Journal of General and Emergency Medicine

Research Article

Prochlorperazine/Diphenhydramine vs Ketorolac for Treatment of Acute-on-Chronic Back Pain Exacerbations in the Emergency Department

This article was published in the following Scient Open Access Journal:
Journal of General and Emergency Medicine
Received : June 19, 2017; **Accepted** August 04, 2017; **Published** August 11, 2017

Jennifer Stahl*, Kori Brewer and William Meggs

East Carolina University/Brody School of Medicine, USA

Abstract

Back pain is one of the most commonly reported chief complaints for Emergency Department visits. Non-narcotic treatment strategies are ideal for this patient population. In this study, we investigate whether treatment with prochlorperazine and diphenhydramine would provide significant pain relief for acute exacerbations of chronic back pain.

Methods: Patients who presented to the ED with a chief complaint of lower back pain and met study criteria were randomized into two arms of treatment. One group received prochlorperazine 10 mg plus diphenhydramine 50 mg intravenously (IV) and the other group received standard of care treatment with ketorolac 30 mg IV. Patients were monitored for relief of symptoms for 1 hour.

Results: In this study, 6 patients were enrolled and received prochlorperazine and diphenhydramine treatment. Pain scores for these patients were: 0 minutes (baseline) mean = 9.5 (95% CI = 8.6-10), 30 minutes mean = 7.3 (95% CI = 5.5-9.2), and 60 minutes mean = 6.7 (95% CI = 4.2-9.1). The change in pain from 0 minutes (baseline) to 30 min was mean = 2.2 (95% CI=0.6-3.7) with p=0.01, and the change from baseline to 60 minutes was mean = 2.8 (95% CI=0.6-5.1) with p<0.01.

Conclusions: Patients who received prochlorperazine and diphenhydramine treatment demonstrated pain relief at 30 minutes that persisted at 60 minutes. Pain was improved at 60 minutes with statistical significance when compared to baseline. This study shows the potential of prochlorperazine and diphenhydramine as a treatment modality for acute exacerbations of chronic back pain.

Keywords: Back pain, Prochlorperazine, Diphenhydramine, Ketorolac

Introduction

Back pain is one of the most common presenting complaints to the Emergency Department, with acute-on-chronic back pain comprising a large proportion of these visits. Back pain can often become difficult to treat given variable pain tolerance and response to treatments. In 2007, a systemic review of pharmacologic treatments for back pain was published. In this systematic review, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) showed improvement of symptoms in both acute and acute on chronic back pain when compared to placebo [1]. NSAIDs have been the mainstay of treatment for acute-on-chronic back pain in most Emergency Department settings. A recent update to the 2007 guidelines found new evidence that NSAIDs had a smaller benefit for chronic back pain than was previously observed [2]. Many patients in the Emergency Department setting have variable response to NSAID treatments and often require alternative pharmacologic therapy for pain relief.

In an era of national prescription drug abuse, non-narcotic treatment options would be ideal if adequate pain relief could be demonstrated. Prochlorperazine is a main staple in the Emergency Department setting for use in acute migraine pain. Prochlorperazine is a dopamine D_2 receptor antagonist and has been postulated to induce a central anti-nociceptive effect mediated by a central cholinergic mechanism [3]. It has also been shown to be effective as an antiemetic as well as abortive pain reliever in migraine headache attacks [4]. Prochlorperazine is part of the phenothiazine class of antipsychotics and carries a risk of akathisia (25-44%) [5,6].

***Corresponding Author:** Jennifer Stahl, Clinical Assistant Professor of Emergency Medicine/Internal Medicine and Critical Care Medicine, East Carolina University/Brody School of Medicine, USA, Tel: (252) 744-4757, Email: stahlj@ecu.edu

	Compazine 10 mg + Benadryl 50 mg			Toradol 30 mg		
Time	**0 min**	**30 min**	**60 min**	**0 min**	**30 min**	**60 min**
	10	9	9	8	8	8
	10	7	6	8	5	3
	10	6	4			
	9	6	6			
	8	6	5			
	10	10	10			
Average	9.5	7.33	6.66	8	6.5	5.5

Table 1: Visual Analog Scale (VAS) Pain Scores.

The use of diphenhydramine (anticholinergic) in combination with prochlorperazine has been shown to decrease the risk of akathisia to approximately 14% in one trial [6]. In this study, we investigated the use of combination prochlorperazine and diphenhydramine in comparison to ketorolac (NSAID) for the treatment of acute-on-chronic back pain in patients presenting to the Emergency Department. Ketorolac was used as a standard NSAID therapy treatment for comparison. Our primary outcome was reduction in pain utilizing a visual analog pain scale (VAS) (Table 1).

Materials and Methods

This study was performed between May and August 2014 in the Emergency Department (ED) of a 900-bed tertiary care hospital with 120,000 annual ED visits. Following Institutional Review Board (IRB) approval, adult patients presenting to the ED with a chief complaint of "back pain" were screened for enrollment in our study. Inclusion criteria included: a history of chronic low back pain, chief complaint of acute exacerbation of the chronic low back pain, normal neurologic exam, no traumatic injury preceding the onset of back pain, 18 to 65 years of age, and no fever. Exclusion criteria were: Age < 18 or > 65 years of age, pregnant women, history of QT prolongation (defined as QT >420 ms), abnormal neurological examination, presence of fever (defined as >100.4 degrees Fahrenheit), absence of a prior history of back pain, traumatic injury within the last month (onset of pain with lifting or bending was not considered traumatic injury), any history of cancer, history of gastrointestinal bleeding within the last month, history of chronic renal disease, history of opioid abuse or opioid seeking behavior (determined by electronic chart review), current enrollment in another clinical trial, presence of another acute complaint at the time of the visit, and history of allergy or intolerance to the study drugs.

Once enrolled in the study patients were randomized into two pharmacologic treatment arms. The first treatment arm included administration of prochlorperazine 10 mg intravenously along with diphenhydramine 50 mg intravenously. The second treatment arm included administration of ketorolac 30 mg intravenously. The patient, study investigators, treating providers, and nurses administering the drugs were blinded to treatment arms. Patient pain severity levels were obtained using visual analog scale (VAS) scoring with values 0 to 10. Scores were obtained at 0 minutes (prior to medication administration), and then at 30 minutes and 60 minutes from medication administration. Patients were given only the study treatments for the first 60 minutes of their care. After the 60-minute VAS measurement was obtained the patient could receive any further treatment deemed necessary by the treating provider if the patient's pain was not adequately relieved. Patients were monitored for any adverse events during their emergency room visit.

Results

In this study, 75 patients were screened for enrollment in this study with only 8 patients meeting inclusion criteria and willing to participate. Of the 8 patients enrolled, 6 (75%) received prochlorperazine and diphenhydramine treatment, while 2 received ketorolac treatment (25%). Enrollment in the study was terminated prematurely due to shortage/availability of prochlorperazine and IRB approval expiring.

Changes in pain ratings over time were analyzed using RMANOVA followed by Fisher's post-hoc test. Of note, there were no comparisons made between treatment arms due to the study limitation of only 2 patients in the ketorolac treatment arm. Of the 6 patients who were enrolled and received prochlorperazine and diphenhydramine treatment, pain scores for these patients were: 0 minutes (baseline) mean = 9.5 (95% CI = 8.6-10), 30 minutes mean = 7.3 (95% CI = 5.5-9.2), and 60 minutes mean = 6.7 (95% CI = 4.2-9.1). The change in pain from 0 minutes (baseline) to 30 min was mean = 2.2 (95% CI=0.6-3.7) with p=0.01 and the change from baseline to 60 minutes was mean = 2.8 (95% CI=0.6-5.1) with p<0.01. The change in pain from 30 to 60 min had a mean improvement of 0.67, without statistical significance, p= 0.1.

During the ED visit no patients were noted to have any adverse reactions or events to the study drugs. No symptoms of akathisia specifically were noted of the patients given prochlorperazine and diphenhydramine there appeared to be a trend towards improvement in pain relief at 30 minutes which persisted for 60 minutes. However, none of the patients reported complete pain relief, and 1 reported no relief at all (Figures 1 and 2).

Discussion

Acute-on-chronic back pain plagues many patients in the United States every year, prompting frequent visits to the Emergency Department for acute symptom relief. Treatment of these patients is often difficult due to suboptimal and often ineffective treatment options. While NSAIDs have been a mainstay of treatment in the ED, many patients do not achieve adequate relief. While other treatments are available such as muscle

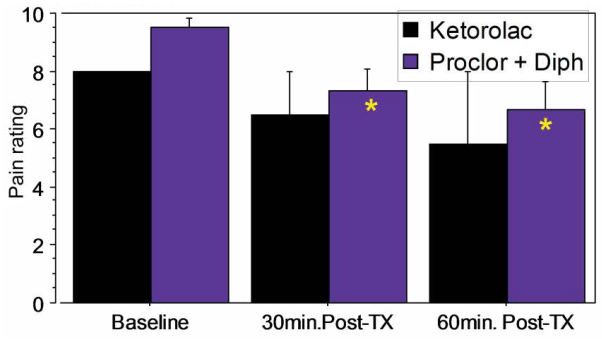

Figure 1: pain scale scores reported prior to treatment, 30 minutes and 60 minutes after treatment. For the group, mean baseline pain scores =9.5(95% cl = 8.6-10), 30 minutes mean = 7.3 (95% cl = 5.5-9.2), and 60 minutes mean = 6.7 (95% cl = 4.2 -9.1). Pain scores decreased significantly from baseline to 30 min (mean change = 2.2, 95% cl = 0.6-5.1;p<0.02. No significantly side effects were noted. *=p<0.05.

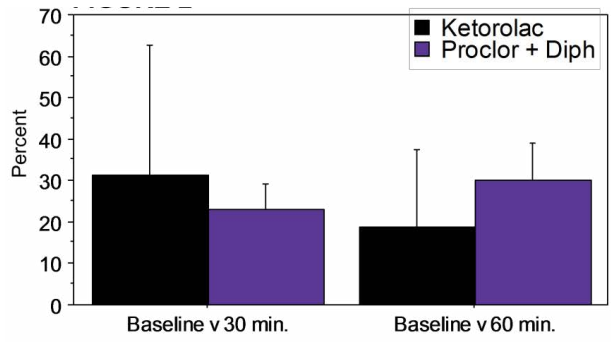

Figure 2: Mean percentage decreases in pain score over time.
For the experimental group, mean pain score improvement at 30 min = 2.1 (25%) and at 60 minutes = 2.8(27.5%)

relaxants, benzodiazepines, acetaminophen, antidepressants, etc., their performance often is suboptimal as well. Narcotic medications run the risk of addiction and over-sedation, and therefore are not recommended as first line agents. As a result, other alternative pharmacologic agents that could provide analgesic relief with low side effects would be ideal.

Prochlorperazine has proven to be a very effective treatment choice for acute migraine headaches and has been well studied in the Emergency Department setting [4,7-10]. It has shown efficacy when compared to ketorolac in treatment of pediatric migraine headaches as well as more effective than metoclopramide in the adult migraine population [4,9]. The pharmacologic properties of prochlorperazine indicate a nociceptive effect and potential treatment for other types of pain. In a recent trial, prochlorperazine was used for treatment of postoperative pain following laporoscopic-assisted distal gastrectomy (LADG) in combination with tramadol/acetaminophen, and celecoxib, and showed equal effectiveness in comparison to epidural anesthesia [11]. The main side effect of prochlorperazine is akathisia which has been shown to decrease with concomitant diphenhydramine administration [6].

An obvious limitation of this study was the low number of study subjects. During enrollment, we had difficulty finding patients who met inclusion/exclusion criteria and were willing to participate in the study during the IRB approved study period, we faced a national pharmaceutical shortage of the study drug prochlorperazine which further hindered patient enrollment. Although only 8 patients were enrolled in this pilot study, our results showed that patients who received prochlorperazine and diphenhydramine treatment demonstrated pain relief at 30 minutes, which persisted at 60 minutes. Pain was improved at both 30 and 60 minutes with statistical significance when compared to baseline scores with $p = 0.01$, and $p < 0.01$ respectively. In each group, one patient showed no improvement in pain over time. There were no adverse events and patients tolerated medications well during their visit. Other limitations of this study (other than study number) include treatment of only acute on chronic back pain, minimal follow up time, and reliance of patient reported pain scale. Future studies could look at a larger patient population which would improve statistical significance, potentially expanding inclusion criteria, and having longer a follow up time including repeat visits for the same complaint.

This study indicates that the use of prochlorperazine and diphenhydramine as a treatment modality for acute exacerbations of chronic back pain may be beneficial. Patients presenting with chronic back pain are often difficult to manage and treat. Many of these patients have a high potential for abuse and dependency when narcotic medications are initiated. In an effort to lower prescription abuse and opiate prescribing, adding another non-narcotic alternative for treatment of chronic pain syndromes has tremendous clinical and practical implications as well as potential for further research. While this project served as a pilot study, expanding this study to include more patients will further determine the efficacy of the use of prochlorperazine and diphenhydramine as a treatment option.

References

1. Chou R, Huffman LH, American Pain Society, American College of Physicians. 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*. 2007;147(7):505-514.
2. Chou R, Deyo R, Friedly J, et al. Systemic pharmacologic therapies for low back pain: A systematic review for an american college of physicians clinical practice guideline. *Ann Intern Med*. 2017;166(7):480-492.
3. Ghelardini C, Galeotti N, Uslenghi C, Grazioli I, Bartolini A. Prochlorperazine induces central antinociception mediated by the muscarinic system. *Pharmacol Res*. 2004;50(3):351-358.
4. Friedman BW, Esses D, Solorzano C, et al. A randomized controlled trial of prochlorperazine versus metoclopramide for treatment of acute migraine. *Ann Emerg Med*. 2008;52(4):399-406.
5. Wijemanne S, Jankovic J, Evans RW. Movement disorders from the use of metoclopramide and other antiemetics in the treatment of migraine. *Headache*. 2016;56(1):153-161.
6. Vinson DR, Drotts DL. Diphenhydramine for the prevention of akathisia induced by prochlorperazine: A randomized, controlled trial. *Ann Emerg Med*. 2001;37(2):125-131.
7. Bachur RG, Monuteaux MC, Neuman MI. A comparison of acute treatment regimens for migraine in the emergency department. *Pediatrics*. 2015;135(2):232-238.
8. Becker WJ. Acute migraine treatment in adults. *Headache*. 2015;55(6):778-793.
9. Brousseau DC, Duffy SJ, Anderson AC, Linakis JG. Treatment of pediatric migraine headaches: A randomized, double-blind trial of prochlorperazine versus ketorolac. *Ann Emerg Med*. 2004;43(2):256-262.
10. Marmura MJ, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: The american headache society evidence assessment of migraine pharmacotherapies. *Headache*. 2015;55(1):3-20.
11. Mikami J, Takiguchi S, Miyazaki Y, et al. Novel management of postoperative pain using only oral analgesics after LADG. *Surg Today*. 2016;46(1):117-122.