

A Randomized Controlled Trial on the Effectiveness of *Zingiber officinale* Ointment versus Placebo Ointment Among Patients with Acute Musculoskeletal Complaints

Melissa Claire L. Masaluña, MD

Background: Complementary and alternative medicine is becoming popular among Filipino patients. Ginger is one promising herbal plant in the management of musculoskeletal complaints. Studies showed significant reduction of the pain after oral intake of either ginger extract or tablet with reported occurrence of mild gastrointestinal side effects. Hence this study aimed to assess the effectiveness of using 10% ginger ointment as a treatment for acute musculoskeletal pain.

Objective: This study determined the effectiveness and safety profile of topical application of ginger ointment as compared to a placebo ointment in the reduction of pain severity in patients with musculoskeletal complaints.

Subjects and Setting: The study participants consisted of adults aged 19-59 years old who have acute musculoskeletal pain. The study was done in Canossa Health and Social Center in Tondo, Manila.

Design: Ginger ointment was compared to a placebo ointment in 60 patients with acute musculoskeletal complaints in a single blinded randomized controlled trial. Study participants were randomized into two groups of thirty (N=30), the experimental group (ginger) and the placebo group.

Data Collection: The clinical assessment included a visual analog scale (VAS) for pain at baseline, 30 minutes and 60 minutes after intervention. Paracetamol and diclofenac tablets were prescribed as rescue medication. Reduction of pain was computed using mean, standard deviation and groups were compared using students' t-test. The frequency of the adverse reaction to the ointment was summarized using cross tabulations.

Results: There was decrease in the severity of the pain reported by study participants for both ginger and placebo ointment. At 60 minutes post-intervention, a greater decrease on pain scores among participants receiving the ginger ointment ($X=1.37$; $SD\pm 1.22$) was noted compared to the participants receiving placebo ointment ($X=2.07$; $SD\pm 1.90$). However, the differences between intervention groups were not statistically significant, $p>0.05$. There were no reported adverse reactions for both intervention groups.

Conclusion: Ginger ointment 10% was not effective in decreasing pain scores when compared to placebo ointment. No adverse event was reported within 60 mins of intervention among adult patients with musculoskeletal complaints.

Keywords: musculoskeletal complaints, ginger ointment

INTRODUCTION

Musculoskeletal complaints are one of the most common causes of severe long term pain and physical disability. They

include a range of conditions from acute onset-short duration to lifelong disorders such as osteoarthritis, rheumatoid arthritis, osteoporosis, and low back pain.¹

More than 315 million office visits each year were due to musculoskeletal complaints, which also account for more than 10% of all outpatient visits in general medical practice.² Locally, it has a prevalence of 16.3% (95% CI 8.6-24.0) among the adult population in a Filipino urban community.³

* From the Department of Family and Community Medicine, University of the Philippines – Philippine General Hospital

Musculoskeletal complaints are managed with simple analgesics, non-steroidal anti-inflammatory drugs, opioid analgesics and muscle relaxants.⁴ Paracetamol is widely advocated for pain associated with rheumatic disease and has proven beneficial for a significant minority of patients. However, some patients prefer to use complementary and alternative medicine which has a documented utilization prevalence of 68.4% in rural and 51.1% in urban areas.⁵

Ginger (*Zingiber officinale*) has been used for acute pain of musculoskeletal disorders albeit with conflicting results on effectiveness. Wigler et al in 2003 showed significant reduction of the pain after oral intake of either ginger extract or tablet while Haghghi et al reported similar efficacy between the ginger extract and ibuprofen in reducing the pain on patients with osteoarthritis.^{6,7} On the other hand, based on the recommendations of the Philippine Clinical Practice Guideline of Medical Management of Knee Osteoarthritis (2009), concentrated standardized ginger preparation will provide moderate relief on pain of knee osteoarthritis and patients are warned of potential adverse events with the intake of oral preparations.⁸

Topical ginger preparations as compress or patch for pain of osteoarthritis will have potential benefits in terms of adverse events and local availability. However, there is limited evidence of its efficacy in terms of acute pain relief among adult patients presenting with mild to moderate pain due to musculoskeletal disorders. This study therefore aimed to assess the effectiveness of using 10% ginger ointment as a treatment for acute musculoskeletal pain.

METHODS

Collection of the Ginger Rhizome

The ginger rhizomes were procured from an Organic Farm in Amadeo, Cavite and brought to the Philippine National Museum for certification. The rhizomes were gathered and properly placed in a plastic bag for transport to the Department of Industrial Pharmacy of the University of the Philippines Manila for processing.

Preparation of the Ointments

The *Zingiber officinale* ointment and placebo ointment were prepared independently by the staff of the Department of Industrial Pharmacy of the University of the Philippines Manila. Both the experimental and control drugs were prepared in the form of an ointment.

Preparation of the *Zingiber officinale* Ointment

The procured ginger plant was dried in the shade and extraction of plant materials thru cold maceration and 95% ethanol was done. The method of Haghghi et al. (2005) was adopted for the extraction. Ten percent (10%) ginger ethanolic extract was used in this study. Two grams of ginger ointment was placed in a 5g white plastic jar and labelled with the appropriate code.

Preparation of the Placebo ointment

The 2 gram placebo ointment was formulated to mimic the ginger using the FD&C colorants, placed in a 5g white plastic jar and labelled with the appropriate code.

Patient Selection and Study Design

The study was a single blinded randomized controlled trial carried out at Canossa Health and Social Center in Tondo, Manila. All the study participants had acute musculoskeletal complaints (upper and lower extremities, torso and back) with a pain score of 3 – 6 cm (mild – moderate pain) on a 10 cm visual analog pain scale, no intake of anti-inflammatory medications for at least 24 hours and/or a diagnosis of osteoarthritis, rheumatoid arthritis and gouty arthritis. The exclusion criteria were a pain score of 7-10 cm (severe pain) on a 10cm visual analog pain scale, intake of steroids within the prior 4 weeks, Intra-articular corticosteroid treatment within the previous 3 months, open wound on the site of the pain, allergy with ginger plant, paracetamol and diclofenac, severe medical disorders (diagnosis of Cancer / Neurological Disorder) and history of dyspepsia and gastroesophageal reflux.

The sample size was based on the assumptions that topical ginger will improve pain scores by 30 ± 3.7 from the baseline compared to 56.5 ± 3.6 in the placebo group (Alpha of 5%, Beta of 20% and a confidence interval of 95%).⁷ . The total computed sample size was 30 for each group.

Conduct of the Study Intervention

A thorough history and physical examination was done by the primary investigator. The selected subjects were randomized using the random number generator in Excel into the ginger and the placebo ointment groups.

The study participants were asked to identify the painful part and point out the severity of the pain using the visual analog scale. The primary investigator applied all the contents in the container to the painful part of the body and

was observed for a total of 60 minutes for reduction of the severity of the pain and occurrence of any adverse events such as erythema or rashes. The pain scores and the time of measurement were recorded prior to the application of the ginger and placebo ointment and during the observation period.

The patients were given rescue medications depending on the VAS score at the end of the one (1) hour observation period: mild pain (1-3cm VAS), a 500mg paracetamol; moderate pain (4-6cm VAS), 50mg diclofenac.

The data were analyzed using an evaluation copy of on-line SPSS IBM. The study protocol was submitted to the University of the Philippines Manila Research Ethics Board (UPMREB) PGH Review Panel for ethics review and approval prior to implementation.

RESULTS

A total of sixty (60) patients were randomized in the two treatment groups: 30 in the ginger ointment and 30 in the placebo ointment. There was no significant difference between the groups in terms of age, sex, anthropometric measurements, past medical histories, vital signs and site of pain at baseline (Table 1). Likewise, pain scores of the two groups were similar at the start of the intervention (Table 2). There were no drop-outs or exclusion of study participants during the study period.

Overall, there was reduction on the severity of the pain for both ginger and placebo ointment interventions (Figure 1). Although, there was a greater decrease in pain scores among participants receiving the ginger ointment during the 60 minutes intervention (Table 2), the difference between the two groups was not significant. Likewise, there were no reported adverse reactions for both intervention groups.

Table 1. Baseline demographic characteristics of participants who have acute musculoskeletal pain randomized to Ginger Ointment vs Placebo.

Variables	Treatment Ginger (N=30)	Control Placebo (N=30)	p value
Age, (X±SD)	44.27 (SD±11.61)	48.33 (SD±8.56)	0.128
Sex			
Females	21 (70%)	26 (86.7%)	0.117
Males	9 (30%)	4 (13.3%)	
Anthropometric Measurement			
Height, (X±SD)	157.07 (±7.01)	156.10 (±5.27)	0.548
Weight, (X±SD)	54.2 (±8.78)	53.02 (±53.01)	0.576
Presence of Allergy to Food/Medications	0 (0%)	2 (6.6%)	0.152
Presence of Chronic Illness	3 (10%)	6 (20%)	0.278
Presence of Conditions Related to the Musculoskeletal System	2 (6.6%)	6 (20%)	0.126
Maintenance Medications	3 (10%)	5 (16.7%)	0.067
Vital Signs			
Heart Rate, (X±SD)	74.57 (±7.32)	74.63 (±7.15)	0.972
Respiratory Rate, (X±SD)	17.70 (±1.24)	17.67 (±1.21)	0.916
Temperature, (X±SD)	36.60 (±0.50)	36.57 (±0.51)	0.798
Site of pain*			
Lumbar Area	7 (23%)	4 (13.3%)	0.330
Knee	4 (13.3%)	7 (23%)	0.330
Upper Back	3 (10%)	7 (23%)	0.175

*Only the top highest sites of pain were included

Table 2. Treatment outcomes after 60 minutes of application of ginger ointment and placebo ointment among participants with acute musculoskeletal pain

Variables	Treatment Ginger (N=30)	Control Placebo (N=30)	p value
Pain Score, Mean SD			
Before Treatment	4.83 (SD ± 1.177)	5.03 (SD ± 1.098)	0.499
First 30 minutes	2.27 (SD ± 1.337)	2.90 (SD ± 1.845)	0.134
Second 30 minutes	1.37 (SD ± 1.217)	2.07 (SD ± 1.964)	0.104
Adverse Reactions	0 (0%)	0 (0%)	

*p value computed using students t-test, significant at <0.05

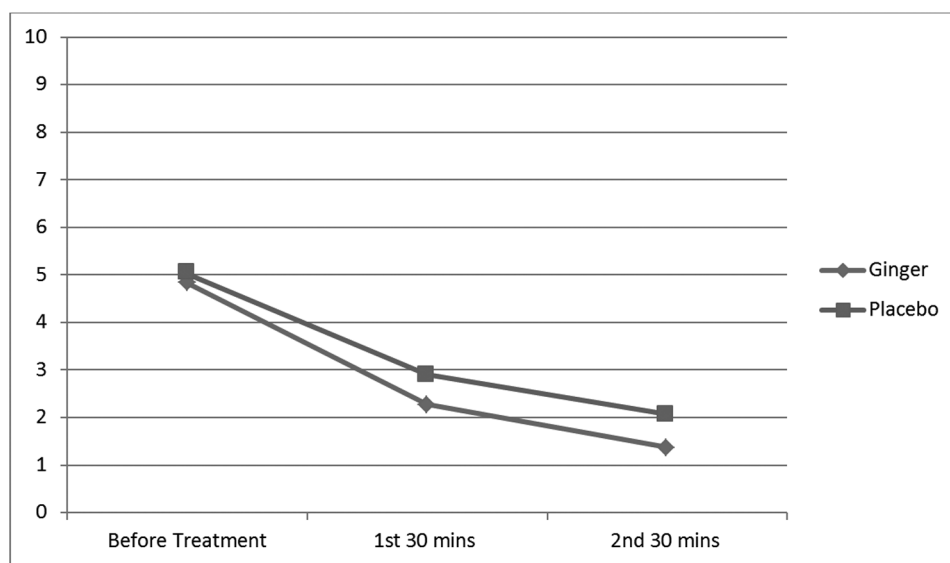


Figure 1. Effect of ginger and placebo ointment on VAS score of adult patients treated for acute musculoskeletal pain

DISCUSSION

The findings of this study demonstrate a reduction on the severity of the pain in adults with musculoskeletal complaints after application of both ginger and placebo ointment. Although, there was greater decrease on pain scores among patients receiving the ginger ointment, the difference between the two groups was not statistically significant. The safety profile was also similar as there were no reported adverse reactions for both groups during the intervention period.

Complementary and alternative medicine is gaining popularity among patients with musculoskeletal complaints. Ginger has been recognized with its various uses especially as an anti-inflammatory agent. Several studies have been conducted using an oral form of ginger and it has been shown to be superior to placebo.^{6,9,10,11}

Ginger constituents, mainly the gingerols and shogaols, showed strong inhibitory effects on COX-2 enzyme activity on intact cells and excellent inhibition of LPS-induced PGE2 production.^{12,13} Ginger also showed a good potential for skin penetration wherein amounts of gingerol extract using a plaster was absorbed transdermally through human epidermis as well as having an effective anti-inflammatory response on mouse skin.¹⁴ These findings also support the study done by Therklason (2013) using a ginger compress versus a ginger patch for the treatment of osteoarthritic symptoms which showed a potential to relieve symptoms.¹⁵

In this study, although the pain reduction between the 2 treatment groups was not statistically significant, the results showed a trend towards greater pain reduction among study participants who received the ginger ointment as treatment for a musculoskeletal complaint. The greater decrease in pain severity

may be clinically significant for patients with musculoskeletal pain.

The lack of dose-gradient for the ginger ointment and placebo effect among study participants were considered to be the limitations in the study. No studies showed an effective dose of the ginger ointment to use among adults with musculoskeletal complaints.^{16,17,18} The dose of 10% Ginger ethanolic extract was based on the percent weight of the ginger extract where the 10 grams of ginger ethanolic extract is contained per 100g of the ointment. This limitation may have affected the results since only one dose was used as the intervention and higher doses may prove the dose effectiveness of topical ginger.

Secondly, the placebo group was observed to have improvement comparable with that of the treatment group. It is noted that placebo treatments are also considered healing agents as its influence lies in the psychobiological context surrounding treatment thereby resulting in an active response in the brain and body of the patient.¹⁹

The study showed that ginger ointment can decrease pain scores of patients with musculoskeletal disorders. Future trials should aim at testing the effective topical dose that could bring about significant pain relief on a larger population and should also consider testing against a conventional topical NSAID.

CONCLUSION

Ginger ointment 10% was not effective in decreasing pain scores when compared to placebo ointment. No adverse event was reported within 60 mins of intervention among adult patients with musculoskeletal complaints.

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REFERENCES

1. Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. Bull World Health Organ. 2003; 81(9): 646–56.
2. Palmer T, Toombs JD. Managing joint pain in primary care. J Am Board Fam Pract 2004; 17 Suppl: S32-42.
3. Dans LF, Tankeh-Torres S, Amante CM and Penserga EG. The prevalence

- of rheumatic diseases in a Filipino urban population: a WHO-ILAR COPCORD study. J Rheumatol 1997; 24, 1814–19.
4. Australian Acute Musculoskeletal Pain Guidelines Group (AAMPGG). Evidence based management of acute musculoskeletal pain. Australian Academic Press, Brisbane (2003).
5. Dahilig VRA and Salenga RL. Prevalence, perceptions and predictors of complementary and alternative medicine use in selected communities in the Philippines. JAASP 2013; 1(1): 16–24.
6. Wigler I, Grotto I, Caspi D, Yaron M. The effects of Zintona EC (a ginger extract) on symptomatic gonarthrosis. Osteoarthritis Cartilage 2003; 11(11): 783-9.
7. Haghghi M, Khalvat A, Toliat T, Jallaei S. Comparing the effects of ginger (*Zingiber officinale*) extract and ibuprofen on patients with osteoarthritis. Arch Iran Med 2005; 8(4): 267–71.
8. Penserga E and Knee OA. CPG Technical Working Committee. The Philippine Rheumatology Association Clinical Practice Guidelines for the Medical Management of Knee Osteoarthritis. PPD's Compendium of Philippine Medicine 12th Edition 2010.
9. Srivastava KC, Mustafa T. Ginger (*Zingiber officinale*) and rheumatic disorders. Med Hypotheses 1989; 29(1): 25-8.
10. Bliddal H, Rosetzky A, Schlichting P, Weidner MS, Andersen LA, Ibfelt HH, Christensen K, Jensen ON, Barslev J. A randomized, placebo-controlled, cross-over study of ginger extracts and ibuprofen in osteoarthritis. Osteoarthritis Cartilage 2000; 8(1): 9-12.
11. Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. Arthritis Rheum 2001; 44(11): 2531-8.
12. Tjendraputra E, Tran V H, Liu-Brennan D, Roufogalis BD and Duke CC. Effect of ginger constituents and synthetic analogues on cyclooxygenase-2 enzyme in intact cells. Bioorganic Chemistry 2001; 29: 156-63.
13. Jolad SD, Lantz RC, Solyom AM, Chen GJ, Bates RB and Timmermann BN. Fresh organically grown ginger (*Zingiber officinale*): Composition and effects on LPS-induced PGE2 production. Phytochemistry 2004; 65: 1937-54.
14. Minghetti P, Sosa S, Cilurzo F, Casiraghi A, Alberti E, Tubaro A, Montanari L. Evaluation of the topical anti-inflammatory activity of ginger dry extracts from solutions and plasters. Planta Medica 2007; 73: 1525-30.
15. Therklason T. Topical ginger treatment with a compress or patch for osteoarthritis symptoms. J Holist Nurs 2013; 32(3): 173-82.
16. Terry R, Posadzki P, Watson LK, Ernst E. The use of ginger (*Zingiber officinale*) for the treatment of pain: a systematic review of clinical trials. Pain Med 2011; 12(12):1808-18. doi: 10.1111/j.1526-4637.2011.01261.x. Epub 2011 Nov 4.
17. Chrubasik S, Pittler MH, Roufogalis BD. *Zingiberis rhizoma*: a comprehensive review on the ginger effect and efficacy profiles. Phytomedicine 2005; 12(9): 684-701.
18. Ding M, Leach MJ, Bradley H. A systematic review of the evidence for topical use of ginger.
19. Moerman D E and Jonas WB. Deconstructing the placebo effect and finding the meaning response. Ann Intern Med 2002; 136(6): 471–6.