adding SMRs to short-term pain relief compared with a placebo [12]. This current study explored the combination of a skeletal muscle relaxant - Orphenadrine citrate 50mg, and an analgesic -paracetamol 650 mg (Norgesic ® Forte) in moderate to severe low back pain in a real-world setting.

Methods

A prospective, multicenter, uncontrolled, open-label, longitudinal study on the effectiveness of Orphenadrine citrate 50 mg + paracetamol 650 mg in alleviating the low back pain of adult Filipino patients who presented with acute moderate to severe non-specific low back pain in a real-world setting was conducted. This study has been approved by the University of the East Ramon Magsaysay Memorial Medical Center Ethics Research Committee (1552/P/2023/123).

They were prescribed by their attending physicians with Orphenadrine citrate 50 mg + paracetamol 650 mg (Norgesic ® Forte). Excluded were those who were hypersensitive to orphenadrine citrate or paracetamol, had used any other oral preparations like NSAIDs, cyclobenzaprine, methocarbamol, or opioids for the past 48 hours before initiation of treatment, those who were having other nonpharmacologic therapies for their low back pain, including complementary and alternative medicine modalities (e.g., acupuncture, acupressure, therapeutic massage, etc.), were pregnant, with glaucoma, prostatic hypertrophy, obstruction at the bladder neck or myasthenia gravis, and / or diagnosed with any of the following: scoliosis, spondylosis, spondylolisthesis, spondylitis, herniated nucleus pulposus, psychogenic lumbago, secondary to renal colic due to urolithiasis.

They were followed up until the total resolution of the lower back pain or up to a maximum of ten (10) days. The prescribed dosage was 1-2 tablets three times a day for a maximum of 10 days. Sixty (60) tablets of Orphenadrine citrate 50 mg + paracetamol 650 mg were given for free to the patients upon consultation. Participating physicians included primary care physicians, general medical practitioners, family physicians, community medicine and public health practitioners, general internists, rehabilitation medicine practitioners, and orthopedic surgeons practicing in the country.

Patient demographic and baseline characteristic data were collected on all patients as well as relevant medical history / current medical condition data.

The primary endpoints of interest were (1) the decrease in VAS scores for pain from the baseline until the total resolution of low back pain, possibly with no recurrence for a maximum of 10 days, and (2) the decrease in physical disability scores from baseline until completion of study, and (3) the up time to total resolution of low back pain after use of Orphenadrine citrate 50 mg + paracetamol 650 mg, again with nonrecurrence. The secondary endpoints of interest were: (1) the time to total resolution of low back pain after use of Orphenadrine citrate 50 mg + paracetamol 650 mg, again with nonrecurrence, (2) the decrease in VAS score of 2 from baseline, (3) time to onset of pain relief after the first dose, (4) duration of pain-free period after the first dose, (5) the decrease in physical disability scores from baseline until completion of study, and (6) occurrence of adverse effects, including but not limited to, hypersensitivity reaction.

Roland-Morris Disability Questionnaire was used to assess self-rated physical disability caused by low back pain. They were obtained at baseline and on study completion (Day 11) [13].

A daily dose of Orphenadrine citrate 50 mg + paracetamol 650 (Norgesic ® Forte) was described, and the number of drugs per day was tabulated. Patients discontinuing Orphenadrine citrate 50 mg + Paracetamol 650 mg (Norgesic ® Forte) use was reported, and reason/s were described.

Since this was an observational, uncontrolled study, no special protocol-mandated visits or procedures were associated with the investigation. During the study, patients were allowed to switch to other pain relievers/muscle relaxants other than the prescribed medications. However, they were encouraged to remain on the study medications. However, attending physicians advised study subjects to have at least one follow-up period (i.e., on Day 11 as the end of treatment). Follow-up consultations were done via face-to-face or tele-consult. The VAS and physical disability scores were obtained after ten days of initiation of treatment.

For selected safety outcomes, incidence rates with respective 95% confidence intervals (CI) were calculated when applicable.

Continuous variables were expressed as mean ± SD or median (min and max) for non-normally distributed data. Categorical variables were expressed as percentages. Significant differences in Visual Analogue Scale (VAS) scores and the number of tablets consumed between baseline and each succeeding day up to 10 days

were determined using the Wilcoxon signed rank test. Likewise, differences in physical disability scores between baseline and end of the study period were determined using the Wilcoxon signed rank test. A p-value <0.05 was accepted to be statistically significant. Data was analyzed using Stata version 13 software.

Results

There were 181 participants, 55.3% females and 44.7% males with a mean age of 38.8 SD ± 11.1 years. Majority were from Luzon (63%) and the National Capital Region (28.2%). There was an almost equal distribution of white and blue-collared workers (Table 1).

Gender (n, %)	
Male	81 (44.7)
Female	100 (55.3)
Age in years (mean, sd)	38.8, 11.1
Residence	
National Capital Region (NCR)	51 (28.2)
Luzon	
Visayas	114 (63.0) 15 (8.3)
Mindanao	1 (0.5)
Work/Profession	
White-collared (clerk/office staff , teacher, nurse, laboratory assistant, administrative/HR/IT personnel, etc.)	64 (35.8)
Blue-collared (machine operator, factory worker, driver, maintenance personnel, vendor, security guard, carpenter, construction worker, plumber, etc.)	66 (36.9)
Unemployed	49 (27.4)
No response	2 (1.1)

Table 1: Demographic profile of respondents.

A few (n=7) had diagnostic examinations showing elevated LDL-Cholesterol (1), high Uric Acid (1) and normal Urinalysis (1) test results. Lumbosacral spine-ray showed lumbar straightening in one and unremarkable pelvic x-ray in another (Table 2).

Laboratory	**No. (%)**
LDL	1
Uric Acid	2
Urinalysis	1
Radiologic	
X-ray of lumbosacral spine	2
X-ray of the pelvis	1

Table 2: Diagnostic examinations done.

Among those who had baseline vital sign measurements, heart rate, respiratory rate, systolic and diastolic blood pressures and temperature were within normal in most. The median onset of pain relief occurred an hour after the first dose of: Orphenadrine citrate 50 mg + paracetamol 650 mg (Norgesic ® Forte) tablet, the fastest at 5 min and the slowest at 8 hours. The median length of time after the first dose and before the next episode of pain was 6 hours, with 3 hours as the shortest and 24 hours as the longest period of relief from pain. Eighty-one percent were adherent to the medications with 19% reporting to forgetting to take the medications as the primary reason for non-compliance (Table 3).

Baseline Vital Signs	No. (%)
Heart rate (beats/min)	
Normal (60-100)	100 (99.0)
Decrease (<60)	1 (0.1)
Respiratory rate (breaths/min)	
Normal (12-20)	95 (94.1)
Increased (>20)	6 (5.9)
Systolic blood pressure (mmHg)	
Normal (90-130)	85 (83.3)
Elevated (>130)	17 (16.7)
Diastolic blood pressure (mmHg)	
Normal (60-100)	102 (100)
Temperature (oC)	
Normal (<37.6)	98 (100)
Clinical Outcomes	
Onset of pain relief in hours after the first dose (median, min/max)	1 (5 min, 8 hours)
Duration of pain-free period before the next dose in hours after the first dose (median, min/max)	6 (3 hours, 24 hours)
Compliance to medications	
Yes	146 (80.7%)
No	35 (19.3%)

Table 3: Clinical profile and outcome of respondents.

At baseline, the median VAS score was 7, the lowest was 2 and the highest was 10. Except for a unit increase in median VAS score on the morning of day 2, generally there was a decreasing trend observed on subsequent time points which differed significantly from baseline ($p<0.0001$). By day 5 VAS scores dropped to 0 until day 10. The median number of Orphenadrine citrate 50 mg + paracetamol 650 mg (Norgesic ® Forte) tablets consumed for pain relief likewise decreased from 3 tablets on day 1 to 1 tablet on day 6 to none on day 8 and beyond. The number of tablets consumed on days 2 and 3 did not differ significantly with day 1 (baseline) ($p=0.0777$ and $p=0.6326$, respectively). But by day 4 and each succeeding day the differences from baseline intake was significant ($p<0.0001$) (Table 4).

	VAS scores		p-value*	Number of tablets consumed		p-value*
	Median	Min. Max		Median	Min. Max	
Day 1	-	-	-	3	1, 6	-
Baseline	7	2, 10	-	-	-	-
After 60 minutes	5	0, 9	<0.0001	-	-	-
At bedtime	4	0, 9	<0.0001	-	-	-
Day 2				3	0, 6	0.0777
After 60 minutes	5	0, 10	<0.0001	-	-	-
At bedtime	3	0, 9	<0.0001	-	-	-
Day 3				3	0, 6	0.6326
After 60 minutes	3	0, 9	<0.0001	-	-	-
At bedtime	2	0, 9	<0.0001	-	-	-
Day 4	1	0, 8	<0.0001	3	0, 6	<0.0001
Day 5	0	0, 8	<0.0001	2	0, 4	<0.0001

Day 6	0	0, 7	<0.0001	1	0, 4	<0.0001
Day 7	0	0, 7	<0.0001	1	0, 3	<0.0001
Day 8	0	0, 6	<0.0001	0	0, 3	<0.0001
Day 9	0	0, 5	<0.0001	0	0, 3	<0.0001
Day 10	0	0, 5	<0.0001	0	0, 3	<0.0001

*Wilcoxon signed-rank test

Table 4: VAS scores and number of tablets consumed from Day 1 to Day 10.

The mean duration of symptoms before total resolution of low back pain, which meant having a VAS score equal to 0 with no recurrence of symptoms, was 4.3 SD ± 2.0 days. As much as 72.4% of the participants' VAS scores decreased by 2 points from baseline as early as day 1. This increased to 86.2% by day 3 and levelled off subsequently between 80% to 84% from day 4 onwards. The highest observed proportion of respondents with at least 2 points decrease from baseline VAS scores was on day 3. There were 39 participants, though, who were still symptomatic by the end of the observation period but the VAS scores in 33 out of 39 (84.6%) exhibited a decrease of ≥ 2 points from baseline (Table 5).

Complete resolution (VAS score=0) reached 37.6% by day 4, a 19.4 percentage points difference with day 3 versus an 8.8 percentage points difference with day 5 suggesting that most cases were completely resolved by day 4. Succeeding time points showed increments ranging from 1-5 percentage points in the proportion of resolved cases. (Table 5).

Duration of low back pain before complete resolution (VAS=0) with no recurrence in days (mean, sd)		**4.3, 2.0**
Time in days	**Proportion of those whose VAS scores decreased by at least 2 points from baseline, n (%)**	**Proportion of those with complete resolution (VAS=0), n (%)**
Day 1	131 (72.4)	17 (9.4)
Day 2	148 (81.8)	21 (11.6)
Day 3	156 (86.2)	33 (18.2)
Day 4	149 (82.3)	68 (37.6)
Day 5	152 (84.0)	84 (46.4)
Day 6	151 (83.4)	94 (51.9)
Day 7	149 (82.3)	96 (53.0)
Day 8	145 (80.1)	102 (56.4)
Day 9	145 (80.1)	107 (59.1)
Day 10	144 (79.6)	113 (62.4)

Table 5: Duration of symptoms before complete resolution and proportion of resolved cases.

The median physical disability score on day 1 was 9, with a minimum value at 1 and a maximum value at 23. On day 11 this decreased significantly to 1, with values ranging from 0 to 11 (p<0.0001) (Table 7).

Physical Disability Scores	**Median**	**Min, Max**	**p-value***
Day 1	9	1, 23	<0.0001
Day 11	1	0, 11	

*Wilcoxon signed-rank test

Table 7: Physical disability scores.

There were 13 participants who developed adverse events. The adverse events reported were nausea & vomiting (1), dry mouth (4), dizziness (7), somnolence (5), blurring of vision (2), difficulty of breathing (2) and abdominal discomfort (1). They were generally mild with few moderate cases, lasting for a minimum of less than a day to a maximum of 5 days. Most resolved with observation (Table 7).

Adverse Event	Total	Severity	Duration (days)	Action	Outcome
Nausea & vomiting	1	Mild	< 1	Observation	Resolved
Dry mouth	4	Mild (3) Moderate (1)	<1 to 2	Observation (1) Fluids (2) Pharmacotherapy (1)	Resolved
Dizziness	7	Mild (6) Moderate (1)	<1 to 3	Observation (3) Rest (2) Pharmacotherapy (1) NR (1)	Resolved
Somnolence	5	Mild (3) Moderate (1) NR (1)	1-5	Observation (2) Sleep (1) Pharmacotherapy (1) NR (1)	Resolved
Blurring of vision	2	Mild	1-5	Observation	Resolved
Difficulty of breathing	2	Moderate	< 1	Observation	Resolved
Abdominal discomfort	1	Mild	1	Observation	Resolved

Table 7: Adverse events.

Discussion

In 2020, the global burden of low back pain is approximately 619 million, which is estimated to rise to 843 million by the year 2050 [14]. This is mainly due to population expansion and aging. Around 40% is attributed to modifiable risk factors [15]. Locally, a survey revealed that back pain is the most common type of occupational disease, accounting for 35% of occupational diseases [16].

The participants' baseline median Visual Analog Scale (VAS) was 7, a value higher than the baseline median VAS reported in several studies, ranging between 4-7 [17-19]. With the administration of the Orphenadrine citrate 50 mg + Paracetamol 650 mg (Norgesic ® Forte), except for a unit increase on the morning of day 2, a generally decreasing trend was observed at subsequent time points. This trend differed significantly from the baseline, with a notable reduction (VAS=0) starting on Day 5. These findings suggest a faster onset of relief than other studies involving myorelaxants and NSAIDs, which typically reported reduced acute LBP at approximately one week [20]. Skeletal muscle relaxants are effective for acute lower back pain but have adverse effects such as drowsiness, dizziness, and nausea [21-23].

Physical functioning was assessed through the Roland Morris Disability Questionnaire (RMDQ), yielding a baseline score of 9. By Day 11, this score decreased to 1, signifying a notable improvement. The initial score aligns with other studies on acute low back pain, where baseline scores typically range from 9 to 14 [22]. The substantial 8-point reduction is particularly noteworthy, as clinical guidelines often consider a 5-point decrease indicative of the largest benefit [24].

Combined with Paracetamol, Orphenadrine produces a synergistic effect on providing musculoskeletal pain relief. Previous studies that compare muscle relaxants and placebo show statistically significant relief and efficacy of muscle relaxants on musculoskeletal pain [25]. A study on Cyclobenzaprine 5 and 10 mg. Hydrochloride demonstrated that the median time for patients to achieve "complete relief" from starting backache was three days. However, the sedation produced at its 10mg dose limits its use [26]. Currently, no known study has mentioned the duration of symptoms before total resolution with the use of Orphenadrine citrate 50 mg + Paracetamol 650 mg (Norgesic ® Forte). The results of this study showed that the mean duration of symptoms before total resolution of low back pain, or having a VAS score equal to 0, was 4.3 SD ± 2.0 days. This also meant no recurrence of symptoms.

As early as day one, 72.4% of the participants reported a decrease in VAS scores by 2 points from baseline. Relief of pain is expected on the first day due to the pharmacokinetics of the combination drugs; Paracetamol's analgesic effect is known to take effect within 10-60 minutes after oral administration, while Orphenadrine's onset of action is 1 hour after oral intake, with both medications lasting 4-6 hours per dosage [27]. VAS scores decreased to 86.2% by day three and leveled off between 80% and 84% from day four onwards. However, the highest observed proportion of respondents with at least two 2-point decreases from baseline VAS scores was on day 3.

Clinical guidelines using a 100-point visual analog pain scale (or equivalent) benchmark a mean improvement of 5 to 10 points to be small or slight, 10 to 20 points to be moderate, and more than 20 points substantial [24]. Other studies show that a 13mm (1.3) decrease in VAS is the minimum clinically significant difference in acute pain [28]. Thus, Orphenadrine citrate 50 mg + Paracetamol 650 mg (Norgesic ® Forte), is a promising remedy for patients with acute low back pain.

Generally, both Paracetamol and Orphenadrine have a favorable safety profile and often do not cause serious adverse effects. The

commonly reported adverse events are attributed to the antimuscarinic properties of Orphenadrine, including but not limited to dryness of mouth, tachycardia, palpitations, nausea, and headache 16. Among the 181 participants, there were 13 who developed adverse events. The most frequently reported adverse event is dizziness, followed by somnolence and dry mouth. Other reported adverse events were nausea and vomiting, difficulty breathing, blurring of vision, and abdominal discomfort. All of the mentioned adverse events are anticipated occurrences and are documented on the medication's safety information sheet [27]. They were generally reported as mild, with a few cases categorized as moderate, and had durations ranging from less than a day to a maximum of 5 days. The majority were resolved through observation without requiring active management.

The onset of action of Paracetamol as an analgesic occurs within 40 minutes and 1 hour for Orphenadrine, both following oral intakes. As reported in this study, the onset of pain relief generally occurred an hour after the first intake, with the fastest at 5 min and the slowest at 8 hours, consistent with the pharmacodynamics of both Paracetamol and Orphenadrine.

The median length of time after the first dose and before the next pain episode was 6 hours, with 3 hours being the shortest and 24 hours being the longest period of relief from pain. Orphenadrine is a derivative of diphenhydramine, an antihistamine known for its utility as a muscle relaxant and an analgesic. It is widely used with Paracetamol for relieving pain due to muscle spasms. Although shown by studies [29] to be effective when used separately, multiple controlled studies have demonstrated that combining Orphenadrine and Paracetamol produces a synergistic effect, providing better musculoskeletal pain relief than when each is used alone [25]. This is in line with pain management guidelines, which recommend the use of combination therapy in targeting pain, given the multiple pathways involved in pain [30]. One study showed that there were no significant pharmacokinetic alterations between Orphenadrine and Paracetamol; however, the dosages used were 35 mg and 450 mg, respectively, and thus further studies can be conducted to evaluate their pharmacokinetics at higher doses, such as in this study [31]. The analgesic efficacy of this combination has also been evaluated in other types of pain. A randomized controlled trial showed that the orphenadrine-paracetamol combination provided significant relief of postoperative oral surgical pain [32].

The study has some limitations; there may be genetic differences among the participants that could interact with and/or alter the pharmacokinetics of Orphenadrine and Paracetamol. Although the use of non-pharmacological therapies and medications such as other oral painkillers or muscle relaxants before treatment was indicated as part of the exclusion criteria, the use of these modalities after the initiation was not checked. In addition to the frequency of AEs, the duration and time to onset of AEs can be obtained to provide more information on the AEs, which may be helpful, especially when advising patients in general practice. Since this was an uncontrolled observational study, different biases can obscure any true causal association. The nature of the medical consultation (i.e., face-to-face vs. tele-consult) curtailed thorough physical examination of the back and other pertinent organ systems.

Results from this study indicate that Orphenadrine citrate 50 mg + Paracetamol 650 mg (Norgesic ® Forte) provides pain relief compared to the baseline. In addition to its analgesic effects, its use proves beneficial in improving physical function, as evidenced by the significant decrease in the physical disability scores and, subsequently, an improvement in the quality of life (QoL) of these patients. The pain relief scores can be measured in addition to pain intensity to further support its beneficial impact on the QoL since pain relief scales are deemed more sensitive [33]. More studies may also be done to evaluate the effectiveness of the same combination (same dose or lower dose preparation) on pain of other types and severity, such as mild-moderate low back pain, post-surgical pain, neuropathic pain, or chronic low back pain.

Conclusion

Low back pain is a common condition that significantly affects millions of people worldwide and is a leading cause of disability, leading to significant economic and social losses. Because of its burden, there is a need for its appropriate management, including both nonpharmacologic and pharmacologic therapies. Many medications have been marketed as effective musculoskeletal pain relievers, one of which is the combination of Orphenadrine citrate 50 mg + Paracetamol 650 mg (Norgesic ® Forte), which provides a synergistic effect as an analgesic and a muscle relaxant. Multiple studies have demonstrated its effectiveness in pain relief, but its impact on the local population has yet to be evaluated. The results of this study show that Orphenadrine 50 mg + Paracetamol 650 mg (Norgesic ® Forte) provides pain relief for acute low back pain in adult Filipino patients. Regarding its safety profile, this combination was well-tolerated, with no serious adverse events noted. The most common AEs were dizziness, somnolence, dry mouth, and nausea and vomiting, all of which were self-limiting. Overall, the fixed combination of Orphenadrine 50 mg + Paracetamol 650 mg (Norgesic ® Forte) may provide an effective therapeutic option for treating acute low back pain.

References

1. Woolf AD, Pfleger B (2003) Burden of major musculoskeletal conditions. Bull World Health Organ 81(9):646-56.
2. Deyo RA, Tsui-Wu YJ (1987) Descriptive epidemiology of low-back pain and its related medical care in the United States. Spine (Phila Pa 1976). 12(3):264-268.
3. Cassidy JD, Carroll LJ, Côté P (1998) The Saskatchewan health and back pain survey. The prevalence of low back pain and related disability in Saskatchewan adults. Spine (Phila Pa 1976). 23(17):1860-1866.
4. Rudy TE, Weiner DK, Lieber SJ, Slaboda J, Boston RJ (2007) The impact of chronic low back pain on older adults: a comparative study of patients and controls. Pain 131(3):293-301.
5. Weiner SS, Nordin M (2010) Prevention and management of chronic back pain. Best Pract Res Clin Rheumatol 24(2):267-279.
6. Hoy D, March L, Brooks P, Blyth F, Woolf A, et al. (2014)

The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis 73(6):968-974.
7. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, et al. (2020) Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet 396(10258):1204-1222.
8. Boros L (2018) GSK Global Pain Index 2017 Global Research Report. 13.
9. Chou R (2010) Low back pain (chronic). BMJ Clin Evid 2010:1116.
10. Chou R, Deyo R, Friedly J, Skelly A, Hashimoto R, et al. (2017) Nonpharmacologic Therapies for Low Back Pain: A Systematic Review for an American College of Physicians Clinical Practice Guideline. Ann Intern Med 166(7):493-505.
11. Friedman BW, Cisewski D, Irizarry E, Davitt M, Solorzano C, et al. (2018) A Randomized, Double-Blind, Placebo-Controlled Trial of Naproxen With or Without Orphenadrine or Methocarbamol for Acute Low Back Pain. Ann Emerg Med 71(3):348-356.e5.
12. Qaseem A, Wilt TJ, McLean RM, Forciea MA Clinical Guidelines Committee of the American College of Physicians, et al. (2017) Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med 166(7):514-530.
13. Roland M, Fairbank J (2000) The Roland-Morris Disability Questionnaire and the Oswestry Disability Questionnaire. Spine (Phila Pa 1976). 25(24):3115-3124.
14. WHO (2023) Low back pain [Internet]. World Health Organization. 2023 [cited 2023 Nov 13]. Available from: https://www.who.int/news-room/fact-sheets/detail/low-back-pain
15. Ferreira ML, De Luca K, Haile LM, Steinmetz JD, Culbreth GT, et al. (2023) Global, regional, and national burden of low back pain, 1990–2020, its attributable risk factors, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. The Lancet Rheumatology 5(6):e316-329.
16. Philippine Statistics Authority. Home [Internet]. [cited 2023 Nov 10]. Available from: https://psada.psa.gov.ph/home
17. Aoki Y, Sugiura S, Nakagawa K, Nakajima A, Takahashi H, et al. (2012) Evaluation of Nonspecific Low Back Pain Using a New Detailed Visual Analogue Scale for Patients in Motion, Standing, and Sitting: Characterizing Nonspecific Low Back Pain in Elderly Patients. Pain Research and Treatment 2012:1-4.
18. Karasel S, Oncel S, Sonmez I (2021) The Effect of Short-Wave Diathermy and Exercise on Depressive Affect in Chronic Low Back Pain Patients. Med Arch 75(3):216.
19. Kim SK, Min A, Jeon C, Kim T, Cho S, et al. (2020) Clinical outcomes and cost-effectiveness of massage chair therapy versus basic physiotherapy in lower back pain patients: A randomized controlled trial. Medicine 99(12):e19514.
20. Baroncini A, Maffulli N, Al-Zyoud H, Bell A, Sevic A, et al. (2023) Nonopioid pharmacological management of acute low back pain: A level I of evidence systematic review. Journal Orthopaedic Research 41(8):1781-1791.
21. Hall H, McIntosh G (2008) Low back pain (acute). BMJ Clin Evid 2008:1102.
22. Chou R, Deyo R, Friedly J, Skelly A, Weimer M, et al. (2017) Systemic Pharmacologic Therapies for Low Back Pain: A Systematic Review for an American College of Physicians Clinical Practice Guideline. Ann Intern Med 166(7):480.
23. Van Tulder MW, Touray T, Furlan AD, Solway S, Bouter LM (2003) Muscle Relaxants for Nonspecific Low Back Pain: A Systematic Review Within the Framework of the Cochrane Collaboration: Spine 28(17):1978-1792.
24. Chou R, Huffman LH (2007) Medications for Acute and Chronic Low Back Pain: A Review of the Evidence for an American Pain Society/American College of Physicians Clinical Practice Guideline. Ann Intern Med 147(7):505.
25. Hunskaar S, Donnell D (1991) Clinical and pharmacological review of the efficacy of orphenadrine and its combination with paracetamol in painful conditions. J Int Med Res 19(2):71-87.
26. Toth P, Urtis J (2004)Commonly used muscle relaxant therapies for acute low back pain: a review of carisoprodol, cyclobenzaprine hydrochloride, and metaxalone. Clinical Therapeutics 26(9):1355-1367.
27. Norgesic/Norgesic Forte Full Prescribing Information, Dosage & Side Effects | MIMS Philippines. [cited 2023 Nov 10]. Available from: https://www.mims.com/philippines/drug/info/norgesic-norgesic%20forte?type=full
28. Sadovsky R (2002) Clinically Important Changes in Pain Severity on VAS. Afp 65(9):1916-1921.
29. Schaffler K, Reitmeir P (2004) Analgesic effects of low-dose intravenous orphenadrine in the state of capsaicin hyperalgesia. A randomised, placebo-controlled, double-blind cross-over study using laser somatosensory evoked potentials obtained from capsaicin-irritated skin in healthy volunteers. Arzneimittelforschung 54(10):673-679.
30. Anekar AA, Hendrix JM, Cascella M (2023) WHO Analgesic Ladder. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Nov 10]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK554435/
31. Saano V, Elo HA, Paronen P (1990) Effect of central muscle relaxants on single-dose pharmacokinetics of peroral paracetamol in man. Int J Clin Pharmacol Ther Toxicol 28(1):39-45.
32. Winter L, Post A (1979) Analgesic Combinations with Orphenadrine in Oral Post-Surgical Pain. J Int Med Res 7(3):240-246.
33. McQuay H, Moore R (2006) Methods of Therapeutic Trials: Pain Measurement for Trials. Edinburgh, United Kingdom: University of Oxford; 2006. Report No.: 5.