Journal of Manipulative and Physiological Therapeutics
Volume 22 • Number 9 • November/December 1999
0161-4754/99/$8.00 + 0 76/1/102743 © 1999 JMPT

A Randomized, Placebo-Controlled Clinical Trial on the Efficacy of Chiropractic Therapy on Premenstrual Syndrome

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ABSTRACT

Objective: To evaluate the efficacy of chiropractic therapy on the treatment of symptoms associated with premenstrual syndrome.

Design: A prospective, randomized, placebo-controlled, crossover clinical trial.

Setting: Multicenter private clinics.

Subjects: Twenty-five subjects with diagnosed premenstrual syndrome (with a Moos premenstrual syndrome questionnaire plus daily symptom monitoring).

Intervention: After randomization, 16 of the subjects received high-velocity, low-amplitude spinal manipulation plus soft tissue therapy 2 to 3 times in the week before menses for at least 3 cycles. The remaining 9 subjects received a placebo treatment with a spring-loaded adjusting instrument wound down for minimum force. After a 1-cycle washout, the 2 groups changed over.

Outcome Measure: Daily rating of symptom level, comparing total scores for premenstrual week with baseline for treatment and placebo phases.

Data Analysis: The data were analyzed with paired Student *t* tests and Wilcoxon signed rank tests, with the statistical significance set at $P < .05$.

Results: There was a significant decrease in scores after treatment compared with baseline scores ($P = .00001$) and a statistically significant decrease in scores for the treatment phase compared with the placebo ($P = .006$). For group 1 (n = 16), there was a significant decrease in scores after treatment compared with baseline scores ($P = .0001$) and a statistically significant decrease in scores for the treatment phase compared with the placebo ($P = .041$). For group 2 (n = 9), there was a significant decrease in scores during treatment compared with the baseline ($P = .01$); however, there was no difference at the $P = .05$ level between treatment and placebo scores.

Conclusions: Within the limitations of the study, the results support the hypothesis that the symptoms associated with PMS can generally be reduced by chiropractic treatment consisting of adjustments and soft-tissue therapy. However, the role of a placebo effect needs further elucidation, given that the group receiving the placebo first, although improving over the baseline, showed no further improvement when they had actual treatment. (J Manipulative Physiol Ther 1999;22:582-5)

Key Indexing Terms: Premenstrual Syndrome; Chiropractic Manipulation

INTRODUCTION

Premenstrual syndromes (PMS) are a group of menstrually related, chronic, cyclical disorders characterized by emotional, behavioral, and physical symptoms in the second half (luteal phase) of the menstrual cycle.[1] In its more severe form, the syndrome has been referred to by the American Psychiatric Association as premenstrual dysphoric disorder and is categorized as a depressive mood disorder.[2]

Estimates of prevalence vary from 10% to 90%, depending on the mode of assessment used, with some 10% to 20% of women of reproductive age having premenstrual dysphoric disorder with severe or disabling symptoms.[3,4]

Apart from social and work-related problems, suicide and criminal behavior can also occur. PMS has been accepted as a mitigating factor in crimes committed in the United Kingdom, and France has permitted PMS as grounds for a plea of temporary insanity. In 1983, Kramer[5] estimated that PMS affected 5 million women in the United States and that at least $30 billion in wages had been lost as a result of PMS.

The lack of a uniformly accepted definition or diagnostic criteria has inhibited research and advances in the management of PMS; however, it is generally recognized that a true diagnosis can only be made after a prospective recording of symptom severity on a daily basis for a minimum of 2 cycles.[6,7] Most current therapeutic interventions (eg, drugs, vitamin supplements, and psychotherapy) have been found to be ineffective compared with placebo treatments, to have undesirable side effects,[7,8] or to have low patient treatment satisfaction.[1] Recent research[9,10] has indicated that drugs such as fluoxetine (Prozac) and sertraline, which affect serotonin activity and reuptake, may be effective in the treatment of PMS and premenstrual dysphoric disorder. There is only minimal evidence in the literature about the use of chiropractic treatment or spinal manipulation for the care of PMS. Anecdotal evidence of the effectiveness of chiropractic manipulative therapy in reducing the symptoms associated with PMS is abundant, but no clinical trials have been performed. Published case studies[11-14] offer some support for the anecdotal evidence.

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This study was funded by the Australian Spinal Research Foundation.

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Paper submitted February 3, 1999; in revised form March 30, 1999.

METHODS

The trial design was a randomized, single-blind, placebo-controlled, crossover clinical trial. The study was approved by the Royal Melbourne Institute of Technology University Human Ethics Committee. All participating subjects gave written informed consent after reading information about the study. Fifty-four subjects were recruited by media articles and advertising and were of reproductive age with diagnosable PMS (according to DMS-IV-R criteria) and regular menstrual cycles. Subjects were excluded from the study if they had medically diagnosed psychiatric, gynecologic, or hormonal disorders, had undergone chiropractic treatment in the previous 6 months, were taking medication that affected the menstrual cycle, or had contraindications to chiropractic manipulation.

All subjects underwent an initial interview during which they completed a Moos Menstrual Distress Questionnaire to determine a provisional diagnosis of PMS. A full medical history and physical examination was conducted by a qualified medical practitioner to rule out exclusion diagnoses and pathologic conditions. The chiropractic examination was performed by 1 of 2 qualified, registered chiropractors. Forty-five subjects satisfied the DSM-IV criteria for PMS as indicated by the Moos questionnaire, had no contraindications to chiropractic therapy, and were admitted to the study. These subjects monitored their major PMS symptoms on a daily basis for a minimum of 2 complete cycles before any intervention with a PMS-Cator disc, developed and validated at Royal Melbourne Institute of Technology by Magos and Studd.[15] This was necessary to confirm a diagnosis of PMS and establish a baseline. On the basis of the baseline daily rating of symptoms, all 45 subjects were confirmed as having PMS and were then randomly assigned to 2 groups. Group 1 (n = 28) initially received chiropractic treatment for 3 cycles, followed by the placebo, consisting of a sham adjustment for an additional 3 cycles after a 1 cycle washout. Group 2 (n = 17) received the placebo first, then the treatment. The flowchart in Figure 1 summarizes the phases of the trial.

Treatment and Placebo Regimens

Treatments and placebos were delivered at 7 separate private clinics by fully qualified, registered chiropractors with a minimum of 10 years clinical experience.

Treatment consisted of standard high-velocity, low-amplitude spinal manipulations delivered either manually or by drop tables and soft-tissue therapy as clinically indicated. Low-force techniques such as adjusting instruments or pelvic blocking were not used. The sham treatment used a Activator Adjusting Instrument (Activator Methods Inc., Phoenix, Ariz) wound fully down to minimize the impulse, which was delivered away from the normal segmental contact point. Both treatment and placebo were given an average of 3 times over a 10-day period before start of menses for each cycle. For group 1, the range of total number of real treatments per subject was 6 to 11 with an average of 7.9, whereas for group 2, the range was 6 to 9 with an average of 6.7 treatments per subject.

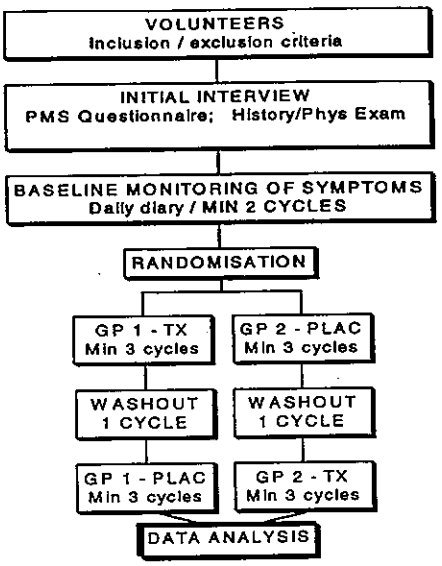

Fig 1. *Flow chart showing phase of study.*

Blinding

All data analysis was performed by one of the authors (M.J.W.) and an independent statistical consultant. The treating practitioners had no access to or knowledge of the outcomes of treatment at any stage during the trial and were requested not to discuss PMS symptom levels with the subjects they were treating. All subjects were told that they would be receiving spinal manipulation in all visits, but 2 different methods were to be used.

Outcome Measure

Subjects monitored their PMS symptoms on a daily basis with the PMS-Cator disc for the full course of the trial. Up to 7 symptoms were scored as follows: 3 = severe; 2 = moderate; 1 = mild; 0 = none. A global score composed of the total score for all symptoms over a 7-day period before menses was calculated for each cycle as a measure of the symptom severity for the premenstrual week for all phases of the trial. The average global score was calculated for the baseline, treatment, and placebo phases.

Data Analysis

The average global symptom scores for the premenstrual week for the baseline phase were compared with those for the treatment phase, and the treatment phase scores compared with those for the placebo phase. In each case, the data were analyzed with paired Student t tests with the statistical significance set at $P < .05$. Wilcoxon signed rank tests were performed, verifying that the data fit a normal distribution.

The minimum sample size for statistical significance was 20 for the crossover design used in this study. This figure was calculated by an independent consultant based on data from a previously conducted pilot study.[14]

RESULTS

A total of 25 subjects completed all phases of the study. There were 20 dropouts from the 45 initially accepted into

Table 1. *Characteristics of the study population at the initial interview, level of completion, and according to group*

	Initial (n = 45)	Total completed (n = 25)	Dropouts (n = 20)	Group 1 (n = 16)	Group 2 (n = 9)
Mean baseline score	55.7 (31.1 SD)	54.0 (26.0 SD)	57.8 (37.5 SD)	54.4 (29.8 SD)	53.1 (13.2 SD)
Mean age (y)	35.7 (6.9 SD)	35.3 (7.1 SD)	36.3 (6.7 SD)	35.0 (7.4 SD)	36.0 (7.0 SD)
Age range (y)	20-47	20-45	25-47	20-45	23-42
Mean cycle length (d)	28.0 (2.4 SD)	27.9 (2.4 SD)	28.4 (2.1 SD)	27.8 (2.7 SD)	28.3 (1.0 SD)
No. of children	2.1	1.1	2.7	1.2	0.7

SD, Standard deviation.

Table 2. *Major PMS symptoms monitored*

Symptom	No. of subjects with symptoms: Total (n = 25)	Group 1 (n = 16)	Group 2 (n = 9)
Irritability and/or anxiety	25	15	9
Moodiness and/or anger	16	13	5
Depression	16	10	6
Bloating	13	8	5
Headache	11	8	3
Breast tenderness	11	7	4
Fatigue	11	4	7
Low-back pain	9	5	4
Abdominal cramps	8	5	3

the study: 5 withdrew after the baseline monitoring; 6 withdrew because of illness or injury; 3 were away for a significant period of time; 3 did not have time to continue participating; and 3 became pregnant during the study.

Table 1 shows the subject characteristics for the initial cohort, the dropouts, the total subjects who completed, and each of the 2 study groups. There were no differences among any of the study groups in terms of initial level of PMS symptom severity, age, cycle length, and number of children. Similarly, there were no statistical differences (chi-square test) for the same characteristics, including initial PMS scores between the dropout group and the study group.

The major symptoms monitored for the study group (Table 2) showed a similar distribution and frequency as reported in the literature about women with PMS.[4,5,16] The distribution was similar in both study groups.

Comparisons of average global scores (as calculated from daily symptom ratings) for the baseline, treatment, and placebo phases of the study are shown in Table 3 and Figure 2. For the total group, there was a significant decrease in the mean global scores in the treatment phase compared with both the baseline and the placebo phases. This result was also seen for the treatment-first group (group 1). For the placebo-first group (group 2), there was a significant decrease in scores during treatment compared with the baseline; however, there was no difference at the $P = .05$ level between treatment and placebo scores.

Twenty-three of the 25 subjects who completed the trial had a mean score for the treatment phase lower than the mean baseline score. Fourteen subjects had a reduction in treatment scores of 30% or more compared with baseline, which is considered to be clinically significant.[17]

DISCUSSION

The results of the study support anecdotal and case study evidence that chiropractic therapy consisting of spinal manipulation and soft-tissue therapy can reduce symptom levels in some women with PMS. Just over half of the subjects who completed the trial showed a significant improvement in symptom levels after treatment.

There are a number of limitations to the study that need to be taken into account in applying the trial results to the general population of women with PMS. The relatively small sample size, although large enough for statistical purposes, makes it difficult to apply the results to the general population, despite the appearance that the study sample was a representative sample. As a result of the long trial period (each subject was required to be in the study for a minimum of 9 months), compliance was difficult; a large number of participants dropped out, with the effect on the results not known. Follow-up effects were not obtained so that the longer-term effects of the treatment are not known. Informal indications from subjects were that the effects were short-lived, with regular treatment needed on a monthly or bimonthly basis. This aspect requires further investigation. The inability to blind the treating practitioners to the type of intervention delivered is a problem associated with all manual therapy trials. Similarly, the development of an appropriate placebo has been a major problem. The placebo in this trial involved the use of a spring-loaded, adjusting instrument that was turned down maximally to minimize the impulse delivered away from the normal point of contact. Haas et al[18] found that this procedure was satisfactory. However, it can be argued that it is impossible to remove all effects of a placebo used in manual therapy trials; this would account for a part of the apparent placebo effect with group 2. In general, the presence of the Hawthorne effect, in which the construct validity of a study is compromised by the introduction of subjects' and practitioners' expectation bias, would contribute to a possible placebo effect.

There are several theoretical models that could provide a basis for the role of chiropractic treatment in PMS management. Normalizing neurologic activity is a fundamental premise of chiropractic treatment.[19,20] In particular, the somatovisceral reflex hypothesis states that somatic sensory input arising from the richly innervated soft-tissue structures of the vertebral motion segments may initiate or modify a visceral activity such as abdominal cramping and vascular headaches.[21,22]

A more recent hypothesis involves the role of endogenous opiate peptides. There is evidence that aberrant cyclic changes in circulating endogenous opiate peptide levels may play a role in the pathophysiology of PMS. In particular, an excessive drop of endogenous opiate peptides during the premenstrual weeks in women with PMS has been found, which may account for a number of PMS symptoms.[23] Chiropractic manipulative therapy may cause a change in β-

Table 3. *Summary of results*

	Mean global scores (SD)			Tx vs baseline	Tx vs placebo
	Baseline	Treatment	Placebo		
Total (n = 25)	54.0 (26.0)	34.9 (25.3)	43.11 (26.2)	Reduced 35.4% $P = .00001$	Reduced 19.0% $P = .006$
Group 1 (n = 16)	54.4 (29.8)	36.7 (27.7)	44.2 (28.6)	Reduced 32.5% $P = .0001$	Reduced 17.0% $P = .041$
Group 2 (n = 9)	53.1 (13.2)	30.3 (19.0)	40.1 (20.4)	Reduced 42.9% $P = .010$	Reduced 24.4% $P = 0.21$

SD, Standard deviation; *Tx*, chiropractic treatment.

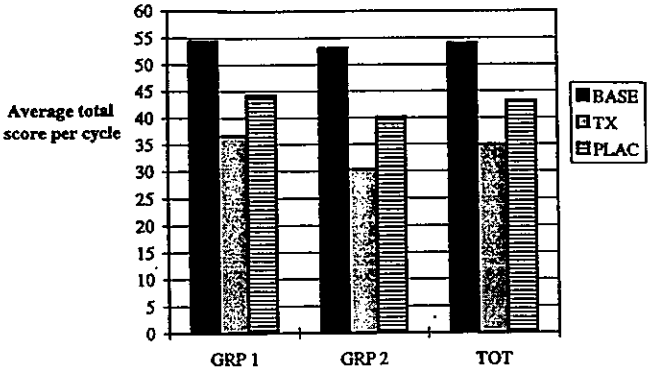

Fig 2. *Comparison of average total scores for baseline, treatment, and placebo phases.*

endorphin (an endogenous opiate peptide) levels. This has been used to explain the pain relief obtained from chiropractic manipulative therapy.[24,25]

A further theory implicates prostaglandins in PMS. Abnormal production of prostaglandins has been found in women with PMS. Abnormal prostaglandin levels can give rise to symptoms similar to those found in PMS.[26] There is some evidence that spinal manipulation may be associated with a reduction in plasma levels of prostaglandins.[27]

CONCLUSIONS

Within the limitations of the study, the results support the hypothesis that the symptoms associated with PMS can generally be reduced by chiropractic treatment consisting of adjustments and soft-tissue therapy. However, the role of a placebo effect needs further elucidation, given that the group receiving the placebo first, although improving over the baseline, showed no further improvement when they had actual treatment.

ACKNOWLEDGMENTS

We thank Associate Professor Seba Chandraraj and the private practitioners who participated in the trial.

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