



RANDOMIZED CONTROLLED COMPARATIVE STUDY

Effects of traditional Thai massage versus joint mobilization on substance P and pain perception in patients with non-specific low back pain

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Received 11 July 2005; received in revised form 16 October 2005; accepted 1 November 2005

KEYWORDS

Non-specific low back pain;
Traditional Thai massage;
Joint mobilization;
Substance P

Summary Although both Traditional Thai Massage (TTM) and joint mobilization have been practiced in Thailand to reduce musculoskeletal pain, a comparative study of these in relieving pain is not been found in the literature. The purpose of this study was to examine the immediate effects of TTM versus joint mobilization on substance P and pain perception in patients with non-specific low back pain. Sixty-seven adults with non-specific low back pain were randomly assigned to receive either TTM (35 people) or joint mobilization (32 people). The duration of each treatment was 10 min. The levels of substance P in saliva and a visual analog scale (VAS) were measured before and 5 min after each treatment. Paired *t*-test was used to compare outcome variables at baseline with outcome measures 5 min after each treatment. An analysis of covariance (ANCOVA) was performed to compare the difference between groups. Both groups showed a decrease in the level of substance P after treatment when compared with levels pre-treatment (73.86 ± 62.31 pg/ml versus 50.43 ± 64.39 pg/ml in TTM and 80.61 ± 85.26 pg/ml versus 56.27 ± 72.77 pg/ml in joint mobilization; $p = 0.019$ and 0.006 ; 95%CI: 4.03–42.82 and 7.48–41.19, respectively). Additionally, there was a marked decrease in VAS after treatment in both groups (4.22 ± 1.98 versus 2.45 ± 1.75 in Thai massage and 4.35 ± 1.71 versus 3.39 ± 1.66 in joint mobilization; $p = 0.000$ and 0.002 , 95%CI: 1.12–2.40 and 0.37–1.55, respectively). There was no significant difference in the substance P level after treatment between the two groups. However, the VAS pain score was slightly different between the groups after treatment (0.88; 95% CI: 0.16–1.59;

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$p = 0.017$), where the TTM group reported less pain than the joint mobilization group (2.48 ± 0.25 versus 3.36 ± 0.25 VAS, respectively). Both TTM and joint mobilization can relieve pain in patients with non-specific low back pain. However, TTM yields slightly more beneficial effects than joint mobilization.
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Background

Chronic low back pain is the most common condition in musculoskeletal disease. Previous epidemiologic studies have indicated that approximately 70–90% of the population experience low back pain at one time or another in their lives (Waddell, 1987; Nachemson et al., 2000). In the United States \$25 billion is spent annually on medical care services for back problems and another \$50 billion is spent on lost productivity and disability payments (Frymoyer and Cats-Baril, 1991). Low back pain and its sequelae place an enormous burden on society, the health care system and the economies of developed countries (Deyo et al., 1991). In Thailand, the incidence of non-specific low back pain has increased in all age ranges. The number of patients with low back pain at Srinakarind Hospital (Khon Kaen University Hospital) in 2002 was about 1740. Therefore, low back pain is an important health problem in Khon Kaen province.

The physiology involved in the production and response to chronic back pain is associated with activation of the group C afferent nerve fibers and is usually accompanied by a greater degree of tissue damage. This damage to the tissue cells results in the release of chemical mediators, such as bradykinin, substance P, histamine, serotonin and prostaglandins from the damage cells and activated nociceptor nerve endings. These chemical mediators, especially substance P, sensitize the nociceptors response to normal stimuli by altering the transduction properties of the free nerve endings (Wood, 2002). So the role of this peptide is in initiating and propagating the pain impulse and also in the neural circuitry that sustains chronic pain (Adam, 1997).

Substance P is a well-known neuropeptide that has a crucial role in nociceptive signal transmission. Structurally, it is an 11-amino acid polypeptide whose C-terminal amino acid sequence is essential for its pharmacologic activities. It preferentially binds to the neurokinin 1 (NK1) receptor. After binding to its receptor, substance P modifies Ca^{2+} and K^+ currents at the cellular level. The following sequences are recognized: (1) activation of the enzyme phospholipase C results in the cleavage of membrane-bound phosphatidylinositol biphosphate into two second messengers: Inositol-1-1, 4,5-triphosphate and diglyceride, thus activating the

release of calcium from intracellular stores and influx of calcium into cells. (2) Elevation of the intracellular level of cyclic adenosine monophosphate (cAMP). (3) Elevation of the intracellular level of cyclic guanosine monophosphate. (Radhakrishnan and Henry, 1995). The cellular responses include prolonged depolarization and increased response to C-fibers. The NK1 receptors are found throughout the peripheral and central nervous system with preferential distribution in the dorsal root of the spinal cord (Otsuka and Takahashi, 1977).

Substance P appears to play a role in chronic back pain (Parris et al., 1990) and arthritis (Levine et al., 1984). There is growing awareness that the knowledge of substance P may help to develop new methods to treat pain. For example, the role of substance P in the pathophysiology of clinical syndromes such as headaches (Marukawa et al., 1996), inflammatory joint disease (Anichini et al., 1997; Appellgren et al., 1998), fibromyalgia (Sprott et al., 1998; Schwarz et al., 1999; Fields et al., 2002) and diseases with chronic neuropathic and inflammatory pain in general (Nichols et al., 1999) is becoming more clear. It can be expected that the development of drugs and interventions aimed at the modulation of substance P will be able to help treatment of pain from these diseases. Many studies used the level of substance P in saliva to indicate the level of pain (Fields et al., 2002; Parris et al., 1990; Marukawa et al., 1996) in many chronic pain conditions, because the amount of substance P is significantly greater in saliva than in plasma. Also, the noninvasive nature of saliva collection suggested that substance P in saliva may be useful as an alternative neurochemical correlation with chronic low back pain (Parris et al., 1990).

Evidence-based treatment of chronic back pain suggests that: (1) drugs are used if exercise induces pain (Fulan et al., 2001); (2) exercise, physical therapy programs and manipulation were recommended to reduce pain (Van Tulder et al., 2000); (3) multidisciplinary treatment provided to greater benefit to patients (Kitti 2002). However, pain was still the most important factor in chronic back pain. Studies of the effectiveness of intervention to relieve pain are challenges that are currently being given much attention by associated health-care professionals.

Spinal mobilization is a passive movement of a spinal segment within and occasionally beyond its active range of motion. It is a well-known treatment to reduce pain and improve mobility of the vertebrae in chronic low back pain (Vansudevan, 1997). Thirty-six randomized controlled trials (RCTs) on the effectiveness of acupuncture, massage and spinal manipulation concluded that the efficacy of spinal manipulation for patients with acute or chronic low back pain might be effective in some subgroups of patients with the pain (Koes et al., 1991). However, spinal mobilization has a prominent role in all national guidelines on the management of back pain (Koes et al., 2001).

The popularity of alternative medical treatment for many conditions has increased during recent years and massage has been documented as one of the most frequently used alternative treatments for back pain (Eisenberg et al., 1998). Traditional Thai massage (TTM) is a deep massage with prolonged pressure (5–10s per point) on the muscles along with passive stretching. Pressure-point massage along the body's 10 major energy channels or "sen" lines is believed to release blocked energy, increasing awareness and vitality. Gentle stretching of the joints and muscles relieves tension, enhances flexibility, and induces a deep state of tranquility. (Tapanya, 1993).

Although, TTM is very popular, not only in Thailand but also in other countries in the world, controlled studies to support the effectiveness of TTM for treatment of pain conditions are very thin on the ground. Therefore, we conducted a randomized clinical trial to assess the effectiveness of TTM in the treatment of non-specific low back pain, in order to contribute much-needed knowledge to this field of alternative medicine. The aim of this study was to determine the effect of TTM in comparison with comparable Western forms of mobilization on pain levels and pain perception.

We hypothesized that TTM could reduce pain more than joint mobilization in non-specific low back pain patients.

Methods

Design and setting

A randomized clinical trial was conducted on a parallel group at the Department of Physiotherapy at Khon Kaen University, Thailand. The ethical committee of Khon Kaen University approved the research protocol.

Participants

Potential participants, aged 20–60 years, were recruited through public announcement broadcasts by local radio stations and through flyers posted around the city of Khon Kaen during a 9-month period between July 2003 and May 2004. These recruitment announcements called for individuals who had experienced persistent chronic low back pain (more than 12 weeks) to volunteer to take part in the study. Participants for inclusion in the study were selected by a physical therapist and/or a physical medicine and rehabilitation doctor who conducted a detailed physical examination and collected baseline data from them. Non-specific low back pain is defined as having no evidence of underlying diseases or anatomical abnormalities. (e.g. malignancy, osteoporosis, spondylolisthesis, herniated nucleus pulposus, spondylosis and others). Furthermore, patients were excluded if their condition had improved significantly during the previous 2 weeks.

Even if subjects met the above criteria, individuals were not included if they had at least one of the following conditions: menstruation; pregnancy; a body temperature of more than 38.5 °C on the day of examination; a history of acute trauma, back-surgery, spinal fracture, joint subluxation or instability, inflammatory joint disease (RA or Gout), muscle disease, malignancy or infection; evidence of neurologic deficits, multiple sclerosis, hemi/para paresis or myelopathy, skin diseases, or infectious diseases (tuberculosis or AIDS). Any individual considered unable to commit to the full course of treatment was also excluded.

Informed consent was obtained prior to the baseline examination.

Procedure

Randomization

There were 67 patients who met the above inclusion criteria and they were randomly assigned to one of the two treatment arms using block-randomized allocation with block sizes of 2, 4, and 6. Groups were assigned using a pre-generated random assignment scheme enclosed in envelopes, which resulted in a total of 35 patients for TTM and 32 patients for mobilization.

Treatment

Part 1: Time course responses of substance P. This study was the first study to measure the level of substance P in Thai people so we had to study the time responses of substance P in both TTM and

mobilization groups. Ten patients were randomly selected to receive either TTM to the back muscles (5 people) for 10 min or mobilization grade 2 (5 people) 5 min/set, 2 sets/level at lumbar spinous process of L2–L5. TTM was performed according to the system of royal Thai massage, which applies the theory of “10 Sens”, based on the concept of energy lines (Sens) running through the body (Tapanya, 1993). Massage and joint mobilization points of this study are shown in Figs. 1 and 2.

The patients were asked to reflect on chewing a sour lemon and this produced adequate quantities of saliva in all cases. About 2 ml of saliva was easily obtained. Saliva was collected into a sterile bottle over four time periods: pre-treatment, immediately post-treatment, 5 and 10 min post-treatment. Saliva specimens were immediately cooled in ice and centrifuged at 10,000g at 4 °C for 15 min to obtain the supernatant, and stored at –70 °C until measurement. Saliva substance P was detected

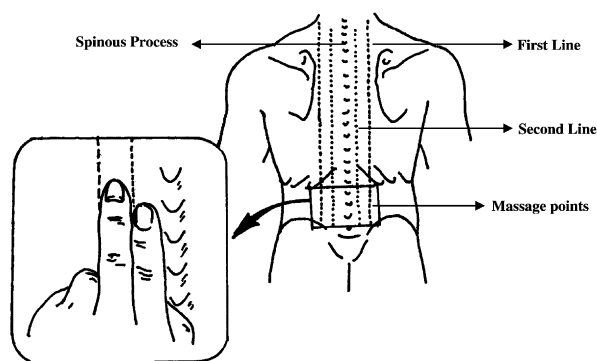


Figure 1 The massage points: running from low back muscles between L2 and L5. Each point in the first line is one finger's breadth from the spinous process. The second line is two finger's breadth from the spinous process.

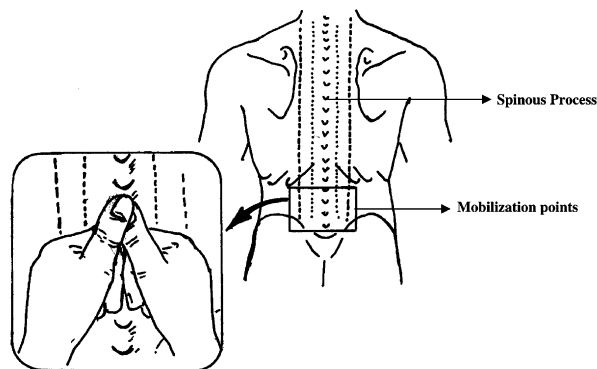


Figure 2 The mobilization points: lying on spinous process of L2–L5.

using a competitive enzyme-linked immunosorbent assay. Flat-bottomed 96-well microtiter plates (Cayman Chemical, USA) were obtained pre-coated with mouse monoclonal anti-SP antibody. Acetylcholinesterase linked to SP, antiserum, and samples were added to the wells and incubated for 24 h at 4 °C. The plates were washed five times with phosphate-buffered saline (PBS) containing 0.05% Tween-20 (PBS-Tween 20), then Ellman's Reagent (which contains the substrate for acetylcholinesterase) was added to each well, and the absorbance was measured at 405 nm with a microplate reader (Dade Behring BEP, Germany). The intra-assay and inter-assay precision was coefficients of variation of approximately 10%. The result showed that substance P changed within 5 min after treatment and returned to the baseline value within 10 min after treatment. So saliva was collected before and 5 min after treatment to detect the exact value of substance P changes after treatment in Part 2 of the experiment.

Part 2: Substance P and visual analogue scale before and after mobilization and TTM. Sixty-seven non-specific low back pains were diagnosed by a doctor and selected for this study. All subjects signed an informed consent form prior to participation in the study. The patients were randomly allocated to receive either TTM (35 people) on low back muscles between L2 and L5 or joint mobilization (32 people) on spinous process of L2–L5 by experienced physiotherapist. The duration of each treatment was 10 min. The level of substance P in saliva and visual analogue scale (VAS) were measured before and 5 min after each of the treatments.

Data analyses

The outcome measures were analyzed as continuous variables and presented as the mean \pm SD. Paired *t*-test was used to compare outcome variables at baseline (measures before each treatment), with outcome measures 5 min after each treatment. Since the randomization method did not guarantee that baseline characteristics would be the same between groups, an analysis of covariance (ANCOVA) was performed to take account of chance imbalances at baseline between the treatment groups, using a pre-test as a covariate variable. (Vickers and Altman, 2001). This analysis was used to compare differences in outcome measures between the two treatment groups and to estimate the adjusted mean differences and the 95% confidence intervals for each outcome measure at each treatment. Analyses were performed using STATA Version 7. (StataCorp LP, 4905 Lakeway Drive College Station, TX 77845, USA).

Results

Demographic and baseline characteristic

Details of demographic are shown in Table 1. Most patients (61.19%) were women. The average age of patients who participated in both groups was not different. In TTM it was 38.97 ± 7.85 and in the mobilization group it was 38.57 ± 7.66 years old. Also there was no difference in the type of work between the two groups, typically government service, private officer, student and business owner.

Outcomes measure

Substance P level

Table 2 shows substance P levels before and after treatment in both groups. There were significant decreases of substance P levels after treatment in both groups when compared with pre-treatment levels (73.86 ± 62.31 pg/ml versus 50.43 ± 64.39 pg/ml in TTM and 80.61 ± 85.26 pg/ml versus 56.27 ± 72.77 pg/ml in joint mobilization; $p = 0.019$ and 0.006 ; (95%CI: 4.03–42.82 and 7.48–41.19, respectively). However, substance P levels between the two groups were not significantly different (95% CI: -21.6 to 24.08 ; $p = 0.914$) (Table 3). Therefore, overall results indicate that

both treatments can be pain relief mediators in non-specific low back pain but there was no marked difference between two groups.

Visual analogue scale

Table 4 shows that patients in both groups reported improvements in the visual analogue scale after treatment. However, the VAS pain score was slightly different between the groups after treatment (0.88; 95% CI: 0.16–1.59; $p = 0.017$), whereas the TTM group reported less pain than the joint mobilization group (2.48 ± 0.25 versus 3.36 ± 0.25 VAS, respectively) (Table 5).

Discussion

The present study examined the acute effect of TTM and joint mobilization on pain levels and pain perception in non-specific low back pain. The findings suggested that both treatments could temporarily relieve pain. Although there was no significant difference between two treatments in their substance P level, VAS in the TTM group was slightly lower than that of the joint mobilization group. This result supported our hypothesis that TTM could slightly reduce pain more than joint mobilization.

Table 1 Demographic and baseline characteristic.

| Group | Sex | | Occupation | | | | Age (year) mean \pm SD |
|--------------|------|--------|--------------------|-----------------|---------|----------------|--------------------------|
| | Male | Female | Government service | Private officer | Student | Business owner | |
| TTM | 12 | 23 | 18 | 11 | 1 | 5 | 38.97 ± 7.85 |
| Mobilization | 14 | 18 | 15 | 11 | 3 | 3 | 38.57 ± 7.66 |

Table 2 Substance P levels in saliva before and after treatment (pg/ml).

| Group | Pre-treatment | Post-treatment | Difference (95% CI) | <i>P</i> -value |
|--------------|-------------------|-------------------|---------------------|-----------------|
| TTM | 73.86 ± 62.31 | 50.43 ± 64.39 | 23.42 (4.03–42.82) | 0.019 |
| Mobilization | 80.61 ± 85.26 | 56.27 ± 72.77 | 24.34 (7.48–41.19) | 0.006 |

Table 3 Comparison of the adjusted mean and 95% CI of Substance levels in saliva (adjusted for baseline using ANCOVA) after treatment between two groups (pg/ml).

| Group | Adjusted mean (standard error) | Difference (95% CI) | 95% CI | <i>P</i> -value |
|--------------|--------------------------------|---------------------|--------------------|-----------------|
| TTM | 52.60 (7.8) | 1.2 | -21.60 – 24.08 | 0.914 |
| Mobilization | 53.80 (8.3) | | | |

Table 4 Visual analogue scales before and after treatment.

| Group | Pre-treatment | Post-treatment | Difference (95% CI) | P-value |
|--------------|---------------|----------------|---------------------|---------|
| TTM | 4.22 ± 1.98 | 2.45 ± 1.75 | 1.76 (1.12–2.40) | 0.000 |
| Mobilization | 4.35 ± 1.71 | 3.39 ± 1.66 | 0.76 (0.38–1.55) | 0.002 |

Table 5 Comparison of the adjusted mean and 95% CI of visual analogue scales (adjusted for baseline using ANCOVA) after treatment between two groups.

| Group | Adjusted mean (standard error) | Difference (95% CI) | 95%CI | P-value |
|--------------|--------------------------------|---------------------|-----------|---------|
| TTM | 2.48 (0.25) | 0.88 | 0.16–1.59 | 0.017 |
| Mobilization | 3.36 (0.25) | | | |

Substance P level

Substance P levels in saliva have been used in many studies to indicate the severity of chronic pain. The results of this study are consistent with much research into substance P levels in pain conditions: they are higher than in the normal range (for example in chronic low back pain (Parris et al., 1990), migraine and tension headaches (Marukawa et al., 1996) and fibromyalgia) (Fields et al., 2002). Our results were in agreement with Field's et al. (2002): that substance P levels are reduced after massage. Although the techniques of massage were different than in our study, we supposed that either TTM (deep friction kind of massage) or Swedish massage (superficial massage) could affect the same pain chemical mediator.

In terms of the comparison between TTM and joint mobilization, the level of substance P did not significantly differ between the two treatments. This is the first study that has quantified the pain levels after TTM (and also the first scientific document) to suggest that TTM can temporarily reduce pain in non-specific low back pain.

TTM and joint mobilization may modulate pain transmission at spinal cord level by closing the gate; i.e. inhibiting transmission cell (T cell) activity via substantia gelatinosa (SG cells). Both techniques stimulate mechanosensitive afferent fibers in muscles and spinal joints that influence SG cells. Activation of low-threshold, large diameter mechanoreceptive afferent fibers stimulates the SG cells via an excitatory synapse, increases the amount of pre-synaptic inhibition acting on the nociceptor afferent terminals, and prevents the transmission of nociceptive information to higher center (Wood, 2002). They also temporarily decrease the level of pain in biochemical transmission, substance P, so the nerve conductivity to a higher center was limited.

In addition, information is also passed to a higher center via the multisynaptic spinoreticular tract. This pathway sends projections from several brain-stem terminations via the intralaminar nucleus of the thalamus to areas such as the hypothalamus, the frontal lobe and limbic system of the brain. These areas coordinate the autonomic, psychological and emotional responses to pain. We suggested that both treatments could relax patients and modulate emotional and psychological changes, therefore affecting pain perception at brain stem level. Thus, the pain signal that is sent to the cerebral cortex is modified and eventually pain perception is decreased.

Non-specific low back pain manifests itself as pain, muscle tension or stiffness. Both mobilization and massage can reduce muscle tension and improve blood flow to stiff muscles and joints, so the pain metabolite such as substance P, H⁺ and lactic acid are washed out. In addition, nutrients and oxygen are raised by more blood flow to these tissues. Ischemic pain of non-specific low back pain is temporarily decreased.

This study demonstrated acute effects of both TTM and manipulation on pain chemical mediators. Future studies need to verify the long-term effects of both treatments to confirm the effectiveness of them, and may apply to the clinical application in non-specific low back pain.

Visual analog scales

Our study found that VAS after treatment in the TTM group declined slightly more than in the mobilization group. The difference in VAS was 0.88 (95% CI from 0.16 to 1.59: $p = 0.017$). However, the overall difference between groups and the lower limit of the 95% CI range were both

less than 1; i.e. not considered to be clinically significant. It should be noted that Thai people may used to TTM more than mobilization. They prefer TTM and may relax and calm down more than after the mobilization technique has been used. So VAS (pain perception by patients) will differ.

VAS and substance P level decreased in consistency after both treatments. We supposed that pain level and perception in non-specific low back pain were affected by manual treatments, such as joint movement and deep friction of muscles around vertebral joints. This result was similar to the findings of the study by Franke et al. (2000). This previous study found that for patients with non-specific low back pain, acupuncture massage (combined with individual or group exercise) was more beneficial in reducing pain than Swedish massage. We suggested that multi-treatment should bring the most benefit for patients with chronic pain.

This study was conducted as a RCT with independent (unbiased) group allocation and evaluation by one person only, who was blind to this treatment group allocation. However, there was lack of a control group due to ethical reasons in comparing treatments. Future studies may use a sham group (e.g. massage with no pressure) as a control group to give a stronger conclusion about the effectiveness of both treatments.

Conclusion

Based on the results of this study, we conclude that both TTM and joint mobilization can temporarily relieve pain in patients with non-specific low back pain. However, TTM yields slightly more beneficial effects than joint mobilization.

Acknowledgements

This study was supported by a 2002–2003 Khon Kaen University research grant, Khon Kaen University, Khon Kaen, Thailand.

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