THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE
Volume 00, Number 00, 2017, pp. 1–9

DOI: 10.1089/acm.2017.0182

CASE STUDY

Somato-Visceral Effects in the Treatment of Dysmenorrhea: Neuromuscular Manual Therapy and Standard Pharmacological Treatment

Giovanni Barassi, PhD, Rosa Grazia Bellomo, PhD, Annamaria Porreca, BSc, Piera Attilia Di Felice, BSc, Loris Prosperi, BSc, and Raoul Saggini, PhD

Abstract

Objectives: This study aims to verify whether neuromuscular therapy (NMT) or pharmacology therapy (PT) is more effective for reducing symptoms in women affected by primary dysmenorrhea and the effects associated with each treatment.

Design: A controlled, randomized, single-blind clinical trial within the framework of the chair of physical medicine and rehabilitation of the University ''G. d'Annunzio'' of Chieti-Pescara. The study was conducted on a sample of 60 women suffering from primary dysmenorrhea. Subjects were randomly divided in two groups (A and B). Group A was treated with NMT and group B with PT. Group B was given ibuprofen or naproxen because they are considered the best painkillers for this condition. Group A was treated with 8 neuromuscular manual lumbosacral and abdominal therapy sessions twice per week for 4 weeks. Results were analyzed at the beginning (T0) and end (T1) of the study with a menstrual distress questionnaire, brief pain inventory, and visual analogue scale. Twenty patients from Group A were selected for evaluation of their maintenance of the eventual improvement that was detected in T1 at follow-up (T2).

Results: Both therapies had significant short-term effects in reducing the perception and duration of pain. However, NMT appears to give more improvements in the duration of pain. NMT had a long-term effect on perception of pain because patients conserved the positive effects of treatment after 4 weeks. NMT also had a long-term effect on duration of pain because patients conserved benefits of treatment, but this improvement started to decrease after 4 weeks.

Conclusions: In the treatment of primary dysmenorrhea, NMT represents a valid therapeutic alternative method to PT. NMT is free from potential adverse effects of analgesics, is noninvasive, and is easy to perform.

Keywords: dysmenorrhea, NMT, pain treatment

Introduction

Dysmenorrhea is a set of pathological symptoms associated with menstruation, such as abdominal cramping and pain during the menstrual period, which interferes with daily activities. Associated general symptoms, such as nausea, vomiting, lumbago, diarrhea, and headache, are also common. Dysmenorrhea is categorized into two types, primary and secondary.[1]

Primary dysmenorrhea refers to menstrual pain without underlying pathology, whereas secondary dysmenorrhea refers to painful menstruation associated with underlying pathology. In both cases, the pain perception could lead not only to physical ailments but also to psychologic and emotional instability.[2–4] It is known that this condition has repercussions on activities and social relationships, and causes a high rate of absenteeism from work.[5,6] Physiopathology distinguishes primary and secondary dysmenorrhea[1]: primary dysmenorrhea indicates pain that is not connected to a pelvic disease, whereas secondary dysmenorrhea is.[7,8]

There are many experimental treatments for this disease, from the most conventional[4,9,10] to those more innovative.[11–14]

Department of Medical and Oral Sciences and Biotechnologies, G. D'Annunzio University, Chieti, Italy.

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) and oral contraceptives is related to side-effects such as nausea, breast tension, bleeding between two consecutive menstrual cycles, and visual and auditory disturbances; in ~25% of patients, NSAIDs are insufficient to solve the problem when they are used without other treatments.[9,15–21] Moreover, several studies have investigated alternative methods for improving symptoms of primary dysmenorrhea, including acupuncture and acupressure, biofeedback, exogenous thermotherapy, transcutaneous electrical nerve stimulation (TENS), and relaxation techniques.[3]

Systematic reviews and meta-analyses were used to determine the effectiveness of the interventions of physiotherapy. In 2009, a systematic review of the efficacy of TENS found a high frequency of use, and demonstrated the effectiveness of this method. Pickles et al. highlighted that an excess of prostaglandins during the menstrual period is correlated with the appearance of painful cramps,[7] and many studies have emphasized the beneficial effects of NSAIDs, which, by inhibiting the cyclooxygenase enzyme, are effective in the treatment of dysmenorrhea (especially in the acute phase, in which a positive response of 75% was found).[5,10,11] Other studies have shown that the use of NSAIDs (before or during the first day of a menstrual cycle) reduces pain if taken at regular intervals to obtain continuous inhibition of prostaglandins.[22–24] Much scientific evidence has demonstrated that morpho-functional alterations of ligament muscle components (interposed between the sacral area and uterus) can induce dysmenorrhea.[25–28]

Recently, young and adult women have been seeking alternative methods to resolve premenstrual symptoms of dysmenorrhea because of the side-effects of medications and aversions to pharmacology therapy (PT) treatments.[29] Many studies (e.g., Demirtürk et al.) have underlined the application of physiotherapy as part of nonpharmacological approaches, and that complementary and alternative therapies have gained popularity in recent years.[29] Another epidemiological study, which strengthens the underlying conditions of this study, conducted with the support of the Japan Ministry of Health and Welfare, revealed that menstrual pain requiring pain medication occurs in 33% of menstruating Japanese women. In 6% of women, pain medications were ineffective and bedrest was needed. This study suggested that 1/3 of women who menstruate may require medical intervention.[1,30]

This study aims to understand whether neuromuscular therapy (NMT) or PT is more effective in reducing symptoms in women affected by primary dysmenorrhea and determine the effects associated with each treatment.

Materials and Methods

Design

Sixty participants gave written informed consent to participate and were randomly assigned to two 30-participant experimental groups, A (NMT) and B (PT). Groups were evaluated at times T0 and T1.

In addition, 20 patients were randomly selected from group A; in conjunction with their next cycles, they also provided questionnaire answers at T2 to evaluate the effectiveness of the therapy over time.

Inclusion criteria

The inclusion criteria for both groups were (1) the presence of gripping pains in the lower area of the abdomen that arise a few hours before or after the start of a cycle and (2) intense pain (>6) as measured with the visual analogue scale (VAS).

Exclusion criteria

The exclusion criteria considered for both groups were the presence of symptoms due to organic diseases, like endometriosis, adenomyosis, ovarian cysts, uterine fibroids, congenital malformations, pelvic inflammations, pelvic varicocele or anatomical alterations, and vascular complications.

Ethical aspects

The trial protocol was in accordance with a local ethics committee, the Ethics Committee of Biomedical Research of ''G. d'Annunzio'' University and the Declaration of Helsinki.

Procedure

The participants were subjected to a medical examination to outline the features of their cycles, including onset of the disorder with respect to menarche; length of cycle; onset and duration of cycle; severity of pain and associated symptoms; influence on activities of daily living (ADLs); and forms of treatment used previously. The examination also excluded secondary dysmenorrhea.

The VAS was used to assess the intensity of pain before and after treatment, from *absence of pain* to *worst pain ever had*. Pain from 7 to 10 is considered severe, from 6 to 5 is moderate, and from 1 to 4 is slight.[31,32] The Brief Pain Inventory questionnaire, which is designed to assess how pain interferes with ADLs, was used to highlight subjects' overall degree of disability related to dysmenorrhea.[33]

The Menstrual Distress Questionnaire comprises 47 questions and was used to evaluate the main characteristics of cycles and typical symptoms of primary dysmenorrhea. For each response, a score from 1 to 5 was given. Responses were used to assess cyclicality of physical symptoms and mood changes in the premenstrual and menstrual phases.[34]

Participants were asked not to change eating habits or lifestyles during treatment. At the end of the therapy and when the next cycle was starting (T1), questionnaires were administered again to verify the effectiveness of the therapy and any variations on menstrual flow. For the follow-up (a subgroup of Group A), the assessment was repeated at T2.

Outcome variables

Perception of pain was measured with VAS (0 = absence of pain; 10 = maximum pain). Duration of menstrual cycle (in days) was assessed through the variable LENGTH, whereas pain length (in days) was assessed by PAIN_LENGTH. Finally, VAS_CH and PAIN_LENGTH_CH indicate the percentage variation of VAS and percentage variation of PAIN_LENGTH from one assessment to the next, respectively.

Intervention protocols

The treatment in Group A was carried out at the ends of menstrual cycles at T0, for a total of eight treatments, twice

a week, for 4 weeks. There were at least 24 h between each session, and each session lasted 30–35 min on average. The whole protocol lasted 4 weeks.

Selected areas for treatment were dysfunctional myofascial structures correlated to the visceral and pelvic regions at functional, neurological, and biomechanical levels. In primary dysmenorrhea, pain is caused by muscular hypertone of myometrium. The increment of basal tone produces a reduction of blood supply, determining hypoxia, ischemia, and release of algogenic substances, which evokes physiologic responses that determine pain.[35]

Different studies have demonstrated that pelvic dysfunction and lumbar-sacral vertebrae mechanical restriction can compromise nervous functionality, blood supply, and fluid drainage. These conditions can generate local inflammation, which creates a nervous hypersensibility to painful stimuli.[25,26] Moreover, all the muscular structures of the lumbar and pelvic areas in this condition are dysfunctional due to the nervous alterations explained. All osteomuscular structures of this region have the same nervous pathways of pelvic organs. Thus, the theory of convergence could explain the referred pain of visceral dysfunction on somatic structures.[25,36]

According to these physiologic phenomena, the structures selected for NMT were the rectum of the abdomen, diaphragm, lumbar-ileum ligaments, sacroiliac ligament, sacrotuberous ligament, iliopsoas, piriform, and quadratus lumborum.

These were treated by specific direct techniques of NMT. Specifically, once the tissue was prepared through superficial massage techniques, direct strokes were performed: stripping, deep transversal friction, longitudinal friction, and pincer pressure.

The stripping technique consists of a progressive and firm pressure along the area of myofascial dysfunction. The deep transversal friction is a deep muscular fiber stimulation by pressure in the transversal direction. The longitudinal friction technique is similar, and is applied in the same direction of muscular fibers. The pincer technique consists of a pincer palpation to individuate dysfunctional areas to be treated with higher pressure, applied in the same position.[37,38]

On the contrary, at the onset of symptoms, Group B was invited to take ibuprofen and/or naproxen.

Statistical analysis

To determine whether NMT or PT is more effective in reducing the symptoms of dysmenorrhea, data from two different time points were analyzed. To verify if the treatments brought statistically significant improvements from T0 to T1, *t*-tests for paired data were used by separately considering the two groups (first for the variable VAS and then for the variable PAIN_LENGTH). To verify if the treatment type resulted in statistically significant differences in the improvement of VAS_CH and PAIN_LENGTH_CH, two parametric analyses of variance (ANOVAs; between groups) were tested; in both ANOVAs, the treatments were PT and NMT and the dependent variables were VAS_CH and PAIN_LENGTH_CH.

To determine if NMT had a long-term effect, a random subgroup of 20 patients was considered (for this sample, data for T2 were collected). To understand if from T0 to T1 the 20 patients experienced improvement, and to check if this improvement was maintained from T1 to T2, a parametric ANOVA for repeated measurements (within groups) was carried out; in this way, it was possible to test if time had a statistically significant effect on VAS and PAIN_LENGTH.

Before carrying out parametric analysis, normality and homogeneity of the variances were tested. Normality was verified with the Jarque-Bera test, and for all variables, the null hypothesis of normality was verified with a significance level of 95%. Subsequently, the homogeneity of the variances between the two groups was controlled using the Bartlett test; all *p*-values were >0.05, thus the null hypothesis of homogeneity of the variances of the two groups can be accepted. The assignment of the participants to the interventions in a randomized controlled trial ensured that the characteristics of the participants between the two groups did not influence the results. All tests were performed using R statistical software.

Results

Table 1 displays that the treatments had similar effects on the improvement of pain (VAS_CH = −49% for PT and −45% for NMT); however, NMT had greater variability (SD = 0.23 against 0.15 for PT). Regarding the reduction of PAIN_LENGTH, NMT is more effective than PT (PAIN_LENGTH_CH = −70% against −31% for PT). For both groups, from T0 to T1, there was a strong reduction of means and minimum values of VAS and PAIN_LENGTH. Figures 1–4 stress this decrease of VAS and PAIN_LENGTH for the greater part of the two samples.

Table 1. Descriptive Statistics of Pharmacology Therapy and Neuromuscular Therapy Groups

		PT group					*NMT group*				
Observation	n	*Mean*	*SD*	*Median*	*Min*	*Max*	*Mean*	*SD*	*Median*	*Min*	*Max*
VAS0	30	8.3	0.84	8	7	10	7.9	0.84	8	6	9
VAS1	30	4.23	1.22	4	1	6	4.3	1.78	4.5	0	7
LENGTH0	30	30.3	3.76	30	22	40	29.9	2.7	29	26	37
LENGTH1	30	30.27	3.41	30	26	41	29.73	4.83	28	23	44
PAIN_LENGTH0	30	2.9	0.76	3	2	5	3.07	0.98	3	1	6
PAIN_LENGTH1	30	1.97	0.67	2	1	4	0.8	0.41	1	0	2
VAS_CH	30	−0.49	0.15	−0.44	−0.88	−0.25	−0.45	0.23	−0.44	−1	0
PAIN_LENGTH_CH	30	−0.31	0.2	−0.33	−0.75	0	−0.7	0.2	−0.75	−1	0
LENGTH_CH	30	0.01	0.12	−0.03	−0.25	0.36	−0.01	0.13	−0.03	−0.18	0.47

NMT, neuromuscular therapy; PT, pharmacology therapy; VAS, visual analogue scale.

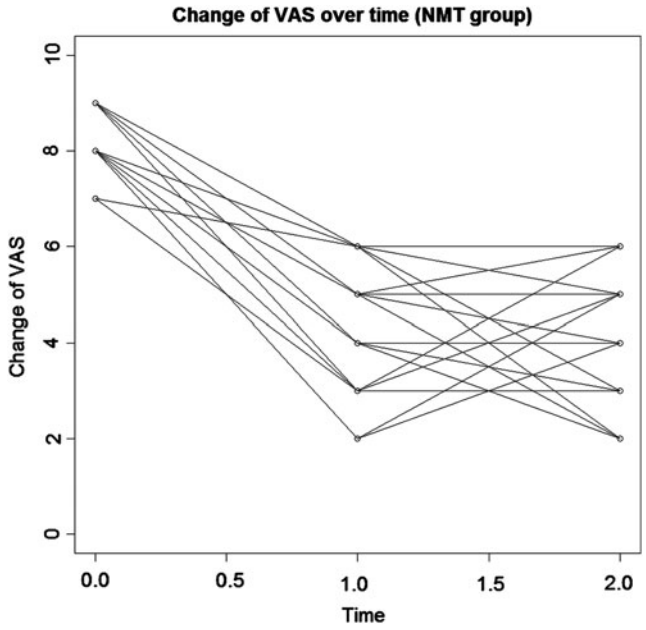

FIG. 1. Change of VAS over the time of NMT group. NMT, neuromuscular therapy; VAS, visual analogue scale.

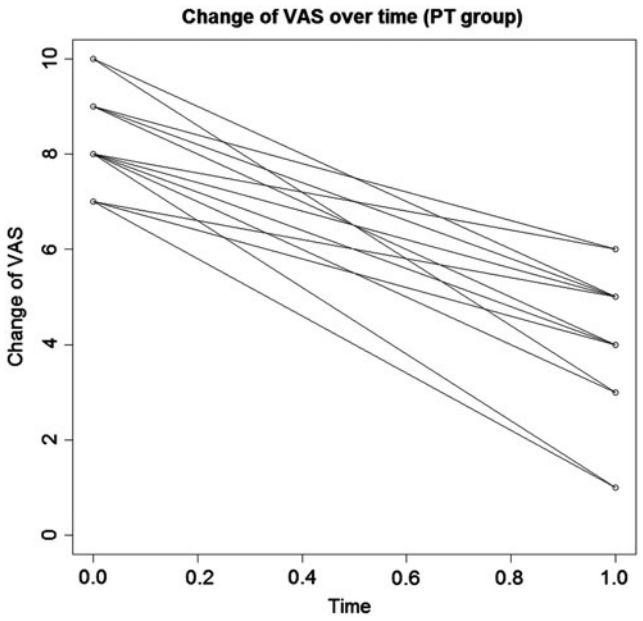

FIG. 3. Change of VAS over the time of PT group. PT, pharmacology therapy.

Table 2 shows the descriptive statistics of the NTM subgroup of 20 patients (for which 3 observations are available). On average, there was a slight increase of PAIN_LENGTH from T1 to T2, but the value was still lower compared with T0. Instead, VAS was stable from T1 to T2. Figures 1 and 2 illustrate the trends of VAS and PAIN_LENGTH for the follow-up group. Table 3 shows the correlation matrices of the two groups, respectively.

The first analysis (two time points) investigated whether the two treatments had a significant effect on VAS through two different *t*-tests for paired data (for group B, $t = 17.337$ and *p*-value <2.2E-16; for group A, $t = 10.999$ and *p*-value = 7.29 e-12). The ANOVA aimed to determine if treatment type had a significant difference on the dependent variable VAS_CH. Table 4 shows that the null hypothesis of equality between averages can be accepted and the type of treatment does not have significant effects on the reduction of pain.

The second analysis (two time points) aimed to verify if the two treatments had a significant effect on the change of PAIN_LENGTH; in this case, two different *t*-tests for paired data were used (for group B, $t = 6.9112$ and *p*-value = 1.355e-07; for group A, $t = 12.459$ and *p*-value = 3.622e-13). The

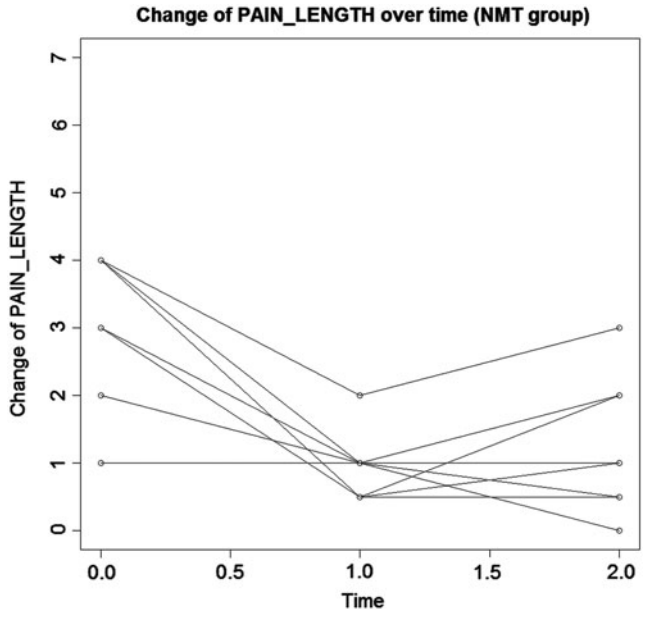

FIG. 2. Change of PAIN_LENGTH over the time of NMT group.

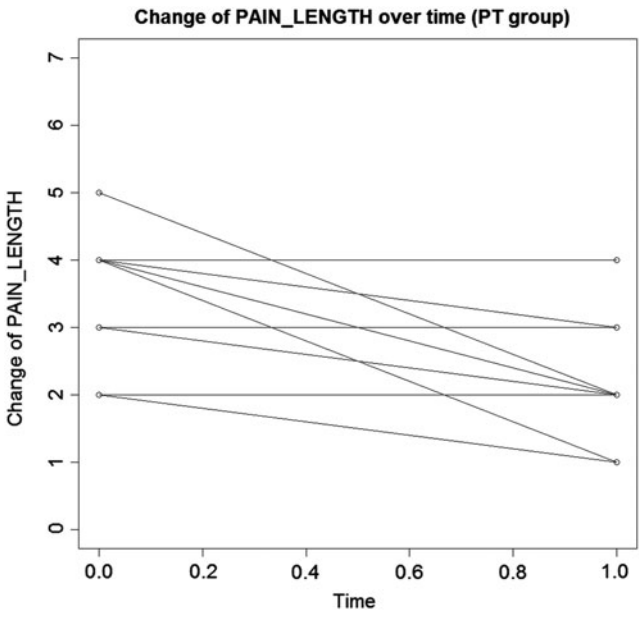

FIG. 4. Change of PAIN_LENGTH over the time of PT group.

Table 2. Descriptive Statistics of Follow-up (Neuromuscular Therapy Subgroup)

Observation	n	*Mean*	*SD*	*Median*	*Min*	*Max*
VAS0	20	8.2	0.62	8	7	9
VAS1	20	4.3	1.38	4.5	2	6
VAS2	20	4.2	1.44	4	2	6
LENGTH0	20	30.65	3	30	26	37
LENGTH1	20	31.3	5.16	31	24	44
LENGTH2	20	31.45	3.8	31.5	25	40
PAIN_LENGTH0	20	3.15	0.75	3	1	4
PAIN_LENGTH1	20	0.88	0.36	1	0.5	2
PAIN_LENGTH2	20	1.25	0.7	1	0	3
VAS_CH	20	–0.47	0.17	–0.47	–0.75	–0.14
VAS_CH2	20	0.11	0.6	0	–0.67	1.5
PAIN_LENGTH_CH	20	–0.69	0.2	–0.75	–0.88	0
PAIN_LENGTH_CH2	20	0.55	0.84	0.75	–1	3
LENGTH_CH	20	0.02	0.15	0	–0.14	0.47
LENGTH_CH2	20	0.01	0.09	0.01	–0.2	0.17

ANOVA aimed to check if the treatment type had a significant effect on the dependent variable PAIN_LENGTH_CH to understand whether NMT or PT had a better effect. Table 4 also shows that the second ANOVA is significant because the p-value <0.05; therefore, the null hypothesis of equality between means can be rejected.

The third analysis considered the follow-up (three time points) by focusing only on the NMT subgroup. A parametric ANOVA for repeated measurements was used to understand if there are significant differences between the means of VAS0, VAS1, and VAS2. Preliminarily, the Mauchly test for checking the assumption of sphericity (homogeneity of covariances) was performed; the results show that this assumption is respected because the p-value is >0.05 ($W = 0.85148$, and p-value = 0.2353). Table 5 confirms that time has a significant effect on VAS; thus, the averages of VAS, measured at different times, are statistically different. In addition, the *post-hoc* Tucky test was performed to understand the pairs that led to the rejection of the null hypothesis of equality between averages. Table 5 also highlights that there are significant differences between the pairs T2-T1 and T3-T1, whereas the pair T3-T2 does not show significant differences.

The fourth analysis was aimed at understanding if there are significant differences between means of PAIN_LENGTH1, PAIN_LENGTH2, and PAIN_LENGTH3. Thus, a parametric ANOVA for repeated measurements was adopted, and the Mauchly test of sphericity confirmed that the assumption is respected ($W = 0.85551$ and p-value = 0.2455). Table 6 confirms that time has a significant effect on PAIN_LENGTH, because the three means are statistically different, and the *post-hoc* tests stress that all the pairs are different.

Discussion

Comparison between NMT and PT (analysis at two time points)

Premenstrual symptoms and dysmenorrhea constitute common problems for which young and adult women seek alternative treatments.[29] In the literature, the analgesic effects of NMT and PT are known; for this reason, in the last few decades, research has focused on the effects of

Table 3. Correlation Matrices of Pharmacology Therapy and Neuromuscular Therapy Groups

	VAS0	*VAS1*	*LEN0*	*LEN1*	*PAIN_LENGTH0*	*PAIN_LENGTH1*	*VAS_CH*	*PAIN_LENGTH_CH*	*LENGTH_CH*
PT group									
VAS0									
VAS1	0.266								
LEN0	0.157	0.239							
LEN1	–0.077	0.15	0.488**						
PAIN_LENGTH0	0.212	0.137	0.301	–0.016					
PAIN_LENGTH1	–0.105	–0.117	0.347	–0.117	0.469**				
VAS_CH	–0.066	0.939***	0.189	0.202	0.039	–0.113			
PAIN_LENGTH_CH	–0.202	–0.304	0.008	–0.189	–0.254	0.689***	–0.244		
LENGTH_CH	–0.255	–0.103	–0.582***	0.400*	–0.266	–0.361	0.005	–0.128	
NMT group									
VAS0									
VAS1	0.226								
LENGTH0	0.162	0.25							
LENGTH1	0.128	0.305	0.596***						
PAIN_LENGTH0	0.217	–0.229	–0.023	0.055					
PAIN_LENGTH1	0.208	0.488**	0.316	0.308	0.172				
VAS_CH	–0.045	0.956***	0.205	0.259	–0.276	0.482**			
PAIN_LENGTH_CH	0.128	0.487**	0.341	0.14	–0.582***	0.583***	0.479**		
LENGTH_CH	0.066	0.207	0.062	0.837***	0.077	0.161	0.175	–0.045	

Computed correlation used Pearson method with listwise deletion.
Significance levels codes: ***0.001, **0.01, and *0.05.

Table 4. Different Analysis of Variance for VAS_CH and PAIN_LENGTH

ANOVA between groups (MAN_TER = 0 for PT, MAN_TER = 0 for NMT)

	Estimate	*Standard error*	t-*Value*	*Pr(>|t|)*
(Intercept)	−0.489	0.035	−13.846	<2e-16***
MAN_TER	0.034	0.049	0.688	0.494

Res. SEM: 0.1934 on 58 DF
R-squared: 0.008102, adjusted R-squared: −0.008999
F-statistic: 0.4738 on 1 and 58 DF, *p*-value: 0.494

	Estimate	*Standard error*	t-*Value*	*Pr(>|t|)*
(Intercept)	−0.308	0.036	−8.531	7.95e-12***
MAN_TER	−0.389	0.051	−7.611	2.76e-10***

Res. SEM: 0.1983 on 58 DF.
R-squared: 0.4997, Adjusted R-squared: 0.491.
F-statistic: 57.92 on 1 and 58 DF, *p*-value: 2.757e-10.

Significance codes: ***0.001.
ANOVA, analysis of variance; DF, degrees of freedom; SEM, standard error of the mean.

nonpharmacological approaches to treat dysmenorrhea on the basis of embryo-physiological principles.[39–41]

Reis et al. applied connective tissue massage to the lumbar region of subjects twice per week for three consecutive menstrual cycle periods in which a cycle was not present.[42] The authors found that the intensity of pain, analgesic drug use, and symptoms were reduced using this technique and a significant improvement in the intensity of pain could also be obtained with both treatments.[42]

In the same way, this study shows that both treatments are effective, confirming the validity of NMT and PT. Specifically, the first set of paired *t*-tests illustrates that both treatments reduce the intensity of pain because the average of VAS at T1 was statistically different from that at T0, and it decreased. In addition, the second set of paired *t*-tests stressed that both treatments reduced the duration of pain because the average of PAIN_LENGTH at T1 was statistically different from that at T0, and it decreased.

Furthermore, the first ANOVA underlined that both treatments had the same beneficial effects on reducing the intensity of pain, but the second ANOVA showed that NMT had better performance in reducing PAIN_LENGTH. In summary, both treatments are good, but NMT has a greater effect than PT regarding reducing duration of pain.

Although the specific techniques used in this study and that of Reis et al. are quite different,[42] both types of manipulations were applied on approximately the same anatomical areas with the same frequency, both evaluated dysmenorrhea symptoms with similar methods and both obtained the same positive results. Both studies showed that NMT can improve the intensity of pain and also reduce its duration better than PT. Moreover, the presence of the PT control group proves that the benefits given by manipulations to dysmenorrheal patients were due to the manipulations themselves and not a placebo effect of empathy perceived by patients, as hypothesized by Reis et al.[42]

These considerations indicate that NMT ensures longer duration effects in the analgesic aspect of therapy and positive repercussions on ADLs. In fact, a stimulus or pulse transmitted through a certain network of neurons tends to follow the same path, and resistance decreases with each application of the same therapy or stimulus.[43–47] Then, under pharmaceutical laws, in the pharmacological group, a negative correlation between the perception and duration of pain highlights the

Table 5. Analysis of Variance for Repeated Measures (Within) for Visual Analogue Scale and *Post-Hoc* Test

ANOVA for repeated measures (within) for VAS

	Df	*Sum Sq*	*Mean Sq*	F-*value*	*Pr(>F)*
TIME	2	208.13	104.07	69.95	1.83e-13***
Residuals	38	56.53	1.49		

Simultaneous tests for general linear hypotheses multiple comparisons of means: Tukey contrasts

	Estimate	*Standard error*	*z-Value*	*Pr(>|z|)*
TIME2–TIME1	−3.900	0.380	−10.245	<1e-05***
TIME3–TIME1	−4.000	0.380	−10.508	<1e-05***
TIME3–TIME2	−0.100	0.380	−0.263	0.963

Significance codes: ***0.001.

Table 6. Analysis of Variance for Repeated Measures (Within) for PAIN_LENGTH and *Post-Hoc* Test

ANOVA for repeated measures (within) for PAIN_LENGTH					
	Df	*Sum Sq*	*Mean Sq*	F-*value*	*Pr(>F)*
TIME	2	59.51	29.754	138.6	<2e-16***
Residuals	38	8.16	0.215		
Simultaneous tests for general linear hypotheses multiple comparisons of means: Tukey contrasts					
	Estimate	*Standard error*	z-*Value*	*Pr(>|z|)*	
TIME2–TIME1	−2.2750	0.1465	−15.526	<0.001***	
TIME3–TIME1	−1.9000	0.1465	−12.967	<0.001***	
TIME3–TIME2	0.3750	0.1465	2.559	0.0283*	

Significance codes: *0.05; ***0.001.

immediacy of the benefits of administering the drugs.[19] By contrast, in Group A, there was a positive correlation between the subjective perception of pain and the same.

NMT follow-up (analysis of three time points)

To evaluate the long-term effectiveness of NMT on the follow-up, two analyses of three time points with two ANOVAs for repeated measurements were performed.

The first ANOVA for repeated measures was used to understand if there were significant differences between the means of VAS0, VAS1, and VAS2. This is significant because VAS1 was different from VAS2 and VAS3. However, VAS2 and VAS3 were not significantly different; this demonstrates that even though the follow-up group was not treated in the month following the end of the rehabilitation protocols, it continued to maintain its improved conditions.

The second ANOVA for repeated measures was used to understand if there were significant differences between the means of PAIN_LENGTH1, PAIN_LENGTH2, and PAIN_LENGTH3. The test is significant and the *post-hoc* tests stress that all pairs were different. Hence, regarding the duration of pain, NMT had a long-term effect because the patients conserved great benefits of treatment, but, differently from perception of pain, this improvement started to slightly decrease after 4 weeks.

Similarly, Reis et al. have pointed out how using the connective tissue massage ''the effect was maintained for more than a menstrual cycle.''[43] In addition, the validity of the NMT is justified by notions of anatomical-physiological[39,29] and embryological[39] of tracks and nervous structures and the muscle-skeletal system.[44,45]

With reference to the theory of gate control, manual therapy by tactile stimuli and pressers would enable the fibers of high caliber Aβ capable of blocking the transmission of signals to pain, which would totally silence the activity of fibers Aδ and C, responsible for painful perception (analgesic).[44] This neurophysiological event is explicable, in turn, from the theory of convergence, according to which, at the level of the same medullary interneuron, different types of nerve fibers converge, each of which carries sensitive information of varying extents, and from the somatic and visceral structures.[48–50] In fact, in the spinal cord, specific neurons are capable of integrating afferent information from somatic structures on both sides of the body with information originating in pelvic viscera and midline regions such as the genitals.[46] In addition, it is important to remember that, as the central nervous system and the skin have the same lead neuroectodermic embryo, a stimulation at the somatic level will have a response even at the level of the nervous system and vice versa.[39]

Thus, the gate control theory may represent an explanation not only for the symptom relief effects of NMT but also for the significantly longer duration of these positive effects compared to PT. In fact, some studies show the efficacy of therapies influencing the gate control pathway, like heat therapy or TENS therapy, in treating primary dysmenorrhea.[51,52] However, gate control alone cannot explain pain reduction, in either the short or long term, from NMT.

According to new theories, it is possible that some intracerebral mechanisms, involving a neuromatrix composed of parallel somatosensory, limbic, and thalamocortical components responsible for the somatory and cognitive-emotional aspects of pain, can be involved in the generation and elimination of chronic and long-term pain.[53,54] It is possible that NMT can also influence these new patterns because of the corticalization effect of somatic stimulation of local muscular manipulations in NMT. This can bring further integration of positive relief stimuli, explaining in a broader way the longer duration of analgesic effects attributable to NMT.

Finally, the influence of an endogenous opioid release mechanism, in particular β endorphins, in both the generation and maintenance of NMT analgesic effects cannot be excluded. This mechanism is well known to be responsible for pain relief effects attributed to a wide range of therapies like acupuncture, TENS, and connective tissue massage.[55–57] It is possible that this specific analgesic pathway plays only a minor role in NMT's positive effects.

It could be assumed that the combination and interaction of all these pathways may be the explanation of the analgesic effects of NMT both in the short and long term in primary dysmenorrhea.[58]

Strengths and weaknesses

A larger sample of patients than was used in this study may be preferable. Moreover, a control group in which patients are treated with both PT and NMT could provide an interesting point of evaluation of the interaction between the two treatments in the long term.

Another limit of this study is that the results cannot be extended to other somato-visceral issues because these

conditions were not investigated. Dysmenorrhea is the only focus of this study, and so, although the mechanism used in this study is similar to other somato-visceral problems, further studies are needed to extrapolate the results.

One crucial argument of this study is that somatic stimulation could exert visceral reflex effects, representing a new, safer approach to the treatment of dysmenorrhea; hence, it could also be a valid alternative to PT for this pathology.

Conclusions

This research focused on the comparison between NMT and PT to understand which is more effective for reducing symptoms in women affected by primary dysmenorrhea, as well as the effects associated with each treatment. A follow-up group was considered to detect the long-term effects of NMT. In summary, considering the ratio between benefits and side-effects, in the case of dysmenorrhea, NMT is equally as effective as PT in the short and long term, whereas NMT is more effective for relieving the duration of menstrual pain. NMT could be a valid alternative to PT in treating women affected by primary dysmenorrhea.

Author Disclosure Statement

No competing financial interests exist.

References

1. Ikeda T, Suzuki Y, Maeda T, Harada T. Analysis of dysmenorrhea-associated factors and relaxation methods in highschool students. Bosei Eisei 2011;52:129–138.
2. Lefebvre G, Pinsonneault O, Antao V, et al. Primary dysmenorrhea consensus guideline. J Obstet Gynaecol Can 2005;27:1117–1146.
3. Proctor M, Farquhar C. Diagnosis and management of dysmenorrhoea. Br Med J 2006;332:1134.
4. Marjoribanks J, Proctor M, Farquhar C, et al. Nonsteroidal anti-inflammatory drugs for primary dysmenorrhoea. Cochrane Database Syst Rev 2003:CD001751.
5. Harlow Siobán D, Meekyong P. A longitudinal study of risk factors for the occurrence, duration and severity of menstrual cramps in a cohort of college women. Br J Obstet Gynaecol 1996;103:1134–1142.
6. Hillen TI, Grbavac SL, Johnston PJ, et al. Primary dysmenorrhea in young Western Australian women: Prevalence, impact, and knowledge of treatment. J Adolesc Health 1999; 25:40–45.
7. Pickles V, Hall W, Best F, et al. Prostaglandins in endometrium and menstrual fluid from normal and dysmenorrhoeic subjects. J Obstet Gynaecol Br Commonw 1965;72: 185–192.
8. Smith RP. Cyclic pelvic pain and dysmenorrhea. Obstet Gynecol Clin North Am 1993;20:753–764.
9. Shapiro SS. Treatment of dysmenorrhoea and premenstrual syndrome with nonsteroidal anti-inflammatory drugs. Drugs 1988;36:475–490.
10. Owen PR. Prostaglandin synthetase inhibitors in the treatment of primary dysmenorrhea: Outcome trials reviewed. Am J Obstet Gynecol 1984;148:96–103.
11. Liu YQ, Ma LX, Xing JM, et al. Does traditional Chinese medicine pattern affect acupoint specific effect? Analysis of data from a multicenter, randomized, controlled trial for primary dysmenorrhea. J Altern Complement Med 2013;19:43–49.
12. Reyes-Campos MD, Díaz-Toral LG, Verdín-Terán SL, et al. Acupuncture as an adjunct treatment for primary dysmenorrhea: A comparative study. Med Acupunct 2013; 25:291–294.
13. Taylor D, Miaskowski C, Kohn J. A randomized clinical trial of the effectiveness of an acupressure device (relief brief) for managing symptoms of dysmenorrhea. J Altern Complement Med 2002;8:357–370.
14. Yeh ML, Hung YL, Chen HH, Wang YJ. Auricular acupressure for pain relief in adolescents with dysmenorrhea: A placebo-controlled study. J Altern Complement Med 2013;19:313–318.
15. Vane JR, Botting RM. Anti-inflammatory drugs and their mechanism of action. Inflamm Res 1998;47:78–87.
16. Vane, John R. The Mechanism of Action of Anti-Inflammatory Drugs. Advances in Eicosanoid Research. Berlin, Heidelberg: Springer, 2000:1–23.
17. Sachs CJ. Oral analgesics for acute nonspecific pain. Am Fam Physician 2005;71:913–918.
18. Wong CL. Oral contraceptive pill as treatment for primary dysmenorrhoea. Cochrane Database Syst Rev 2009;2:CD002120.
19. Giovannini M. Ibuprofen versus steroids: Risk and benefit, efficacy and safety. La Pediatr Med Chir 2013;35:205–211.
20. Matteson KA. Non-surgical management of heavy menstrual bleeding: A systematic review and practice guidelines. Obstet Gynecol 2013;121:632.
21. Harel Z. Dysmenorrhea in adolescents and young adults: From pathophysiology to pharmacological treatments and management strategies. Expert Opin Pharmacother 2008;9: 2661–2672.
22. Ozgoli G, Goli M, Moattar F. Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in women with primary dysmenorrhea. J Altern Complement Med 2009;15:129–132.
23. Witt J, Strickland J, Cheng AL, et al. A randomized trial comparing the VIPON tampon and ibuprofen for dysmenorrhea pain relief. J Womens Health 2013;22:702–705.
24. Abadian K, Keshavarz Z, Mojab F, et al. Comparison the effect of mefenamic acid and Teucrium polium on the severity and systemic symptoms of dysmenorrhea. Complement Ther Clin Pract 2016;22:12–15.
25. Proctor M, Hing W, Johnson TC, et al. Spinal manipulation for dysmenorrhea. Cochrane Database Syst Rev 2010;3: CD002119.
26. Genders WG, Hopkins SS, Lean EK, et al. Dysmenorrhea and pelvic dysfunction: A possible clinical relationship. Chiropractic Journal of Australia 2003;33:23–29.
27. Holtzman DA, Petrocco-Napuli KL, Burke JR. Prospective case series on the effects of lumbosacral manipulation on dysmenorrhea. J Manipulative Physiol Ther 2008;31:237–246.
28. Kokjohn K, Schmid DM, Triano JJ, et al. The effect of spinal manipulation on pain and prostaglandin levels in women with primary dysmenorrhea. J Manipulative Physiol Ther 1992;15:279–285.
29. Demirtürk F, Yilar Erkek Z, Alparslan Ö, et al. Comparison of reflexology and connective tissue manipulation in participants with primary dysmenorrhea. J Altern Complement Med 2016;22:38–44.
30. Kim YH, Cho SH. The effect of foot reflexology on premenstrual syndrome and dysmenorrhea in female college students. Korean J Women Health Nurs 2002;8:212–221.
31. Hawker GA, Mian S, Kendzerska T, et al. Measures of adult pain: Visual analog scale for pain (VAS pain), numeric rating scale for pain (NRS pain), mcgill pain questionnaire

(MPQ), short-form mcgill pain questionnaire (SF-MPQ), chronic pain grade scale (CPGS), short form-36 bodily pain scale (SF-36 BPS), and measure of intermittent and constant osteoarthritis pain (ICOAP). Arthritis Care Res 2011;63: 240–252.
32. Wewers ME, Lowe NK. A critical review of visual analogue scales in the measurement of clinical phenomena. Res Nurs Health 1990;13:227–236.
33. Cleeland CS, Ryan KM. Pain assessment: Global use of the brief pain inventory. Ann Acad Med Singapore 1994;23: 129–138.
34. Moos RH, Rudolf H. The development of a menstrual distress questionnaire. Psychosom Med 1968;30:853–867.
35. Selzer, MW, A. Spencer. Convergence and reciprocal inhibition of visceral and cutaneous afferents in lumbar spinal cord. Federation proceedings. Federation Amer Soc Exp Biol 1967;26.
36. Baker PK. Musculoskeletal origins of chronic pelvic pain. Diagnosis and treatment. Obstet Gynecol Clin North Am 1993;20:719–742.
37. Robinette R. Trigger Point Therapy. Italian Edition curated by Barassi G, Bellomo RG, Saggini R. Padova, Italy: Piccin, 2014.
38. Granger J. Neuromuscular Manual Therapy. Italian Edition curated by Barassi G, Bellomo RG, Saggini R. Padova, Italy: Piccin, 2010.
39. Silverthorn DU, Ober WC, Garrison CW, et al. Human Physiology: An Integrated Approach. San Francisco: Pearson/ Benjamin Cummings, 2009.
40. Siegelbaum SA, and Hudspeth AJ. Principles of Neural Science. Kandel ER, Schwartz JH, Jessell TM, eds. Vol. 4. New York: McGraw-Hill, 2000.
41. Moore KL, Persau, TVN, and Shiota K. Color Atlas of Clinical Embryology. Elsevier Health Sciences, 2000.
42. Reis CAAS, Hardy E, Sousa MH. The effectiveness of connective tissue massage in the treatment of primary dysmenorrhea among young women. Rev Bras Saúde Mater Infant Recife 2010;10:247–256.
43. Melzack R, Wall PD. Pain mechanisms: A new theory. Science 1967;150:89–90.
44. Selzer M, Spencer WA. Convergence of visceral and cutaneous afferent pathways in the lumbar spinal cord. Brain Res 1969;14:331–348.
45. Mørch CD, Hu JW, Arendt-Nielsen L, et al. Convergence of cutaneous, musculoskeletal, dural and visceral afferents onto nociceptive neurons in the first cervical dorsal horn. Eur J Neurosci 2007;26:142–154.
46. Honda CN. Visceral and somatic afferent convergence onto neurons near the central canal in the sacral spinal cord of the cat. J Neurophysiol 1985;53:1059–1078.
47. Sato A. Spinal and medullary reflex components of the somatosympathetic reflex discharges evoked by stimulation of the group IV somatic afferent. Brain Res 1973;51:307–318.
48. Cervaro F, Connell LA. Distribution of somatic and visceral primary afferent fibres within the thoracic spinal cord of the cat. J Comp Neurol 1984;230:88–98.
49. Cervaro F, Wolstencroft JH. A positive feedback loop between spinal cord nociceptive pathways and antinocicptive areas of the cat's brain stem. Pain 1984;20:125–138.
50. Bolton PS, Budgell B. Visceral responses to spinal manipulation. J Electromyogr Kinesiol 2012;22:777–784.
51. Rigi SN, Navidian A, Safabakhsh L, et al. Comparing the analgesic effect of heat patch containing iron chip and ibuprofen for primary dysmenorrhea: A randomized controlled trial. BMC Womens Health 2012;12:25.
52. Wang SF, Lee JP, Hwa HL. Effect of transcutaneous electrical nerve stimulation on primary dysmenorrhea. Neuromodulation 2009;12:302–309.
53. Melzack R. From the gate to the neuromatrix. Pain 1999;82: 121–126.
54. Melzack R. Gate control theory: On the evolution of pain concepts. Pain Forum 1996;5:128–138.
55. Liu CZ, Xie JP, Wang LP, et al. Immediate analgesia effect of single point acupuncture in primary dysmenorrhea: A randomized controlled trial. Pain Med 2011;12:300–307.
56. Kaada B, Torsteinb O. Increase of plasma β-endorphins in connective tissue massage. Gen Pharmacol 1989;20:487–489.
57. Coutaux A. Non-pharmacological treatments for pain relief: TENS and acupuncture. Joint Bone Spine 2017 [Epub ahead of print]; DOI: 10.1016/j.jbspin.2017.02.005.
58. Paungmali A, O'Leary S, Souvlis T, Vicenzino B. Naloxone fails to antagonize initial hypoalgesic effect of a manual therapy treatment for lateral epicondylalgia. J Manipulative Physiol Ther 2004;27:180–185.

Address correspondence to:
Giovanni Barassi, PhD
Department of Medical and Oral Sciences and Biotechnologies
G. D'Annunzio University
Chieti 60100
Italy

E-mail: coordftgb@unich.it