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Randomized Pilot Study

Oral Versus Topical Ibuprofen for Chronic Knee Pain: A Prospective Randomized Pilot Study

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Background: Topical ibuprofen provides an alternative treatment to oral ibuprofen for the treatment of chronic knee pain.

Objective: To compare the efficacy of topical versus oral ibuprofen in chronic knee pain treatment.

Study Design: Prospective, randomized, unblinded pilot study.

Setting: A private pain management practice.

Methods: Twenty patients received either ibuprofen tablets 3 times daily (2400 mg total) or 4% topical gel 4 times daily (320 mg total) for 2 weeks. Subjects completed the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index, the Medical Outcomes Study 12-Item Short Form (SF-12v2) Health Survey, and a satisfaction questionnaire.

Results: Comparison of WOMAC and SF-12v2 mean changes from baseline showed no differences between groups. Patient satisfaction and study treatment convenience were rated equivalently between groups. Within the topical group, significant improvements ($P < 0.05$) were experienced in the mean differences of WOMAC Pain scores from baseline to 2 weeks (-82.6, -158.3 to -6.8), WOMAC Stiffness scores from baseline to one week (-25.3, -50.0 to -0.6) and baseline to 2 weeks (-47.8, -95.7 to 0.1), WOMAC Physical Function scores from baseline to one week (-175.9, -348.6 to -3.2) and baseline to 2 weeks (-312.1, -580.5 to -43.7), and patient satisfaction scores from baseline to one week and baseline to 2 weeks. Within the oral group, significant improvements ($P < 0.05$) were experienced in mean differences of WOMAC Physical Function from baseline to one week (-342.6, -638.1 to -47.1) and baseline to 2 weeks (-323.2, -637.1 to -9.2).

Limitations: As this was a preliminary investigation, the sample size of 20 subjects is a limitation in this study.

Conclusion: Treatment of chronic knee pain with topical ibuprofen provided comparable clinical efficacy and patient satisfaction as oral ibuprofen in this pilot study.

Key words: Topical ibuprofen, knee osteoarthritis, chronic pain

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Chronic knee pain is a prevalent condition in the older population. While it is estimated that 12% of Americans aged 25 to 74 are clinically diagnosed with osteoarthritis (OA), the prevalence among men and women over 60 years of age is 17% and 30% respectively (1). The Framingham study reported 33% of participants aged 63 to 93 had radiographic evidence of knee OA and 9.5% had symptomatic knee OA (2). Additional population-based studies report rates of 33% in patients over 65 and 38% in patients over 60 (3,4).

Oral ibuprofen is routinely prescribed for the

treatment of knee OA and provides successful pain relief (5-8) despite serious side effects which include increased risk of gastrointestinal adverse effects (9-13), cardiovascular events (14-16), and renal toxicity (17-18). The use of topical ibuprofen is not new in the treatment of musculoskeletal pain and has been shown to provide adequate pain relief while potentially avoiding the side effects associated with oral ibuprofen (19-26). However, there are few studies examining its efficacy when compared to its oral counterpart with regard to chronic knee pain (25, 27-29).

The objective of this pilot study was to compare the efficacy of a topical formulation of ibuprofen versus the oral form in treating chronic knee pain in patients 50 years and older treated at a private practice. The primary outcomes measured were Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index Version 3.1 scores for Pain, Stiffness, and Physical Function. Secondary outcomes were the Medical Outcomes Study 12-Item Short Form (SF-12v2) Health Survey subscores as well as patient satisfaction. Patients were followed at one and 2 weeks post-treatment.

Methods

Study design

This prospective, unblinded pilot study was conducted at a single pain management practice of the principal investigator (RLT). A total of 20 patients were randomized via computer-generated number sequence. Using sequentially numbered opaque sealed envelopes, they were assigned to receive either ibuprofen tablets or topical 4% ibuprofen gel for 2 weeks. The objective of this study was to compare efficacy and patient satisfaction at one and 2 weeks after treatment was initiated.

Baseline data were collected during an office visit by study nurse practitioners trained in the study protocol and procedures. Follow-up data at one and 2 weeks after treatment initiation were collected using self-administered questionnaires returned to the study coordinator via postal mail.

Adverse events were reported by patients in the postal surveys as well as directly to the study coordinator during telephone follow-up.

Study Population

After approval of the study protocol by an Institutional Review Board, potential study subjects were recruited from a pain management practice. An advertisement was placed in the general waiting area and interested subjects completed a screening survey. Broad inclusion criteria were applied and patients who fulfilled the following were included in the study:

- ≥ 50 years old
- ≥ 3 months of knee pain
- willing and able to cooperate in the assigned treatment
- willing and able to complete follow-up questionnaires

Patients were excluded from participation if there was any contraindication to ibuprofen usage (known allergy or hypersensitivity, history of gastrointestinal ulcer or bleeding, renal disease, liver dysfunction, consuming >3 alcoholic beverages daily, or anticoagulant treatment), pregnancy, or a scheduled knee procedure within the 2-week follow-up period.

For subjects satisfying study criteria, informed consent was obtained and baseline data were collected, including demographics, concomitant medications and current NSAID use, other bodily pain using a manikin, and Chronic Pain Grade to characterize pain severity (30,31).

For patients experiencing bilateral chronic knee pain, the more severe side was measured and included in the study.

Treatment Intervention

Subjects in the oral ibuprofen group took 800 mg ibuprofen tablets 3 times daily (2400 mg total). Study medication was pre-packaged in pill organizers and given to patients to utilize for the duration of the 2 weeks.

Subjects in the topical ibuprofen group were given tubes of 4% ibuprofen gel supplied by the manufacturer (Helm Pharmaceuticals, Chappaqua, NY) and instructed to apply 2 mL of gel, to a targeted area of an approximately 3.5 cm diameter circle, 4 times daily (320 mg total). A "Gel Application Reference Card" with application instructions illustrated the 3.5 cm diameter circle and accompanied the study medication in order to help patients consistently apply the same amount of gel.

Any subjects taking ibuprofen or other NSAID at the time of enrollment underwent a 2-day washout period before beginning the study treatment. Other medications taken prior to the study were maintained, including those for pain management other than NSAIDs.

Outcome Measures

The primary outcome to measure treatment efficacy was the WOMAC survey consisting of 24 visual analog scale questions to assess pain, stiffness, and physical function with maximum possible scores of 500, 200 and 1,700 respectively (32). Secondary outcomes included the acute SF-12v2 general health survey and a questionnaire assessing patient satisfaction with treatment. The acute SF-12v2 survey assesses the following categories (with a maximum possible score of 100) in reference to the previous week: general health, physical functioning, physical role, bodily pain, vitality, social function, mental health, emotional role, mental component summary, and physical component summary (33). Patients were also asked to provide treatment satisfaction and convenience scores detailed below:

- On a scale from 0 to 10, where 0 is very dissatisfied and 10 is very satisfied, how satisfied were you with the previous treatment of your knee pain (before the study treatment)?
- On a scale from 0 to 10, where 0 is very dissatisfied and 10 is very satisfied, how satisfied were you with the study-prescribed treatment of your knee pain?
- On a scale from 0 to 10, where 0 is very inconvenient and 10 is very convenient, how convenient did you feel the study treatment was?
- Would you undergo this type of treatment again for your knee pain? (YES/NO)

Baseline WOMAC and SF-12v2 scores were obtained at the time of enrollment during the office visit or via postal questionnaire if the patient underwent washout. Subsequent questionnaires were completed at one and 2 weeks and returned via postal service to the study coordinator.

Role of the Funding Source

The funding source solely provided financial support of the study. The funding organization did not participate in any phase of data analysis or manuscript preparation. The principal investigator and research team retained full access to study data.

Statistical Analysis

A full analysis set was analyzed and included all randomized patients receiving the assigned study intervention and providing at least one post-baseline observation. Data are expressed as mean ± standard deviation or mean (95% confidence interval) as noted. Shapiro-Wilk's test was used for normality testing when necessary. Between-groups analysis of continuous data was conducted using independent samples t-tests for normally distributed data and Mann-Whitney U test for nonparametric data. Within-group analysis of continuous data was performed using paired t-tests for normal data and Wilcoxon signed-rank test if parametric assumptions were not met. Categorical data were analyzed using chi-square testing with Fisher's exact test when appropriate. SPSS 16.0 for Windows (SPS Inc, Chicago, IL) was used for all statistic analysis.

Results

During the recruitment period from September 15, 2008 to October 3, 2008, 30 patients were screened for eligibility (Fig. 1). Eight were excluded for not fulfilling study criteria and 2 patients declined participation. A total of 20 participants were enrolled and randomized to treatment groups. Nineteen participants completed the treatment regimen and follow-up questionnaires at one and 2 weeks. One patient in the topical group was lost to follow-up and did not complete study questionnaires.

Adverse events in the oral ibuprofen group included: headache (2 patients), dizziness (2 patients), stomachache (one patient), constipation (one patient) and diarrhea (one patient). One patient in the topical ibuprofen group reported acute skin rash after application and another patient reported dizziness.

The 2 treatment groups were similar in demographic composition and baseline pain severity. As detailed in Table 1, there was no difference in age, gender, body mass index, duration of pain experienced, or baseline Chronic Pain Grade between the groups.

Between Groups

Mean WOMAC Pain, Stiffness, and Physical Function scores are highlighted in Table 2. Though both groups experienced consistent improvement of WOMAC Pain and Stiffness scores, and Physical Function score for the topical group, no significant difference was shown in any WOMAC subcategory between the 2 groups when comparing baseline and follow-up intervals. Likewise, there was no discernable difference between the two groups in reference to SF-12v2 scores (Table 2). Comparison of mean differences between the 2 groups from baseline to one week, one week to 2 weeks, and baseline to 2 weeks is depicted in Table 3 and Fig. 2 (WOMAC subscores). The improvements in WOMAC and SF-12v2 scores were equivalent between the groups and no one treatment group fared better than the other.

Patient satisfaction improved across both groups

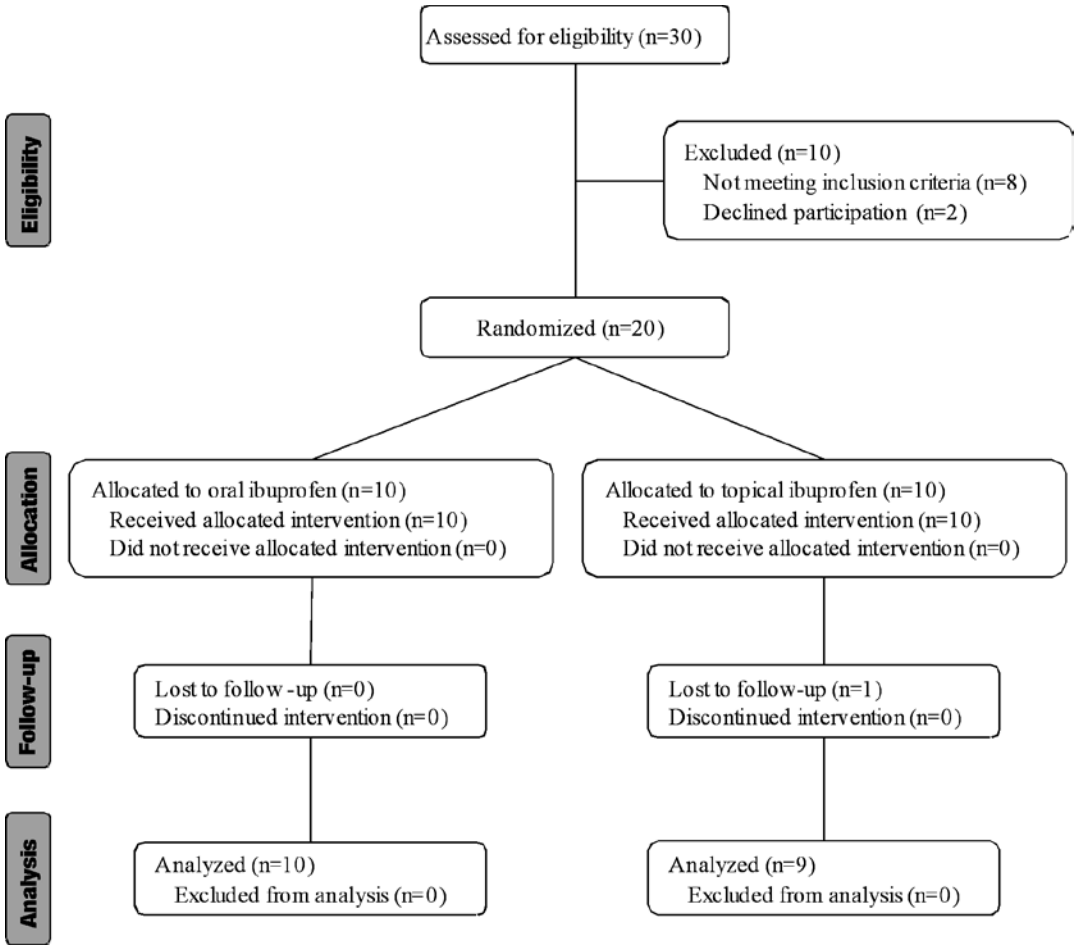


Fig. 1. CONSORT flow diagram.

Table 1. *Demographic and Baseline Characteristics*

	Oral Group (n=10)	Topical Group (n=9)	*P*-value
Gender			
Male	2	0	NS
Female	8	9	
Age, years	57.0 ± 7.9	58.9 ± 10.3	NS
Body Mass Index	30.9 ± 8.0	32.8 ± 6.2	NS
Pain Duration			
3 to 6 Months	1	0	NS
6 to 12 Months	0	0	
> 12 Months	9	9	
Chronic Pain Grade			
0	0	0	
I	0	1	NS
II	1	2	
III	4	3	
IV	5	3	

Mean ± SD. NS=not significant (p≥0.05).

with no one group improving significantly over the other at baseline, one and 2 weeks (Table 4 and Fig. 3). In reference to treatment convenience, though the oral group rated their treatment as more convenient than the topical group, there were no significant differences between the groups. The groups responded equally when asked if they would repeat the assigned study treatment again.

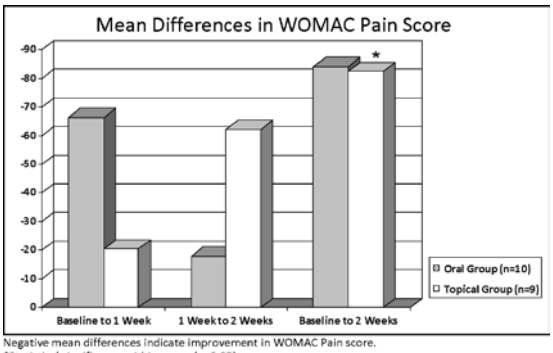
Within Groups

Within the oral ibuprofen group, there were notable improvements in WOMAC Physical Function score mean differences from baseline to one week ($P = 0.028$) and baseline to 2 weeks ($P = 0.045$) and moderate improvements in WOMAC Pain and Stiffness from baseline to one week and baseline to 2 weeks, though not

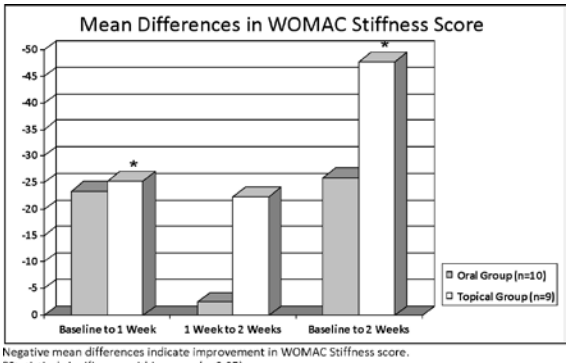
Table 2. *WOMAC and SF-12 scores at baseline, one week, and 2 weeks*

	Oral Group (n=10)	Topical Group (n=9)	p-value
WOMAC Pain			
Baseline	291.7 ± 83.3	305.6 ± 96.6	NS
One Week	225.3 ± 101.5	285.2 ± 105.2	NS
2 Weeks	207.4 ± 127.9	223 ± 125.2	NS
WOMAC Stiffness			
Baseline	131.5 ± 45.2	158.7 ± 29.6	NS
One Week	108.1 ± 49.3	133.3 ± 46.3	NS
2 Weeks	105.6 ± 54.7	110.9 ± 54.1	NS
WOMAC Physical Function			
Baseline	1108.3 ± 302.7	1219.6 ± 201.4	NS
One Week	765.7 ± 293.6	1043.7 ± 343.0	NS
2 Weeks	785.1 ± 460.7	907.4 ± 390.1	NS
SF-12 General Health			
Baseline	44.3 ± 6.2	36.8 ± 9.9	NS
One Week	41.7 ± 6.4	36.8 ± 9.9	NS
2 Weeks	42.3 ± 9.8	36.8 ± 9.9	NS
SF-12 Physical Function			
Baseline	26.4 ± 4.5	25.9 ± 6.2	NS
One Week	29.8 ± 6.4	27.8 ± 7.4	NS
2 Weeks	28.1 ± 5.8	28.8 ± 9.4	NS
SF-12 Role Physical			
Baseline	31.8 ± 8.5	30 ± 6.3	NS
One Week	36.9 ± 8.5	30 ± 8.5	NS
2 Weeks	33.7 ± 6.7	33.1 ± 11	NS
SF-12 Bodily Pain			
Baseline	28.9 ± 9.4	28.0 ± 8.0	NS
One Week	33.0 ± 12.0	31.4 ± 11.5	NS
2 Weeks	34.0 ± 10.8	33.7 ± 14.4	NS
SF-12 Vitality			
Baseline	45.7 ± 6.4	38.8 ± 7.9	NS
One Week	47.7 ± 6.7	42.1 ± 14.3	NS
2 Weeks	48.7 ± 7.4	45.5 ± 8.4	NS
SF-12 Social Function			
Baseline	37.4 ± 12.1	26.3 ± 10.1	NS
One Week	41.5 ± 13.7	33.0 ± 15.2	NS
2 Weeks	40.4 ± 10.9	31.9 ± 13.5	NS
SF-12 Mental Health			
Baseline	42.0 ± 12.2	32.7 ± 10.4	NS
One Week	46.9 ± 14.2	38.1 ± 12.9	NS
2 Weeks	45.1 ± 11.8	36.8 ± 15.3	NS
SF-12 Role Emotional			
Baseline	33.1 ± 17.2	28.7 ± 14.9	NS
One Week	39.9 ± 14.1	29.3 ± 16.3	NS
2 Weeks	37.6 ± 12.1	32.5 ± 15.8	NS
SF-12 Mental Component			
Baseline	44.2 ± 13.8	33.7 ± 11.4	NS
One Week	49.3 ± 15.3	38.4 ± 13.7	NS
2 Weeks	48.1 ± 10.9	38.8 ± 14.2	NS
SF-12 Physical Component			
Baseline	30.5 ± 4.4	30.3 ± 8.1	NS
One Week	32.0 ± 6.2	30.9 ± 7.7	NS
2 Weeks	31.5 ± 5.0	32.9 ± 8.6	NS

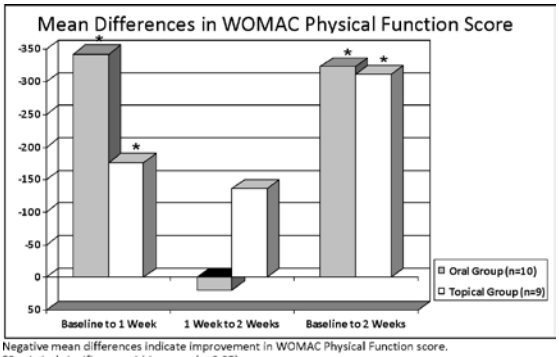
Mean ± SD. NS=not significant ($p \geq 0.05$). WOMAC= Western Ontario and McMaster Universities Osteoarthritis Index. Maximum score for pain, stiffness, and physical function categories is 500, 200, and 1400 respectively. SF-12=Short Form 12. Maximum score for all sub-categories is 100.



Negative mean differences indicate improvement in WOMAC Pain score.
*Statistical significance within group (p<0.05)



Negative mean differences indicate improvement in WOMAC Stiffness score.
*Statistical significance within group (p<0.05)



Negative mean differences indicate improvement in WOMAC Physical Function score.
*Statistical significance within group (p<0.05)

Fig. 2. *Mean Differences in WOMAC Scores.*

to significance. There were no remarkable changes in any SF-12v2 subcategory. The Bodily Pain and Vitality categories showed consistent improvement between intervals, but not to statistical significance. Most other categories (physical function, physical role, social function, mental health, emotional role, mental component summary, and physical component summary) exhibited improvement from baseline to one week and baseline to 2 weeks, but actually declined from one to 2 weeks. Patient satisfaction analysis showed no significant improvement though mean scores from baseline increased favorably during all intervals.

Within the topical ibuprofen group, significant improvements were present in WOMAC Pain scores from baseline to 2 weeks ($P = 0.036$), WOMAC Stiffness scores from baseline to one week ($P = 0.046$) and baseline to 2 weeks ($P = 0.05$), and WOMAC Physical Function scores from baseline to one week ($P = 0.047$) and baseline to 2 weeks ($P = 0.028$). There were consistent, but not significant, improvements in WOMAC Pain, Stiffness, and Physical Function scores from one to 2 weeks in the topical ibuprofen group.

Similar to the oral treatment group, the topical group did not experience any statistically significant improvement of SF-12v2 scores despite overall improved scores in physical function, physical role, bodily pain, vitality, emotional role, mental component summary and physical component summary in all intervals. Certain categories (social function and mental health) showed decreased scores from one week to 2 weeks.

Patient satisfaction scores in the topical group improved from baseline to one week ($P = 0.016$) and baseline to 2 weeks ($P = 0.014$).

Discussion

The subjects in this pilot study benefitted from treatment intervention comparable to other investigations of oral versus topical ibuprofen. The notable Underwood et al (28) trial, a randomized control topical or oral ibuprofen study involving 282 knee pain participants, reported equivalent clinical outcomes between groups for over one year with an absence of clear change in WOMAC scores between baseline and follow-up with both administrations. In our analysis, it is of interest to note that the topical ibuprofen group experienced within-group improvement of WOMAC outcomes not experienced by the oral group. Though it is to be expected that some of the pain relief experienced by the topical group could be attributed to the potential benefits of massaging, several studies dem-

Table 3. *Mean differences in WOMAC and SF-12 Scores at baseline, one week, and 2 weeks*

	Oral Group (n=10)	Topical Group (n=9)	*P*-value
WOMAC Pain			
Baseline to One Week	-66.4 (-167.2 to 34.4)	-20.3 (-75.0 to 34.4)	NS
One Week to 2 Weeks	-17.9 (-95.8 to 60.0)	-62.2 (-130.2 to 5.7)	NS
Baseline to 2 Weeks	-84.3 (-177.9 to 9.3)	-82.6 (-158.3 to -6.8)*	NS
WOMAC Stiffness			
Baseline to One Week	-23.4 (-48.4 to 1.6)	-25.3 (-50.0 to -0.6)*	NS
One Week to 2 Weeks	-2.5 (-41.0 to 36.0)	-22.4 (-75.2 to 30.3)	NS
Baseline to 2 Weeks	-25.9 (-53.6 to 1.8)	-47.8 (-95.7 to 0.1)*	NS
WOMAC Physical Function			
Baseline to One Week	-342.6 (-638.1 to -47.1)*	-175.9 (-348.6 to -3.2)*	NS
One Week to 2 Weeks	19.4 (-249.8 to 288.6)	-136.2 (-382.4 to 110.0)	NS
Baseline to 2 Weeks	-323.2 (-637.2 to -9.2)*	-312.1 (-580.5 to -43.7)*	NS
SF-12 General Health			
Baseline to One Week	-2.6 (-6.6 to 1.4)	0.0†	NS
One Week to 2 Weeks	0.7 (-4.4 to 5.7)	0.0†	NS
Baseline to 2 Weeks	-1.9 (-7.5 to 3.6)	0.0†	NS
SF-12 Physical Function			
Baseline to One Week	3.4 (-0.9 to 7.7)	1.9 (-4.5 to 8.3)	NS
One Week to 2 Weeks	-1.7 (-4.3 to 0.9)	1.0 (-6.0 to 7.9)	NS
Baseline to 2 Weeks	1.7 (-2.2 to 5.6)	2.9 (-5.2 to 11.0)	NS
SF-12 Role Physical			
Baseline to One Week	5.1 (-1.6 to 11.8)	0.0 (-3.5 to 3.6)	NS
One Week to 2 Weeks	-3.2 (-8.9 to 2.4)	3.1 (-4.4 to 10.6)	NS
Baseline to 2 Weeks	1.8 (-1.3 to 5.0)	3.1 (-3.1 to 9.2)	NS
SF-12 Bodily Pain			
Baseline to One Week	4.1 (-5.1 to 13.3)	3.4 (-2.1 to 8.9)	NS
One Week to 2 Weeks	1.0 (-5.4 to 7.4)	2.3 (-6.3 to 10.8)	NS
Baseline to 2 Weeks	5.1 (-3.5 to 13.7)	5.7 (-3.2 to 14.5)	NS
SF-12 Vitality			
Baseline to One Week	2.0 (-2.5 to 6.6)	3.4 (-6.9 to 13.6)	NS
One Week to 2 Weeks	1.0 (-3.1 to 5.1)	3.4 (-2.1 to 8.8)	NS
Baseline to 2 Weeks	3.0 (-2.9 to 8.9)	6.7 (0.0 to 13.4)	NS
SF-12 Social Function			
Baseline to One Week	4.0 (-6.8 to 14.9)	6.7 (-1.9 to 15.4)	NS
One Week to 2 Weeks	-1.0 (-7.3 to 5.3)	-1.1 (-9.3 to 7.1)	NS
Baseline to 2 Weeks	3.0 (-4.6 to 10.7)	5.6 (-3.2 to 14.4)	NS
SF-12 Mental Health			
Baseline to One Week	4.9 (-1.9 to 11.6)	5.4 (-3.8 to 14.6)	NS
One Week to 2 Weeks	-1.8 (-5.4 to 1.8)	-1.4 (-7.4 to 4.7)	NS
Baseline to 2 Weeks	3.1 (-2.5 to 8.6)	4.1 (-6.9 to 15)	NS
SF-12 Role Emotional			
Baseline to One Week	6.7 (-4.9 to 18.3)	0.6 (-15.4 to 16.6)	NS
One Week to 2 Weeks	-2.2 (-10.3 to 5.8)	3.1 (-7.5 to 13.7)	NS
Baseline to 2 Weeks	4.5 (-2.0 to 11.0)	3.7 (-15.0 to 22.5)	NS
SF-12 Mental Component Score			
Baseline to One Week	5.1 (-4.3 to 14.4)	4.7 (-7.4 to 16.9)	NS
One Week to 2 Weeks	-1.2 (-6.4 to 4.0)	0.3 (-3.0 to 3.6)	NS
Baseline to 2 Weeks	3.9 (-2.0 to 9.7)	5.1 (-7.7 to 17.8)	NS
SF-12 Physical Component Score			
Baseline to One Week	1.5 (-1.9 to 5.0)	0.6 (-3.2 to 4.4)	NS
One Week to 2 Weeks	-0.5 (-3.6 to 2.6)	2.0 (-1.9 to 5.9)	NS
Baseline to 2 Weeks	1.1 (-2.8 to 4.9)	2.6 (-0.9 to 6.2)	NS

Mean (95% Confidence Interval).
Negative mean differences in WOMAC scores indicate improvement in corresponding subcategory.
Positive mean differences in SF-12 scores indicate improvement in corresponding subcategory.
*Statistical significance within group ($p < 0.05$), †No Confidence Interval secondary to constant values.

Table 4. *Patient satisfaction and treatment convenience at baseline, one week and 2 weeks*

	Oral Group (n=10)	Topical Group (n=9)	*P*-value
Patient Satisfaction with Treatment			
Baseline (prior to study treatment)	3.0 ± 2.5	2.6 ± 1.7	NS
One Week	5.5 ± 3.3	6.6 ± 3	NS
2 Weeks	5.6 ± 3.2	6.3 ± 2.6	NS
Study Treatment Convenience			
One Week	7.5 ± 2.5	6.2 ± 3.5	NS
2 Weeks	8.2 ± 2.0	6.7 ± 3.2	NS
Would you undergo this study treatment again?			
One Week			
Yes	6	7	NS
No	1	1	
Maybe	3	1	
2 Weeks			
Yes	5	5	NS
No	2	1	
Maybe	3	3	

Mean ± SD.
Maximum score for patient satisfaction and treatment convenience is 10.

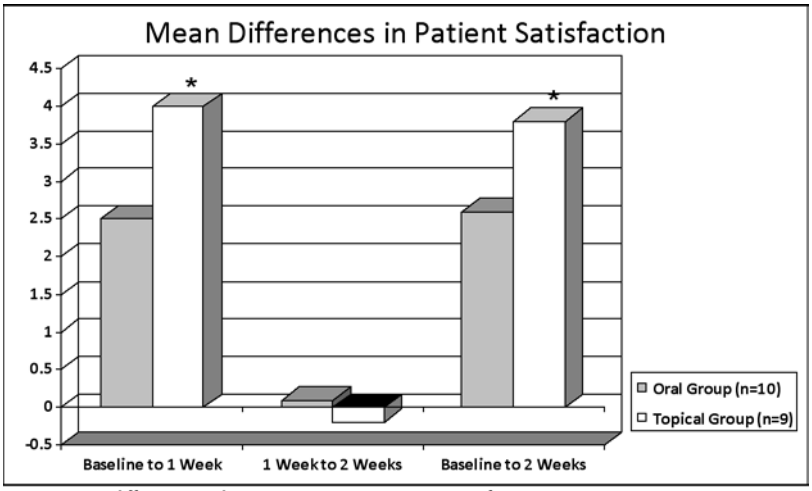


Fig. 3. *Mean Difference in Patient Satisfaction Scores.*

Table 5. *Mean differences in patient satisfaction at baseline, one week, and 2 weeks*

	Oral Group (n=10)	Topical Group (n=9)	*P*-value
Patient Satisfaction with Treatment			
Baseline to One Week	2.5 (-1.0 to 5.1)	4.0 (0.9 to 7.1)*	NS
One Week to 2 Weeks	0.1 (-1.0 to 1.2)	-0.2 (-2.4 to 1.9)	NS
Baseline to 2 Weeks	2.6 (0.0 to 5.2)	3.8 (1.0 to 6.6)*	NS

Mean (95% Confidence Interval).
Positive mean differences in scores indicate improvement in patient satisfaction.
*Statistical significance within group (p<0.05).

onstrate the efficacy of topical NSAIDs over placebo (22,24-25,34). A meta-analysis of topical NSAIDs in the treatment of chronic musculoskeletal pain reported the active topical treatments fared significantly better than placebo in a review of 14 trials involving more than 1,500 patients (26). The mean placebo response rate was 26% compared to the mean treatment response rate of 48%. This suggests that the active treatment provides pain relief beyond the therapeutic effects of massaging.

Intriguingly, the improvement in patients' conditions was quantifiable by the WOMAC survey while SF-12v2 scores for both groups did not capture the same changes within the groups. Similarly, Davies et al (35) in a trial comparing WOMAC and SF-36 scores in patients presenting with hip and knee OA demonstrated that the changes in SF-12v2 scoring were of a lesser magnitude than WOMAC scoring.

The efficiency of the transdermal delivery system is worthy of note as the total daily dose of 320 mg topical ibuprofen represented only a small fraction of the oral dose, yet produced similar clinical outcomes. In a small study with patients with knee disorders, Dominkus et al (36) were able to demonstrate "that the concentrations in tissues directly under the site of topical application lie in the same order of magnitude as those found after peroral treatment." Patients were given oral (2 x 600 mg daily) and topical (3 x 375 mg daily) ibuprofen and significantly higher concentrations of ibuprofen in the subcutis was observed after topical application than oral administration. A higher concentration of ibuprofen in the muscle was also reported in the topical group, but not to significance. Tegeder et al (37) were able to demonstrate in a small crossover study comparing subjects receiving equivalent doses of oral and topical formulations that greater concentrations of ibuprofen were found in the subcutaneous tissue in the topical administration and almost equal peak muscle concentrations were found between the 2 groups while the relative systemic bioavailability of the topical group was 0.6% . These reports might suggest that higher ibuprofen levels present in tissue might have provided a degree of pain relief seen in our treatment population.

This study was designed to evaluate the efficacy of topical and oral ibuprofen when incorporated into the pain management regimen of a typical patient. This often necessitates a multi-modal approach. While the investigation assessed if the addition of topical ibuprofen gel aided in pain reduction, it did not presume to replace ongoing opioid and other pain medication treatment, excluding other NSAIDs. The inclusion of a patient diary tracking other medications taken for pain management would certainly have been of value.

Similarly, in attempting to incorporate topical ibuprofen into the daily routine of patients, we did not formally standardize the amount of gel applied. Though an application card was given to patients to encourage equal amounts of ibuprofen gel, perhaps a syringe or other application aid to measure the quantity of gel would have been appropriate. It should be said that in practical use of the topical gel, the typical patient could be inconvenienced if forced to carry a measuring device at all times.

While there is evidence that topical ibuprofen benefits patients with osteoarthritis (25,27,28), there is scarce literature pertaining to its use in chronic knee pain without a clinical diagnosis of OA. The aim of our investigation was to conduct a preliminary examination of knee pain in the chronic pain population of a pain management practice. Thus, our pilot study did not necessitate a large sample, and treatment effects might be exaggerated due to the small sample size.

Our observations reaffirm the current findings regarding topical ibuprofen and demonstrate efficacy in the broad patient population seen in pain management practices. Additionally, when considering the low ibuprofen blood levels associated with topical application and its implications in avoiding both systemic side effects and adverse drug interactions (36,38,39), concomitant cardioprotective aspirin use in particular (40-51), topical ibuprofen appears to be an efficacious and safe alternative in chronic knee pain treatment. A future larger study of topical ibuprofen with a more extensive follow-up period would be valuable.

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