Original Article
A randomized clinical trial assessment of nonsteroidal anti-inflammatory drugs and Chinese bone setting manipulation therapy in knee osteoarthritis

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Received July 17, 2016; Accepted September 5, 2016; Epub March 15, 2017; Published March 30, 2017

Abstract: Nonsteroidal anti-inflammatory drugs (NSAIDs) have proven to be an effective analgesic in treating knee osteoarthritis (OA). Bone setting manipulation is a representative traditional Chinese manipulation approach in mediating OA. In this work, a randomized controlled trial was conducted to compare the short-term efficacy of NSAIDs therapy (DT) to Chinese bone setting manipulation therapy (MT) for patients with knee OA. Patient subjects were voluntarily enrolled and randomly assigned to either MT group receiving twice weekly sessions of manipulation or DT group receiving medical analgesia. Outcome measures were included the patient-based self-report measures using visual analogue scale (VAS), Western Ontario and McMaster Universities Index of Osteoarthritis (WOMAC) and the performance-based measures using the timed 5-repetition sit-to-stand test and 15 m walk test, the changes were assessed from baseline to 3-week and 6-week follow-up. The both groups demonstrated significant improvements in all the outcome measures in the short-term follow-up (P<0.001). MT group achieved significantly greater improvement than DT group in the timed 5-repetition sit-to-stand test (P=0.0058) and 15 m walk test (P=0.0072) at 6-week assessment. There was no significant difference to be revealed in any of the other measures between the groups (P > 0.05). In summary, the bone setting manipulation seems to be as efficacious as NSAIDs in providing pain relief, function improvement and significantly better in improvement of muscles strength and gait speed in a short term, it may be a reasonable alternative to NSAIDs for patients with knee OA.

Keywords: Manipulation, non-steroidal anti-inflammatory drugs (nsaids), knee osteoarthritis, randomized controlled trial

Introduction
Knee osteoarthritis (OA) is a common chronic degenerative joint disorder that leads to poor quality of life [1]. Individuals with knee OA usually suffer from knee pain, joint stiffness, decreased muscle strength, proprioception deficiency, and limited abilities in walk, stand up, climb stairs, and even increased susceptibility to fall [1-3]. As the leading cause of musculoskeletal handicap in the world (Pitsillides and Beier, 2011), treatment over OA cost millions of dollars [4].

Nonsteroidal anti-inflammatory drugs (NSAIDs) were recommended by the Osteoarthritis Research Society International (OARSI) to treat knee and hip OA [5-7]. However, the use may be restricted by adverse effects, such as cardiovascular, gastrointestinal effects including serious occurrences of bleeding and renal events [8, 9]. In addition, the potential toxic effects of drugs used commonly to treat OA have been especially newsworthy of late [10, 11].

Lately, Non-pharmacological, non-surgical interventions, primarily exercise therapy and more recently manipulation therapy, are recommended as the first line of treatment for hip and knee OA [12, 13]. Extensive progress made in the understanding of efficacy of manipulation has led to growing acceptance of this treatment as a potentially curative therapy for knee OA [14-16]. It is also demonstrated manipulation therapy is useful for the management of knee OA [15, 16]. From the societal perspective, manipulation is generally the most cost...
Comparing nonsteroidal drugs versus Chinese bone setting manipulation in osteoarthritis effective treatment [14, 17]. In the view of this, to develop more effective manual treatment protocols and to better understand the underlying mechanisms of such therapies for OA are warranted.

There are many schools on the manual therapy such as Swedish massage, myofascial, neuromuscular, Chinese, other Asian, medical, osteopathic, or naturopathic manipulative therapies, massage practices are heterogeneous with procedures utilized from these different schools of massage incorporating a variety of techniques [18]. Bone setting manipulation (BSM) is a popular mobilisation treatment especially for musculoskeletal conditions. Patients reported good pain reduction and a relaxing effect as the most positive aspects of BSM [19]. Several studies have evaluated and confirmed the clinical effectiveness of BSM on patients with back pain [20-22].

However, several theoretical and practical aspects of Chinese manipulation distinguish it from occidental manipulation, the concepts of channels and collaterals are key elements in the theory of Chinese manipulation [23]. Soft tissue relaxation and bone setting are the two main components of Chinese BSM: using massage techniques and acupressure to relax the soft tissue and to clear the channels, and utilizing bone setting techniques to restore joint alignment [24-26].

To our knowledge, there is not enough convincing evidence on whether the Chinese BSM is as efficacious as NSAIDs in treating knee OA. Given the limitations and potential adverse events of NSAIDs, it is necessary to evaluate the effectiveness of BSM in management knee OA. The purpose of this study was to compare efficacy of NSAIDs therapy to Chinese BSM therapy on pain, function, muscular strength and gait speed in patients with knee OA.

Participants

Subjects eligible for the study were males or females diagnosed with symptomatic OA. The disease was diagnosed according to the American College of Rheumatology criteria. Participants also have a radiographic inclusion diagnosis with Kellgren Lawrence (K/L) grade of II to III (mild to moderate), which was made by an experienced orthopedic surgeon based on X-ray findings using the standard classification [27, 28].

Participants were excluded if they met the following exclusion criteria: allergy to NSAIDs; the presence of other musculoskeletal problems associated with the knee joint, such as rheumatoid arthritis, inflammatory joint disease; cancer, AIDS or other serious medical conditions; signs or history of gastrointestinal ulcer or bleeding, cardiovascular disease, kidney or liver failure; use of oral corticosteroids within the past 4 weeks; intraarticular hyaluronate within the previous 6 months; significant injury to the knee within the previous 6 months [29, 30].

Randomization

Participants were from the outpatient clinic of the Department of Orthopaedic and Trauma of Xinhua Hospital Affiliated to Shanghai Jiaotong University Medical College Hospital from December 2012 to May 2013. The patients voluntarily enrolled in the tests and were randomly assigned to two groups (both groups consisted of 40 patients): Chinese bone setting manipulation group (MT group) and NSAIDs therapy group (DT group). The allocation was used a computer-generated random table in order to ensure that there were no relevant differences among the study groups with respect to baseline characteristics such as age, sex, etc. The enrolled patients were notified with the tests and signed agreement over these tests.

Interventions

Chinese bone setting manipulation therapy inventions: The MT group protocol for the study intervention consisted of soft tissue relaxation
Comparing nonsteroidal drugs versus Chinese bone setting manipulation in osteoarthritis

Manipulation sessions were 20 minutes long, twice weekly for 6 weeks. Participants were positioned comfortably in supine or prone for the full course of treatment, an experienced trained manual therapist operated the following protocol with varied force according to patient’s response: 1. Soft tissue relaxation step: subject lay supine or prone, the manual therapist used the techniques including rolling, kneading and plucking to act on the lower limb muscles such as quadriceps, hamstring, gastrocnemius muscles and the pressure points around the patella and joint; then pushed the patella back and forth, up and down with gentle force to remiss the synarthrophysis of patellofemoral joint; 2. Bone setting step: subject lay supine, therapist given passive flexion and extension activities to subject and then increased the extent of buckling and hyperextension gradually; bended the knees with knee inward turning, outward turning passive activity; extended the knees with lower limb longitudinal traction.

NSAIDs therapy inventions: In the DT group, participants were given an oral dose of the following drug for 6 weeks: diclofenac slow release 75 mg/once day (Novartis Pharmaceuticals UK Ltd, Camberley, UK), Upset stomach, if any, in the process of treatment, omeprazole and lansoprazole were taken to protect the stomach.

Sample size calculation

As previously described, the minimal clinical important difference to be detected in OA trials is a change of 17% on WOMAC score (White et al., 2010) and a change of 18 mm on VAS score (Bellamy et al., 2005). To detect a clinically relevant difference between each group, 80 subjects are needed with the power of 0.8, alpha level of 0.05. Regarding the effects of the timed sit-to-stand test and 15 m walk test, we were unable to define a clinically significant reduction or to determine a power calculation. In this light, these results could only be labeled as exploratory.

Outcome measures

Outcome measures were included the patient-based self-report measures using visual analogue scale (VAS), Western Ontario and McMaster Universities Index of Osteoarthritis (WOMAC) and the performance-based measures using the timed 15 m walk test, the timed 5-repetition sit-to-stand test. All measurements were collected at baseline and 3-week and 6-week follow-up in both groups. All of the samples were evaluated by an operator who was blinded to the experimental design.

VAS pain score

A 100-mm visual analog scale (0 mm = no pain, 100 mm = worst pain ever), a valid and reliable measure for pain intensity [31, 32]. The experiments were performed at baseline and 3-week, 6-week follow-up, with difference scores used for analysis. The participant draws a line to designate their level of pain at interview.

WOMAC assessment

The Western Ontario and McMaster Osteoarthritis Index (WOMAC) is a self-administered 3-dimensional questionnaire that assesses pain (5 items), stiffness (2 items), and physical functional disability (17 items) in patients with knee and hip OA [33-35]. This disease-specific index has shown excellent validity, reliability and repeatability in numerous studies [33-35]. A negative change in WOMAC scores from baseline indicates improvement of symptoms and limitation whereas a positive change indicates deterioration of symptoms and limitation.

The timed 15 m walk test

The 15 m walk test used to assess physical function in people with hip or knee OA [36]. The operator administered the walk test using a specific measure protocol according to Motyl’s study. All participants who wore comfortable, soft-soled shoes are conducted at a self-selected pace to walk a distance of 15 meters without any walking aids, the investigator recorded the walking time with a stopwatch.

The timed 5-repetition sit-to-stand test: The sit-to-stand test, a more biomechanical instrument identifying how the knee function of the patient is affected is considered to have more practicability and maneuverability [37]. The task will be performed on a standard height chair (at 43 cm in height and 47.5 cm in depth) without a hand support [38, 39]. The test measured the time taken to complete 5 repetitions of the sit-to-stand maneuver.
Safety

A weekly questionnaire was used to monitor clinical adverse events and changes in health status. And adverse drug reactions were also monitored during the course of oral drugs.

Statistical analysis

Statistical analysis was performed using SAS statistical software (version 8.2; SAS Institute, Cary, NC). A $P$ value $<$0.05 was considered to be statistically significant. Descriptive statistics were checked for normality to justify parametric methods. The mean, standard deviation and range were reported for the continuous variables and the analysis used the student $t$-test, whereas the counts described the categorical variables and the analysis used the chi-square test. The paired $t$ test was used to determine differences within groups from baseline to follow-up examination, and repeated measures analysis of variance was used for
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**Results**

**Enrolment and follow-up of participants**

A total of 80 patients were enrolled as participants in this study. Forty patients were randomly allocated to each group. Of these, 74 patients completed the trial (39 in the MT group, 35 in the DT group). Of the 6 patients who withdrew from the study, 3 were lost to follow-up for increased knee pain, 1 for job business, 1 refused to continue drugs intervention for unknown reason. The flow of study participants is shown in Figure 1.

**Demographic and baseline characteristics**

Demographic and baseline characteristics of all subjects were shown in Table 1. No statistical differences were found between the MT group and the DT group regarding the demographic characteristics (sex, age, height, weight, BMI) and disease characteristics (K-L grade, duration of OA). The two groups were also similar with regard to baseline clinical evaluation.

As is shown in Table 2, both MT group and DT group achieved significant decrease in VAS score in 3 weeks follow-up (P<0.001) and up to 6 weeks follow-up (P<0.001). No significant difference was observed between the MT group and DT group in the improvement of VAS pain score (P > 0.05) in 3 weeks time points and in 6 weeks time points (P > 0.05), but the magnitude of the VAS score changes seen in DT group was greater than changes seen in MT group (Figure 2A). Significant improvement was observed in the WOMAC total score and in each domain (pain, stiffness, and functionality) from baseline to 3 weeks and 6 weeks follow-up in both groups (P<0.001) (Table 2). Although almost no statistically significant differences between the MT groups and DT group in the changes. The 95% confidence intervals were determined for changes from baseline.

### Table 1. Baseline Characteristics of the cohort

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>MT group (n=40)</th>
<th>DT group (n=40)</th>
<th>Total (n=80)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic Characteristic</strong></td>
<td></td>
<td></td>
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<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9 (22.5%)</td>
<td>8 (20.0%)</td>
<td>17 (21.25%)</td>
<td>0.7846**</td>
</tr>
<tr>
<td>Female</td>
<td>31 (77.7%)</td>
<td>32 (80.0%)</td>
<td>63 (78.75%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.30 (7.36)</td>
<td>61.90 (6.74)</td>
<td>60.0 (7.13)</td>
<td>0.1043*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>65.08 (10.06)</td>
<td>67.91 (9.70)</td>
<td>66.49 (9.92)</td>
<td>0.2029*</td>
</tr>
<tr>
<td>Height (meters)</td>
<td>161.26 (7.04)</td>
<td>161.36 (6.57)</td>
<td>161.31 (6.77)</td>
<td>0.9478*</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.97 (3.16)</td>
<td>26.07 (3.42)</td>
<td>25.52 (3.32)</td>
<td>0.135</td>
</tr>
<tr>
<td><strong>Disease Characteristic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of OA (month)</td>
<td>43.35 (49.83)</td>
<td>44.96 (67.47)</td>
<td>44.15 (58.94)</td>
<td>0.9038*</td>
</tr>
<tr>
<td>Kellgren-Lawrence grade</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Grade II (mild), n (%)</td>
<td>11 (27.5%)</td>
<td>15 (37.5%)</td>
<td>26 (32.5%)</td>
<td>0.4369**</td>
</tr>
<tr>
<td>Grade III (moderate), n (%)</td>
<td>29 (72.5%)</td>
<td>25 (62.5%)</td>
<td>64 (64.5%)</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline Clinical Evaluation</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>VAS pain score (mm)</td>
<td>54.88 (15.90)</td>
<td>52.43 (17.15)</td>
<td>53.650 (16.48)</td>
<td>0.5096*</td>
</tr>
<tr>
<td>WOMAC score (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain (range 0-500 mm)</td>
<td>124.23. (64.35)</td>
<td>142.25 (63.30)</td>
<td>133.21 (64.14)</td>
<td>0.2104*</td>
</tr>
<tr>
<td>Stiffness (range 0-200 mm)</td>
<td>63.09 (37.91)</td>
<td>64.51 (39.83)</td>
<td>63.79 (38.64)</td>
<td>0.8714*</td>
</tr>
<tr>
<td>Functionality (range 0-1700 mm)</td>
<td>344.63 (160.00)</td>
<td>352.98 (167.89)</td>
<td>348.80 (163.01)</td>
<td>0.8205*</td>
</tr>
<tr>
<td>Total (range 0-2400 mm)</td>
<td>533.06 (233.08)</td>
<td>559.73 (223.81)</td>
<td>546.39 (227.44)</td>
<td>0.6033*</td>
</tr>
<tr>
<td>Time to sit-to-stand (seconds)</td>
<td>15.93 (4.20)</td>
<td>15.50 (4.61)</td>
<td>15.72 (4.39)</td>
<td>0.6642*</td>
</tr>
<tr>
<td>Time to walk 15 m (seconds)</td>
<td>16.03 (3.17)</td>
<td>15.52 (3.15)</td>
<td>15.77 (3.15)</td>
<td>0.4752*</td>
</tr>
</tbody>
</table>

Abbreviations: BMI = body mass index (calculated as weight in kilograms divided by height in meters squared); OA = osteoarthritis; VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; s = seconds; m = meters. Data were given as mean (SD) except where noted. *denotes that P values for the differences between MT group and DT group were obtained from 2-tailed t test. **denotes that P values were obtained from x² test.
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At 3-week follow-up

<table>
<thead>
<tr>
<th>MT group (n=39)</th>
<th>DT group (n=37)</th>
<th>P values</th>
<th>MT group (n=38)</th>
<th>DT group (n=35)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VAS pain score, Mean (SD), 95% CI, (mm)</strong></td>
<td></td>
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</tr>
<tr>
<td>31.64 (19.19)</td>
<td>24.87 (14.98)</td>
<td>&lt;0.001</td>
<td>16.790 (8.87)</td>
<td>12.17 (9.91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(25.16 to 38.12)</td>
<td>(19.87 to 29.86)</td>
<td></td>
<td>(13.88 to 19.70)</td>
<td>(8.77 to 15.58)</td>
<td></td>
</tr>
<tr>
<td><strong>WOMAC score, Mean (SD), 95% CI, (mm)</strong></td>
<td></td>
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</tr>
<tr>
<td>Pain</td>
<td></td>
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<tr>
<td>67.62 (47.47)</td>
<td>73.68 (60.29)</td>
<td>&lt;0.001</td>
<td>44.97 (37.03)</td>
<td>54.69 (37.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(52.22 to 83.00)</td>
<td>(53.57 to 93.78)</td>
<td></td>
<td>(32.80 to 57.15)</td>
<td>(41.78 to 67.59)</td>
<td></td>
</tr>
<tr>
<td>Stiffness</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>38.82 (27.57)</td>
<td>42.95 (26.14)</td>
<td>&lt;0.001</td>
<td>27.21 (19.84)</td>
<td>35.26 (24.66)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(29.88 to 47.76)</td>
<td>(34.23 to 51.66)</td>
<td></td>
<td>(20.69 to 33.73)</td>
<td>(26.79 to 43.73)</td>
<td></td>
</tr>
<tr>
<td>Functionality</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>205.39 (141.92)</td>
<td>219.65 (127.41)</td>
<td>&lt;0.001</td>
<td>129.61 (102.06)</td>
<td>145.91 (79.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(159.38 to 251.39)</td>
<td>(177.17 to 262.13)</td>
<td></td>
<td>(96.03 to 163.18)</td>
<td>(118.51 to 175.33)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
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<tr>
<td>418.87 (257.64)</td>
<td>434.63 (210.52)</td>
<td>&lt;0.001</td>
<td>274.32 (180.43)</td>
<td>325.80 (146.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(335.36 to 502.39)</td>
<td>(362.31 to 506.94)</td>
<td></td>
<td>(215.01 to 333.62)</td>
<td>(275.62 to 375.98)</td>
<td></td>
</tr>
<tr>
<td>Time to sit-to-stand, Mean (SD), 95% CI, (s)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>12.31 (1.72)</td>
<td>14.00 (2.72)</td>
<td>&lt;0.001</td>
<td>10.50 (1.84)</td>
<td>13.25 (2.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(11.75 to 12.87)</td>
<td>(13.09 to 14.91)</td>
<td></td>
<td>(19.89 to 11.11)</td>
<td>(12.26 to 14.26)</td>
<td></td>
</tr>
<tr>
<td>Time to walk 15 m, Mean (SD), 95% CI, (s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.33 (2.70)</td>
<td>13.84 (1.99)</td>
<td>&lt;0.001</td>
<td>11.74 (2.27)</td>
<td>13.46 (1.99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(12.46 to 14.21)</td>
<td>(13.17 to 14.50)</td>
<td></td>
<td>(10.99 to 12.48)</td>
<td>(12.77 to 14.14)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; CI = confidence interval; s = seconds; m = meters. Data were given as mean (SD), 95% CI. P values were for the difference within group from baseline to 3-week and 6-week follow-up.

A similar pattern was observed in the performance-based tests. Both groups demonstrated decreases in the timed 5-repetition sit-to-stand test at 3 weeks (P<0.001) and 6 weeks follow-up (P<0.001) compared to baseline, as did the decreases in the timed 15 m walk test at 3 weeks (P<0.001) and 6 weeks follow-up (P<0.001) compared to baseline (Table 2). At the 3-week assessment, neither in the sit-to-stand test nor the 15 m walk test, no significant differences were revealed between the groups (P > 0.05). However, statistically significant differences were observed between the groups at the 6 weeks assessment in the timed 5-repetition sit-to-stand test (P=0.0058) (Figure 2C) and in the timed 15 m walk test (P=0.0072) (Figure 2D).

Subject were instructed to keep diaries to report adverse events. There were 1 patient in the MT group and 3 patients in the DT group.
reported increased knee pain and refused to return for the follow-up assessment. No other serious adverse event was noticed.

Discussion

The main findings of this study demonstrated that manual therapy using the specific Chinese bone setting technique yielded better results in the timed 5-repetition sit-to-stand test and 15 m walk test, and that it was as efficacious as NSAIDs treatment in the improvement of VAS pain score and WOMAC score in patients with symptomatic knee OA in a short term follow-up.

There are different techniques of Chinese manipulation which are commonly named according to the characteristics of the specific technique or the name of the developers. In general, these manipulation characteristics mainly include relaxation, acupuncture, tendon, pushing skeletal, joint activities, etc. The putative mechanisms of manipulation as related to treating osteoarthritis (relaxation, reducing inflammation, improving flexibility) were considered when designing the protocol [36]. The manipulation technique for this study intervention from Chinese schools was intended to improve musculoskeletal function and pain by addressing not only the target joint (bone setting) but also the quality of associated periaricular soft tissues such as muscles of lower limb structures (soft tissue relaxation). Given the contraindications and potential adverse events of NSAIDs, there was very low quality evidence of this manipulation being a reasonable alternative to NSAIDs medication for patients with knee OA.

The pathological features of knee OA such as progressive degeneration of articular cartilage, sclerosis of subchondral bone, and osteophyte formation can result in pain, impaired mobility, reduced muscle strength, limitation activities of daily living and reduced quality of life. Subjects with knee OA have weaker quadriceps muscles than do subjects without OA (Palmieri-Smith et al., 2010). Slower gait speed is another functional impairment caused by knee OA [20, 21].

The 5-repetition sit-to-stand test and 15 m walk test were used as outcome measures for functional lower limb muscle strength and gait speed [12, 13]. We applied these two performance-based tests combining two patient-based self-report measures (VAS score and WOMAC score) to assess the improvement with two different interventions.

Subjects with knee OA receiving this twice weekly Chinese manual therapy protocol showed immediate improvements in pain, function, sit-to-stand and walking time. Our results are consistent with these prior studies that manual therapy demonstrated significant improvements in level of VAS score, WOMAC score (pain, stiffness, functional disability domains) and walking time [33, 36].

Pain relief is multifactorial and complicated. Initiation of OA was correlated with insufficient blood flow to the subchondral bone that may be associated with delivery of nutrients and gas exchange with the articular cartilage [20, 21], while manipulation increased blood circulation to the muscles promoting gas exchange and delivery of nutrients and removal of waste products, this may be one of mechanisms that manipulation is theorized to work through to relieve pain [40]. In addition, another mechanisms of manipulation to pain relief include immediate hypoalgesia, influenced pain threshold through endorphin release [41].

As 5-repetition sit-to-stand test and 15 m walk test stand for functional lower limb muscle strength and gait speed subjects receiving the manipulation shown better improvement in the performance-based tests compared with those receiving the medical analgesia, we may conclude that this manual protocol has better improvement on muscle strength and gait speed [18, 27].

Some potential proposed mechanisms of manipulation to muscle strength and gait speed include improving the tone of supportive musculature by decreasing muscle strain and balancing muscle tension across the joint, positive mechanical changes in muscles, increased joint flexibility and proprioception, neurophysiological effects and a psychological influence [22].

Local inflammation, the major source of pain, is directly responsible for several clinical symptoms and reflects the progression of OA [42]. NSAIDs have analgesic, antipyretic and anti-
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Inflammatory properties and are extensively prescribed for treating the signs and symptoms of OA.

In our study, subjects receiving NSAIDs treatment improved in WOMAC total scores 44%-50% change from baseline which was considered highly clinically significant according to the minimal clinically important differences (MCID) of 17% change from baseline [17]. This is in agreement with recent studies showing that NSAIDs are able to improve WOMAC scores in patients with knee OA. The improvement in the total WOMAC score is closely related to the decrease in the cytokine concentration [42].

Additionally, we also noted the significant decrease in time to 15 m walk test and 5-repetition sit-to-stand. As pain can lead to limitation of the patients’ life abilities such as the ability to stand up, walk, and climb stairs, and dependency in daily living activities [43]. We speculate that NSAIDs reduced the pain of OA, and the pain relief led to the improvement in the performance-based tests. However, NSAIDs can’t address the underlying degenerative disorder in addition to the potential adverse effects and limitations. The bone setting manipulation seems to be a viable option [44]. However, we noticed that there were some limitations of the current study. The long-term efficacy of the bone setting manipulation was unclear. Therefore future studies about long-term follow-up will be needed; This trial failed to keep patients blinded to the therapy group due to the nature of interventions; The intervention parameters (frequency, duration, techniques and number of sessions) of the manipulation for given population would need to be optimized; In addition, this trial only included a single intervention, the combination therapy-manipulation and medical analgesia compared with MT or NSAIDs alone and the use of placebo were lack of.

Conclusion

In conclusion, this specific bone setting technique from Chinese massage schools has been proven efficacious for patients with symptomatic knee OA. It is as effective as NSAIDs treatment in providing pain relief and functionality improvement, and it is significantly better in improving the performance-based test. Given the limitations and potential adverse effects and these patients who have contraindications to NSAIDS, this manipulation therapy seems to be a reasonable treatment alternative.

Acknowledgements

This work is funded by the Shanghai science and Technology Commission (No: 10DZ19737-00; 13401906500).

Disclosure of conflict of interest

None.

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