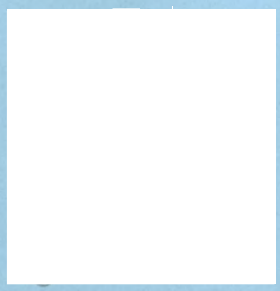
AN EVALUATION OF THE EFFICACY OF A HOMEOPATHIC COMPLEX, PREMENSTRON®, IN THE TREATMENT OF PREMENSTRUAL SYNDROME IN TERMS OF THE PATIENTS' PERCEPTION

by

SHANIE SARAWAN



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Dissertation submitted in partial compliance with the Requirements for the Master's Degree in Technology in the Department of Homeopathy at Technikon Natal.

I, Shanie Sarawan, do hereby declare that this dissertation represents my own work in both concept and execution.

Shanie Sarawan — 18/07/01 Date of signature

APPROVED FOR FINAL SUBMISSION

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THIS DISSERTATION IS DEDICATED TO MY MOTHER, SIMPLY

BECAUSE SHE IS WHO SHE IS.

ACKNOWLEDGEMENTS

The author wishes to express his gratitude to the undermentioned persons for their assistance in the preparation of this dissertation.

Dr. Richard Steele — Supervisor

The staff at the Pavillion Pharmacy

ABSTRACT

The purpose of this double –blind placebo-controlled study was to evaluate the efficacy of a homeopathic complex, Premenstron®, in the treatment of premenstrual syndrome in terms of the patients' perception of the efficacy of the treatment.

Thirty-four patients were selected from volunteers who met the diagnostic criteria developed by Dalton (1984:19). Of these patients thirty completed the study. These patients were divided into two groups according to simple random sampling. Data was collected at the Homeopathic Day Clinic at Technikon Natal.

Half of the patients received a placebo and the other half received the homeopathic complex. Patients were treated over a period of approximately two months (three consultations).

The patients completed the Moos Menstrual Distress Questionnaire at each consultation. The questionnaire consists of 47 symptoms grouped into eight subscales. Results were analysed statistically using the Mann Whitney unpaired test (inter-group comparison) and the Wilcoxon's sign rank test (intra-group comparison).

When the three questionnaires for each patient were compared, it was found that the placebo group did improve in the second consultation (P= 0.016) but the placebo effect did not last through to the third consultation. The treatment group

did show an improvement in the third consultation (P= 0.005) but not significantly enough to consider the complex effective when compared to the efficacy of the placebo. On comparing the two groups with regards to the subscales of the questionnaire, there were no differences in seven of the eight subscales. The only improvement noted was in that of water retention in consultation 3 (P= 0.016).

There were no improvements in the subscales of pain (P= 0.244), concentration (P= 0.091), behavioural changes (P= 0.950), negative effect (P=0.261), autonomic reactions (P=0.950), arousal (P=0.110) and control (P= 0.818) in the third consultations.

Overall, in the placebo group 53.3% of the patients showed an improvement, while 46.7% worsened. In the treatment group 86.7% showed an improvement and 12.3% worsened. However this improvement in the treatment group was not significant enough to verify that the complex was effective when analysed statistically and in comparison with the effects of the placebo.

Therefore the results of this clinical trial demonstrated that the homeopathic complex Premenstron® was ineffective in the treatment of PMS in terms of the patients' perception over the trial period of 2 months.

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DEFINITION OF TERMS

Allopathy: A term applied to that system of therapeutics in which diseases are treated by producing a condition incompatible with or antagonistic to the condition to be cured are alleviated. Called also heteropathy. (Dorland, 1988: 50.)

Climacteric: the syndrome of endocrine, somatic, and psychic changes occurring at the termination of the reproductive period in the female (menopause); it may also accompany the normal diminution of the sexual activity in the male. Called also climacterium. (Dorland, 1988:345.)

Corpus luteum: A yellow glandular mass in the ovary formed by an ovarian follicle that has matured and discharged its ovum. If the ovum has been impregnated, the corpus luteum increases in size and persists for several months. If impregnation has not taken place the corpus luteum degenerates and shrinks. The corpus luteum secretes progesterone. (Dorland, 1988: 385.)

Menarche: The establishment or beginning of the menstrual function (Dorland, 1988:1003).

Menstruation: The cyclical, physiologic discharge through the vagina of blood and mucosal tissues from the non-pregnant uterus. It is under hormonal control and normally recurs, usually at approximately four-week intervals, in the absence of pregnancy during the reproductive period (puberty through menopause) of the female of the human and a few species of primates. It is the culmination of the menstrual cycle. (Dorland, 1988: 1006.)

Ovulation: The discharge of the secondary oocyte from a vesicular follicle of the ovary (Dorland, 1988: 1205).

Pessary: A medicated vaginal suppository (Dorland, 1988: 1267).

Premenarche: The period before menstruation is established; preceding the menarche (Dorland, 1988: 1351).

Premenstruum: The period immediately preceding the occurrences of the menstrual flow (Dorland, 1988: 1351).

Similimum: The single homeopathic medicine, or the drug picture of which most nearly approaches the total symptom complex of the patient, which will certainly cure that patient, if the patient's condition is within reversible limits (Gaier, 1991: 509).

Suppository: A medicated mass adapted for introduction into the rectal, vaginal or urethral orifice of the body (Dorland, 1988: 1614).

CHAPTER 1

1.1. INTRODUCTION

Premenstrual syndrome (PMS) is a condition characterised by a variety of physical and emotional symptoms that occur in women before menstruation (Periodwatch, 2000). PMS was first used as a true medical disorder in 1931 by an American gynaecologist Dr. T. Frank (Lichten, 2000).

According to some studies, 75% of all women suffer from PMS to some degree (Hayman, 1996: 3). Of the estimated 40 million sufferers, more than 5 million require medical treatment for marked mood and behavioural changes (Lichten, 2000). Many women feel that if PMS were a male condition, there is little doubt that much of today's medical research would be devoted to exploring and understanding it. As yet, medical science has still not come up with a definitive treatment for PMS. (Hayman, 3: 1996.)

There are over 150 symptoms that have been attributed to PMS. These symptoms typically begin at or after ovulation, and continue until menstruation begins. Physical symptoms include headaches, fluid retention, fatigue, backache, abdominal cramping and weight gain. Emotional and behavioural symptoms may include anxiety, depression, tension and decreased work or social performance. (Lichten, 2000.)

Approximately 2% to 5% of women have severe PMS but many have only mild or moderate symptoms. PMS is most common in women in their 20's and 30's, and ceases entirely at menopause. (Periodwatch, 2000.)

There are many theories about what causes PMS (Hayman, 60:1996). Hormonal, psychological and nutritional factors may be involved (Periodwatch, 2000). It is not

known why some women have severe symptoms, and some mild while others have none (Lichten, 2000).

PMS is diagnosed by recording symptoms for several menstrual cycles. Symptoms that occur in a predictable pattern (beginning before menstruation and then disappearing when it begins) usually indicate PMS. (Periodwatch, 2000.) PMS may be followed by dysmenorrhoea (Merck, 1792: 1996).

There is much confusion over the treatment of PMS. Much of the previous research has been inconclusive or improperly conducted. (Hayman, 1996: 92.) Treatment usually involves finding the medication or combination of treatments that work for the individual. Dietary changes such as the elimination of salt, caffeine and alcohol and vigorous aerobic exercise are highly recommended. Allopathic treatments include diuretics, oral contraceptives, progesterone and many others. (Periodwatch, 2000)

There has been even less homeopathic research conducted on PMS. Martinez conducted a clinical trial using Folliculinum in 1990, indicating that said remedy did have an effect on PMS (Martinez, 1979: 104-105). Kirtland conducted research in 1994 based on this success, using Folliculinum 15CH with good results (Kirtland, 1994: 3).

As far as it could be ascertained in the literature review, there has been no research into PMS using a homeopathic complex.

Classical homeopathy is based on individualised treatment – finding the right remedy for the individual. Complexes go against this ideal, containing numerous remedies, usually in low potencies. There is a degree of contention between those who use either prescription method in homeopathy.

The purpose of this placebo-controlled clinical trial was to determine the efficacy of Premenstron®, a homeopathic complex, in the treatment of PMS in terms of the patients' perception of the treatment as assessed by the Moos Menstrual Distress Questionnaire (Appendix E).

CHAPTER 2

REVIEW OF THE RELATED LITERATURE

2.1 INTRODUCTION

Over half of the world's adult population experiences menstruation, and most of them, at some time or the other, will probably experience some distressing symptoms, physical or emotional, linked to "that time of the month". One of the most common, and most confusing experience, is premenstrual syndrome (PMS). (Hayman, 1996: vii.)

PMS was first scientifically described in 1931, but despite many studies since then, doctors are really no closer to understanding it. However it does seem to be more common today than in previous times. Some researchers claim that this is due to a general delay in childbirth and the birth of fewer children which results in more periods, while others say that it is due to a more toxic environment. (Kelly, 1992: 32.)

The social and economic implications of PMS are considerable. There is an increased incidence of ant-social behaviour, accidents, illnesses and psychiatric crises in premenstrual women. A 3-5% increase in absenteeism from work occurs around this time. (Lockie, 1992: 66.)

There are ramifications occurring within the family dynamic as well. Strains may be placed on couples due to emotional lability of the female. Children too, are sensitive to the mother's emotional state and have been known to respond to inexplicable mood swings with psychosomatic symptoms. (Lockie, 1992: 66.)

Many people, including health professionals tend to trivialize the impact of PMS, some even denying the existence of it (Lockie, 1992: 66). However, PMS is rapidly

becoming an increasingly recognizable condition which can no longer be brushed aside as a figment of the imagination. (Sandler, 1991: 66.)

2.2 AETIOLOGY

There are many presumed causes of PMS, yet they are only theories - constructed from observations, assumptions and some from sheer hunch. There is as much argument over what causes PMS, as there is over what it is and what might cure it. (Hayman, 1996: 28.)

These are some of the leading theories that have been put forward to explain the phenomenon of PMS:

2.2.1. Oestrogen and progesterone imbalances

It has been suggested that PMS occurs when there is an imbalance in levels of oestrogen and progesterone. These two hormones display marked variations, going through such a rise and fall, the timing of which often parallels the onset and relief of PMS, that it is understandable that they are seen as the cause. (Hayman, 1996: 29.)

The argument is that when a relative drop in progesterone occurs in comparison to oestrogen, or when the body is unable to make use of the progesterone circulating in the system, the uncomfortable reactions known as PMS occur (Hayman, 1996:29).

Whether it is due to an increase in oestrogen secreted by the ovaries during the menstrual cycle, or insufficient secretion of progesterone from the ovary, resulting in relatively high unopposed oestrogen levels, the end result is the same (Sandler, 1991: 67).

Experts believe that this imbalance affects production of brain chemicals such as serotonin and endorphins, and leads to lowered blood sugar (Kelly, 1992: 34). If the oestrogens predominate, women tend to feel anxious, and if progesterone predominates then they tend to feel depressed (Lark, 1984:30).

2.2.2. Prolactin

Another theory for PMS is that high levels of the hormone prolactin cause it. During the luteal phase of a woman's menstrual cycle it has been shown that there are increased levels of prolactin. (Hayman, 1996: 30.)

This hormone is produced by the pituitary gland and stimulates the growth and development of breast tissue, breast lactation and is in control of progesterone released from the corpus luteum in the ovaries (Sandler, 1991: 69).

If too much is produced then this leads to breast tenderness, lumpiness, and enlargement. A secondary effect is that it may alter oestrogen and progesterone balances in the body and affect mood. (Hayman, 1996: 30.)

2.2.3. Prostaglandins

A diet-related explanation for the cause of PMS involves the role of prostaglandins. These are essential fatty acids made by the body which are nutritionally important for growth and health. The most important of these is linoleic acid, a polyunsaturated fatty acid found in cereals and vegetables. If most of the fat in a woman's diet is obtained from animal fat she may have a diet that is low in linoleic acid. (Hayman, 1996: 31.)

Once ingested linoleic acid is converted to other fatty acids and then into prostaglandins. An enzyme called D6D is needed for this conversion, and women lacking this enzyme tend to suffer from PMS. This lack may be genetically

inherited, or may be due to lack of essential substances such as zinc, magnesium, pyridoxine, or due to emotional or physiological stress. (Sandler, 1991: 68.)

Many prostaglandins may have a regulatory effect on hormones such as oestrogen, progesterone and prolactin, ensuring that the correct quantities are produced. A deficiency in these prostaglandins would mean that there might be imbalances in the hormone levels, so causing PMS symptoms. (Hayman, 1996: 31.)

When the prostaglandin levels are low it is postulated that the women become more sensitive to even normal oestrogen-progesterone levels in the second half of their cycle. This oversensitvity to normal hormones can lead to exaggerated effects such as severe breast tenderness, fluid retention and emotional and behavioral disorders. (Sandler, 1991: 68.)

2.2.4. Opioids

One argument is that PMS is linked to opium-like substances which are produced in the brain. These are called endogenous opioid peptides, or endorphins, and are produced in the body to control temperature, bowel movements and whether one feels tired, hungry, happy or sad i.e. regulation of mood changes. (Sandler, 1991: 69.)

Many of the PMS symptoms mimic the symptoms of narcotic withdrawal eg. nausea, cramps and depression. Thus this theory has been advanced, that a lack of natural opioids leads to PMS. (Hayman, 1996: 31.)

Studies have shown that these opioids are not only produced in the brain, but are also affected by chemicals which are produced in the ovaries, and therefore levels may change throughout the menstrual cycle. As a result of these, opioids are at a low level in the premenstuum and may explain a drop in mood. (Hayman, 1996: 32.)

2.2.5. Blood sugar

Another theory is that PMS has to do with low blood sugar or glucose. Glucose is the body's chief source of energy and is carried by the blood to all tissues. If one did not eat for a long period, the blood glucose levels would drop. However, usually the level is kept within fairly narrow limits by the action of various hormones such as insulin, glucagon and adrenaline. Glucose can be stored in the liver and muscles so that if these levels begin to drop these reserves can be released. (Hayman, 1996: 32.)

However the release of adrenaline to stimulate this effect has the side effect of causing stress symptoms, making one tired and jittery. People have been noted to experience sweet cravings, and boosting energy levels by eating chocolates and sweets can actually make the situation worse. There is a quick increase in blood glucose levels followed by an immediate "rebound" reaction where the level falls. (Hayman, 1996: 32.)

This fall stimulates the release of more adrenaline, which starts the vicious cycle all over again. It is also suggested that when adrenaline releases glucose from cells, water takes it's place causing the bloating so may women complain about in PMS. (Hayman, 1996: 32.)

2.2.6. Nutritional deficiencies

Another diet-related argument is that PMS is linked to vitamin or mineral deficiencies. The symptoms of various dietary deficiencies can be shown to be similar to those of PMS, most notably a lack of vitamin B6, E, zinc and magnesium

and others. Modern diets are frequently lacking in these essential dietary factors. (Hayman, 1996: 33.)

In the premenstruum, women often have cravings for the B vitamins, which is similar to a craving for sugar. Instead of ingesting the vitamins, sugar is eaten such as cakes and chocolates and the craving is satisfied (see 2.2.5). These cravings should be dealt with by taking vitamins rather than sugars. (Sandler, 1991: 68.)

2.3. CLINICAL FEATURES

Most women experience some symptoms which are related to the menstrual cycle. In many the symptoms are not disabling and are of short duration, while others may experience a broad range of symptoms that disturb normal ability to function. (Berkow, Fletcher and Beers, 1996: 1791.)

Symptoms usually last from 10 to 12 or more days and usually disappear at the onset of menses. In many women, PMS is followed by dysmenorrhoea. (Berkow, Fletcher and Beers, 1996: 1791.)

PMS is not as specific in it's symptoms as conditions such as influenza or measles – it is a collection of symptoms that come together just before menstruation (Hayman, 1996: 13).

There are over 150 symptoms that have been linked to PMS. These symptoms are both physical and emotional in nature (Hayman, 1996: 13).

The most common symptoms are:

- ***Mood alteration and psychologic effects***

  Irritability; lack of control; agitation; anger; insomnia; difficulty concentrating; lethargy; depression and fatigue.

- ***Fluid retention***

  Oedema; transient weight gain; oliguria; breast enlargement and pain.

- ***Neurologic and vascular symptoms***

  Headache; vertigo; syncope; parasthesias of extremities; easy bruising; cardiac palpitations.

  Epilepsy may be aggravated.

- ***Gastrointestinal symptoms***

  Bloating; constipation; nausea; vomiting and changes in appetite.

- ***Pelvic heaviness or pressure***

- ***Backache***

- ***Skin problems***

  Acne; neurodermatitis; aggravation of other skin disorders.

- ***Respiratory problems***

- ***Eye complaints***

  Visual disturbances; conjunctivitis.

(Berkow, Fletcher and Beers, 1996:1791.)

2.4. TYPES OF PMS

The most common symptoms of which women with PMS complain about can be divided into 4 subgroups:

2.4.1. TYPE A:

This type of PMS is characterised by anxiety, irritability and mood swings. This type of PMS is the most common subtype affecting 65-75% of PMS sufferers. (Lockie, 1992: 67.) In some women the anxiety is followed by depression. The symptoms get worse in the days before the menstrual period and are relieved by its onset. The most likely cause is an imbalance in the circulating oestrogen and progesterone in the body (Lark, 1984: 27.)

2.4.2. TYPE C:

This subtype is characterised by sugar cravings, fatigue, headaches, palpitations and increased appetite. This affects 24-35% of premenstrual women. (Lockie, 1992: 67.) Many women with PMS note an increased craving for refined carbohydrates especially sugar, chocolates and pastries, and eat larger quantities of these foods before their period than they normally would. This craving is made worse during stress. A few hours after indulging in these foods, many women experience fatigue, headaches, shaking and dizziness. (Lark, 1984:29.)

2.4.3. TYPE H:

Women with type H PMS generally complain of abdominal bloating, breast tenderness and heaviness and weight gain. This affects 65-72% of sufferers. (Lockie, 1992: 67.) These women tend to retain excess salt and fluid, caused by an excess production of the pituitary hormone adreno-corticotrophic hormone (ACTH). The ACTH is then circulated via the blood to the adrenal glands. (Lark, 1984: 30.) Aldosterone release causes the kidneys to retain water and salt, so less urine is excreted (Lockie, 1992: 67).

2.4.4. TYPE D:

Depression, confusion, insomnia, crying, and memory loss characterize type D. This affects 23-35% of women and is more commonly found combined with PMS type A. (Lockie, 1992: 67.)

The PMS type A occurs first and is followed by type D symptoms a few days before the onset of the period. (Lockie, 1992: 67.) In these women oestrogen levels are found to be abnormally low, and the depressant effects of high or normal progesterone are not counterbalanced by oestrogen (Lark, 1984: 30). Another theory is that lead poisoning (exhaust fumes and factory outlets) block the action of oestrogen but not progesterone (Lockie, 1992: 30).

This type of PMS can be very serious because sufferers can experience suicidal thoughts (Lark, 1984:30).

At present medical research indicates that each subtype is due to it's own specific chemical imbalance. This shows exactly how multifaceted PMS is, with four different problem entities often coexisting in the same woman. (Lark, 1984: 30.)

2.5. CLINICAL DIAGNOSIS

The American Psychiatric Association has come up with specific diagnostic criteria for what it has termed premenstrual dysphoric disorder, a synonym for premenstrual syndrome. The symptoms largely involve the changes in mood rather than the physical symptoms that may occur in a woman's cycle. In order to diagnose this disorder a woman must have at least 5 of the following symptoms:

- Mood swings
- Decreased interest in usual activity
- Increase/ decrease in appetite
- Physical symptoms such as breast pain, bloating or headache
- Sleep disturbances
- Fatigue

The above symptoms must occur cyclically and during most of the woman's menstrual cycle, and they must be serious enough to interfere with activities. (Carlson, Eisenstat and Ziporyn, 1996: 509.)

Katerina Dalton, an Australian gynaecologist formulated the following criteria for the diagnosis of PMS:

- Symptoms must occur exclusively in the second half of the menstrual cycle.
- Symptoms must increase in severity as the cycle progresses.
- Symptoms must be relieved by the onset of full menstrual flow.
- There must be an absence of symptoms in the postmenstruum.
- Symptoms have to be present for at least 2 consecutive menstrual cycles.

(Dalton, 1984: 19.)

The Moos Menstrual Distress Questionnaire (Moos, 1968) (Appendix E) is one of the methods of assessing premenstrual symptomatology. Other methods include the Premenstrual Assessment Form and daily menstrual charts. There are 47 symptoms in the Menstrual Distress Questionnaire and these are divided into eight sub-scales. These sub-scales are: pain, water retention, negative affect, autonomic reaction, concentration, behavior change, and arousal. The subjects are asked to assign a numerical weight according to their experience of each of the 47 symptoms. (Hawes, 1992.) The Moos Menstrual Distress Questionnaire was the main assessment tool used in this study.

2.6. DIFFERENTIAL DIAGNOSIS

2.6.1 Dysmenorrhoea:

Dysmenorrhoea, the formal name for painful periods, can be classified into primary and secondary dysmenorrhoea. Primary dysmenorrhoea means that one has experienced painful periods since the onset of menstruation. (Hayman, 1996: 67.) This is a cyclical pain associated with the menses during the ovulatory cycle but without demonstrable lesions affecting the reproductive structures (Berkow, Fletcher and Beers, 1996: 1792).

Secondary dysmenorrhoea means that the periods became painful some time after the onset (Hayman, 1996: 63). This pain with the menses is caused by a demonstrable pathology (Berkow, Fletcher and Beers, 1996: 1792).

Primary dysmenorrhoea comes in one of two forms - spasmodic or congestive (Hayman, 1996: 63).

Spasmodic dysmenorrhoea occurs when one experiences severe griping pains that start just before the period or when it begins and can continue until bleeding stops. The cramps are centered in the uterus and affect the groin area and the inner thighs radiating outward. It is often accompanied by nausea and headaches. (Hayman, 1996: 63.)

Congestive dysmenorrhoea describes period pain, which starts some days before the period begins. There is a dull ache, which gradually worsens until the first day of bleeding when it recedes quickly or immediately. Women who suffer from congestive dysmenorrhoea usually have tender and swollen breasts, bloated abdomens, aching joints, swelling of fingers and feet, headaches, sinus problems, acne, clumsiness, insomnia and irritability. (Hayman, 1996: 63.)

2.6.2. Mittelshmertz Phenomenon

This defines a few days of uncomfortable griping pain, which occurs around the time of ovulation, approximately 12 to 16 days before the period starts. At ovulation the follicle in the ovary ruptures or breaks open, throwing out the egg which is then carried through the Fallopian tube to the uterus. (Hayman, 1996: 64.)

2.6.3. Endometriosis

This condition can produce many symptoms which are similar to those of PMS. Pain, especially before a period, depression, tiredness, difficulty in passing urine and bowel upsets are all common symptoms. (Hayman, 1996: 64.) In almost all cases there is severe pelvic pain and dysmenorrhoea (Kumar, 1992: 616).

Endometriosis is a condition in which functioning endometrial tissue is present in sites outside the uterine cavity. Endometriosis is usually confined to the peritoneal or serosal surfaces of abdominal organs, usually the ovaries, broad ligament and Pouch of Douglas. (Berkow, Fletcher and Beers, 1996: 1809.)

Some symptoms of endometriosis may follow a monthly cycle. Discomfort, tiredness and depression may be particularly acute just before a period. The absence or resolution of symptoms after the period begins is not present in endometriosis, while it is in PMS. (Hayman, 1996: 64.) Definitive diagnosis of endometriosis is by means of a laparoscopy (Berkow, Fletcher and Beers, 1996: 1809). Endometriosis is an important clinical condition that may cause infertility (Kumar, 1992: 616).

2.6.4. Peri-menopause

It may be difficult to distinguish peri-menopause from PMS in certain instances. If one is over 40, symptoms such as joint pains, depression, anxiety, forgetfulness, increased urge to pass urine and cystitis may actually be caused by the climacteric. (Hayman, 1996: 65). In addition one should also consider the possibility of

premature menopause in those women who are under the age of 40 (Berkow, Fletcher and Beers, 1992: 1793).

2.6.5. Chronic Pelvic inflammatory disease (PID)

PID is a widespread infection in the reproductive and pelvic organs. When chronic, there may be discharge, pain and general ill health (Berkow, Fletcher and Beers, 1996: 1789). PID may become worse just before a period begins (Hayman, 1996: 66).

2.7. MEDICAL TREATMENT

There is much disagreement about the treatment of PMS. Different treatments work for different women. The main problem is that scientific studies constantly disagree with word-of-mouth evidence about which treatments are effective. (Hayman, 1996: 92.)

2.7.1. Hormonal Treatment

Allopathically PMS may be treated by giving natural or artificial hormones to restore normal balance, based on the theory that PMS is caused by an imbalance in hormone levels associated with the menstrual cycle (Hayman, 1996: 96).

2.7.1.1. Progesterone / Progestogen

Progesterone is used based on the theory that PMS may be due to the body lacking it or having some inability to utilize it. It is offered either as progesterone, which is a naturally occurring form, or as progestogen, a synthetic version. Theoretically progesterone can relieve bloating, period pains and the nausea and diarrhoea often associated with PMS. Since it functions as a muscle relaxant and sedative, it is prescribed for PMS, stress or tension. (Hayman, 1996: 96.)

By boosting progesterone levels in the second part of the menstrual cycle, the luteal phase, these symptoms are relieved (Hayman, 1996: 97).

Progesterone, being difficult to produce in tablet form, is usually given as injections, implants or as suppositories or pessaries. Many doctors are not in favour of using progestogen because they feel it is ineffective or not as effective as progesterone. (Hayman, 1996: 97.)

However there is very little reliable research to show that either of these are outstanding treatments for PMS (Hayman, 1996: 98). Some women report a worthwhile ease of symptoms, while for some women progesterone brings little benefit (Kelly, 1992: 36). Some studies even indicate that taking progesterone may actually worsen symptoms (Carlson, Eisenstat and Ziporyn, 1996: 511).

2.7.1.2. Oestrogen

Oestrogen may be used to alleviate PMS by blocking ovulation. It would be administered as an implant or skin patch. The problem is that continued use of oestrogen in this way has harmful effects on the womb lining. Studies using oestrogen have been inconclusive. (Hayman, 1996: 98.)

2.7.1.3. Oestrogen and progesterone

One obvious way of blocking ovulation would be to use the oral contraceptive pill. The pill not only suppresses ovulation, but also the body's natural hormonal fluctuations. (Kelly, 1992: 36.)

In early studies of the Pill some women claimed that when using it some of their PMS symptoms improved. The studies were not focussing on PMS but on the

contraceptive effectiveness of the Pill, and thus evidence is based on word-of-mouth, and this can't really be said to give an accurate picture. (Hayman, 1996: 99.)

2.7.1.4. Danazol

One theory is that PMS is caused by an imbalance in the progesterone to oestrogen ratio during a particular phase in the menstrual cycle. PMS is not present before menarche, and disappears at menopause. It is also not present in women whose ovaries have been removed. Therefore a possible way to treat PMS is to stop ovarian activity through drug treatment, which Danazol does. (Hayman, 1996: 99.)

Danazol is a synthetic form of the male hormone testosterone, and has an anti-gonadotrophin effect. This means that it interferes with the pituitary's production of follicle-stimulating hormone (FSH) and lutenising hormone (LH). The surge of these two hormones is reduced and oestrogen production is discouraged, resulting in periods and ovulation stopping. (Hayman, 1996: 100.)

Danazol is effective in dealing with breast pain, anxiety, tiredness and food cravings, but is not as effective with other PMS symptoms. The side effects of Danazol include masculinisation of females, weight gain, depression, tiredness and joint pains, hot flushes and increased hair growth. (Carlson, Eisenstat and Ziporyn, 1996: 511.)

2.7.1.5. Gonadotrophin-releasing hormone (GnRH)

Another means of blocking ovulation is by using gonadotrophin-releasing hormone analogues such as Lupron and Synarel (Carlson, Eisenstat and Ziporyn, 1996: 511). These are synthetic substances that act on the pituitary gland by stimulating it to produce the hormones that trigger oestrogen production (Hayman, 1996: 100).

GnRH analogues can either be agonists or antagonists. An antagonist prevents the pituitary gland from producing the hormones, while an agonist stimulates the pituitary, prompting it to produce hormones all the time instead of in pulses as it would normally do (Hayman, 1996: 100).

Side effects to be expected are hot flushes, vaginal dryness, night sweats, loss of libido, breast tenderness, tiredness and irritability (Hayman, 1996: 101). GnRH analogues, as well as being extremely expensive, cannot be used for more than six months without compromising bone density (Carlson, Eisenstat and Ziporyn, 1996: 511).

2.7.2. Non-hormonal Drug therapy

2.7.2.1. Bromocriptine

Bromocriptine is used for conditions due to the overproduction of prolactin. Prolactin stimulates breast tissue. Bromocriptine inhibits the secretion of prolactin from the pituitary gland. It is given to mothers who do not want to breastfeed their infants. (Kelly, 1992: 37.)

Bromocriptine is used to alleviate the symptoms of breast pain or tenderness if taken in the luteal phase of the menstrual cycle (Carlson, Eisenstat and Ziporyn, 1996: 511). It may also be used to treat depression in females due to high prolactin levels (Hayman, 1996: 102).

Side effects are usually dose-related and nausea and vomiting are common (Hayman, 1996: 103). Postural hypotension and drowsiness have also been noted (Lennon Medicines, 1991: 186).

2.7.2.2. Anti-anxiety drugs

Anxiety may be part of or the main symptom in PMS. A woman may experience nervousness or tension with no obvious source. The two main classes of drugs used to deal with anxiety are the benzodiazepenes eg. diazepam, lorazepam and the beta-blockers eg. Propanalol. (Hayman, 1996: 103.)

The benzodiazepenes deal with the emotional results, acting on fear and unhappiness. The beta-blockers act on the physical symptoms of anxiety such as shaking, breathlessness and palpitations. (Hayman, 1996: 103.)

2.7.2.3. Anti-depressant drugs

There are two main types of anti-depressants used - tricyclic anti-depressants and monoamine-oxidase inhibitors (MAOI's). However, the side effects can make themselves felt very quickly. Tricyclic anti-depressants have side effects such as drowsiness, dizziness, blurred vision, constipation, dry mouth and difficulty urinating. (Hayman, 1996: 103.)

This is not a common therapy these days. Depending on what is used, anti-depressants have their own problems, including the risk of dependency. (Kelly, 1992: 37.)

2.7.2.4. Anti-prostaglandin drugs

Prostaglandins are released from cells when they are damaged in any way. The effect is the stimulation of pain, alerting one to the fact that something is wrong. Anti-prostaglandin drugs block the production of prostaglandins, thereby relieving pain, which may be felt before and during the period. Examples of anti-prostaglandin drugs are aspirin, paracetamol and ibuprofen. (Hayman, 1996: 104.)

One of the most effective drugs noted in treating PMS-related pain is Ponstan (mefenamic acid). The side effects of this drug include indigestion and diarrhoea (Hayman, 1996: 105).

2.7.2.5. Diuretics

Many women complain of bloating and cyclical weight gain due to fluid retention. Diuretics help to turn this excess fluid in the body into urine, increasing the frequency and quantity of urine. Side effects of nausea and dizziness are not uncommon. (Hayman, 1996: 106.)

Some research suggests that not only is premenstrual bloating a normal aspect of cyclical change, but that it is not associated with an actual increase in girth. Fluid may shift around the body, and there may be an increase in distension or pressure in the abdomen, but the actual external measurements do not increase. If this is so diuretics would not be an appropriate treatment. (Hayman, 1996: 106.)

2.8. HOMEOPATHIC TREATMENT

Homeopathic medicine has been used for over 200 years to treat a wide variety of illnesses. The word homeopathy means "like suffering". This describes the fundamental principle of homeopathic treatment: that the symptoms that a person experiences can be cured by a substance that would cause the same symptoms if a given to a healthy person i.e. "like cures like". (Rose, 1998: 10.)

This principle was recognized by Hippocrates over 2400 years ago, but was not implemented in a systematic way until Dr. Samuel Hahnemann (1755-1843) began to experiment with other forms of treatment, having grown disillusioned with the brutal medical practices of his day. (Rose, 1998: 10.)

Hahnemann, after experimentation, devised a method of preparing the medicine by systematically diluting the original medicine, or 'mother tincture', and shaking it vigorously between each dilution which enhanced the action of the medicine. He termed this method 'potentisation' and the resultant medicines potencies - thus the highest potencies contain the weakest solutions. (Rose, 1998: 10.)

This method is still in use today. The mother tincture is diluted in one of two scales, either 1 part in 100, the centissimal scale (C) or 1 part in 10, the decimal scale (x) (Rose, 1998: 10).

Giving such small doses has proved to be very controversial among the medical field because the original substance must eventually disappear altogether. It has been found that this occurs at the 12c dilution. It is assumed by homeopaths that the medicine leaves an imprint in the water during the vigorous shaking (succussions) between dilutions and that this message resonates within the body to promote healing. (Rose, 1998: 10.)

Homeopathic prescribing involves taking the whole person into account as far as possible and treating the person simultaneously on all levels - physical, mental and emotional. The idea is to 'treat the person, not the disease'. (Watson, 1993: 71.)

However there are other prescribing techniques within homeopathy, one of which is known as polypharmacy. This method encompasses any prescribing technique in which two or more remedies are prescribed simultaneously, either in alternation with each other or as a combined formula. Classical homeopathy uses one medicine at a time, with infrequent repetitions. (Watson, 1993: 71.)

Polypharmacy may be individualised, whereby several remedies are given either concurrently or alternately depending on what the individual may need. It may disease-based, in which multiple remedies are prescribed on the basis that they all

have a degree of similarity to a particular disease process, with no regard for the individual's peculiarities. (Watson, 1993: 71.)

In polypharmacy low potencies are usually used, within a range of tincture to 6c, and the prescription is repeated on a daily basis. The theoretical advantage is that by combining several remedies the practitioner is able to bypass the necessity to individualize each case, and can give every patient with the same pathology the same prescription. (Watson, 1993: 71.)

The assumption is that whichever remedy in the combination is most similar to the pathology of the person being treated will act while the others will do nothing, or that a group of remedies which have a similarity to the typical symptoms of the pathology, will collectively bring about a curative response. (Watson, 1993: 71.)

Pharma Natura Laboratories in Pretoria have put together a combination of different remedies in order to treat PMS, called Premenstron®. The symptom pictures of the individual remedies are as follows:

2.8.1. Agnus castus D1:

Sadness; absent-minded; nervous depression; difficult concentration; exhilaration alternating with sadness; peevish; lethargy alternating with frenzy; nausea; joint pains; swollen extremities; sleepless; flushes of burning heat.

2.8.2. Chamomilla radix D3:

Restless; impatient; always complaining; spiteful; snappish; hot, clammy sweat on forehead; distended abdomen; nipples inflamed and tender to touch; back pain; weep in sleep.

2.8.3. Lilium tigrinum D3:

Profound depression; anger; fainting in a warm room; nausea; bearing down sensation in lower abdomen; pain in ovaries; bloated feeling; burning in palms and soles; unable to sleep with wild feeling in head.

2.8.4. Caulophyllum thalictroides D4:

Internal trembling and weakness; exhaustion; nervous; excitable; fretful; dyspepsia; discoloration of skin before menstruation.

2.8.5. Equisetum arvense D4:

Bloating in abdomen; retention of water.

2.8.5. Zincum valerianicum D4:

Hysteria; painful affection involving especially the ovaries; violent neuralgic intermittent headaches; sleepless; ovaralgia with pain shooting down limbs, even to foot; can't sit still.

2.8.6. Ignatia amara D6:

Palpitations; headache; functional ovarian cysts; water retention; tendency to depression; before periods sweating is increased, especially axillary region; hair loss.

2.8.8. Kali carbonicum D6:

Irritability; panic attacks; anger; tenseness; hair loss; swelling of the face, especially upper eyelids; pain in vagina on intercourse; swollen, tender breasts; backache; sleepiness.

(Boericke 1997, Vermeulen 1997, Morrison 1993, Jouanny 1994.)

2.9. THE PLACEBO EFFECT

2.9.1 What is a placebo?

The term 'placebo' originates in the 116th Psalm in the Hebrew bible, where through translation errors the Latin version came to contain the "placebo" which literally means "I shall please". In 1785, the word placebo first appeared in a medical dictionary as "a commonplace method or medicine." Two editions later the word placebo meant "a make-believe medicine". (Krentzman, 2000.)

A placebo is an inert substance, or "fake" therapy or surgery. It is most often used as a control in an experiment or is given to a patient for its possible or probable beneficial effect. Why an inert substance, a so-called "sugar pill" would be effective is not completely understood. (Carroll, 2000.)

2.9.2. How does the placebo effect work?

The placebo effect is the measurable or observable effect on a person or group that has been given a placebo (Carroll, 2001). There are two components to the placebo effect. One is the anticipation (usually optimistic) of results because of the expectations associated with medication. This would be regarded as 'suggestibility', 'faith', or 'hope'. (Krentzman, 2000.)

The second component is spontaneous change, and at times this is even more important. If a placebo has been taken before a spontaneous improvement, it may be given the credit for the positive change. Conversely, if someone spontaneously develops a headache or a skin rash after taking a placebo, the placebo would be blamed. (Krentzman, 2000.)

Whether the placebo effect is mainly psychological or misunderstood spontaneous healing or due to some combination of the two cannot be known with complete confidence. But the powerful effect of the placebo is not in doubt. (Krentzman, 2000.)

2.9.3. The placebo effect and homeopathy

Placebo effects play a role in homeopathy, acupuncture, reflexology, bioharmonics, crystal power, etc. (Carroll, 2000). In homeopathy some of the forms of placebo are sugar of milk, cane sugar globules, tablets and alcohol (Dhawale, 1985: 419). In this trial alcohol was used as the placebo.

2.10 PAST RESEARCH

2.10.1. Allopathic research

Allopathic research to date has been far more extensive than those of complementary forms of medicine have. In 1995 research was conducted by Baker et al., the purpose of which was to evaluate the efficacy of progesterone vaginal suppositories in alleviation of nervous symptoms in patients with premenstrual syndrome. From an initial sample size of 25 subjects diagnosed with moderate to severe PMS, 17 females completed the 7-month, double-blind, placebo-controlled trial using 200mg vaginal progesterone suppositories.

Multiple modalities were used to evaluate symptoms, including the Spielberger self-evaluation rating, the Beck depression inventory and the Hamilton anxiety scale. In addition a psychiatrist interviewed each subject every month. Ovulation was determined monthly using a basal body temperature chart. Serum hormonal assays included beta-endorphin, progesterone, follicle-stimulating hormone, lutenizing hormone, estradiol and prolactin.

Hormonal assays confirmed no differences between treatment and control groups. Overall scores on all test vehicles were not significantly different between the two groups. However in the category of nervous symptoms, a significant improvement was found in symptoms relating to tension, mood swings, irritability and lack of control. This study confirmed the utility of twice daily 200mg progesterone vaginal suppositories in the alleviation of some of the PMS symptoms relating to anxiety and irritability. (Baker et al., 1995.)

Steiner et al. conducted research in 1994 to evaluate the efficacy and safety of fluoxetine (which selectively inhibits the re-uptake of serotonin) in the treatment of premenstrual syndrome. The trial consisted of a single-blind, placebo washout period lasting two menstrual cycles, followed by a randomized, double-blind, placebo-controlled trial of fluoxetine at a dose of either 20mg or 60mg per day or placebo for six menstrual cycles. Healthy women suffering from PMS were recruited. The primary outcome measure consisted of visual-analogue scales for tension, irritability and dysphoria.

Of 405 women enrolled in the placebo washout period, 313 entered the randomized part of the study. Only 180 of these women completed the study, which lasted six menstrual cycles. Fluoxetine at a dose of 20mg or 60mg per day was significantly better than the placebo in reducing tension and irritability and dysphoria as measured by the visual-analogue scales ($P < 0.001$). The women who received 60 mg of fluoxetine per reported significantly more side-effects than those receiving 20mg per day or placebo ($P < 0.001$).

Fluoxetine was concluded to be useful in the treatment of premenstrual syndrome. Treatment with fluoxetine at a dose of 20mg per day maximizes therapeutic efficacy while reducing the potential for side-effects. (Steiner et al., 1995.)

In 1993 Berger and Presser conducted a trial to assess the efficacy of alprazolam in the treatment of two groups of women diagnosed with late luteal phase dysphoric disorder (LLPDD), a synonym for PMS. The first group met only the diagnostic criteria for LLPDD. The second group experienced LLPDD and mild symptoms of anxiety and depression in the follicular phase.

A double-blind placebo-controlled crossover design was used in this trial. Patients were treated with alprazolam and placebo for 3 months each and completed daily measures of anxiety, tension, depression, irritability and feelings of being out of control. The response to alprazolam differed significantly by group. For the first group, alprazolam (0.25 mg three times per day) relieved the severity of tension ($P = 0.001$), irritability ($P= 0.005$), anxiety ($P= 0.008$) and feelings of being out of control ($P= 0.012$) more than placebo. The patients reported few side-effects. Alprazolam and placebo did not differ for the second group.

It was concluded that alprazolam benefits women diagnosed solely with LLPDD or PMS, and is not recommended for women who experience LLPDD as well as mild anxiety or depression during the follicular phase. (Berger and Presser, 1994.)

2.10.2. Complementary therapy research

In 1990 research was conducted by Goodale et al. into the alleviation of premenstrual syndrome symptoms with the relaxation response. During a 5 month study the effect of the relaxation response on premenstrual syndrome were examined in 46 women who were randomly assigned to one of three groups: a charting group, a reading group, and a relaxation response group. The relaxation

response group showed significantly greater improvement than both the charting and reading groups on physical symptoms (P less than 0.025 for both comparisons).

Women with severe symptoms in the relaxation response group showed a 58% improvement compared with a 27% improvement for the reading group and a 17% improvement for the charting group. The conclusion drawn from this study was that regular elicitation of the relaxation response is an effective treatment for physical and emotional premenstrual symptoms, and is most effective in women with severe symptoms. (Goodale et al., 1990)

Walsh and Polus (1999) conducted a randomized, placebo-controlled crossover clinical trial on the efficacy of chiropractic therapy on PMS. Twenty-five subjects who were diagnosed with PMS were used in the trial. After randomization, 16 of the subjects received high velocity, low amplitude spinal manipulation plus soft tissue therapy 2 to 3 times a week before the start of the period for at least three cycles. The remaining 9 subjects received a placebo treatment which consisted of spring-loaded adjusting instrument wound down for minimum force.

After a one-cycle washout, the 2 groups changed over. The Moos menstrual Distress questionnaire and daily symptom monitoring were used to assess the progress. The data were analyzed with paired t tests and Wilcoxon's sign rank tests with the level of significance set at $P< 0.05$.

There was a significant decrease in scores after treatment compared with baseline scores ($P= 0.0001$) as well as a statistically significant decrease in scores for the treatment phase compared with the placebo ($P= 0.06$).

For the group initially receiving the active treatment there was a great decrease in scores after treatment compared with the baseline scores ($P= 0.001$). There was also a significant decrease in scores for the treatment phase compared with the placebo ($P= 0.41$). For the group which received the placebo first, there was a

substantial decrease in scores during treatment compared with the baseline. However there was no difference found when the placebo and treatment scores were compared in this group at the P=0.05 level.

The results supported the hypothesis that PMS symptoms can be reduced by chiropractic treatment, which in this experiment consisted of adjustments and soft-tissue therapy. The role of the placebo needs further elucidation as it was found that the group receiving the placebo first showed no further improvement when they had the actual treatment. (Walsh and Polus, 1999)

The efficacy of a standardized Ginkgo biloba extract (EGb761) in treating the congestive symptoms of PMS was evaluated in a controlled multicentric double-blind study versus placebo. The population studied was a group of 165 women aged between 18 and 45 who all suffered from congestive premenstrual troubles during at least 7 days per cycle for at least 3 consecutive cycles. The characteristics of patients and PMS were the same in both groups. The observation of one menstrual cycle confirmed the diagnosis of PMS. The, during the following 2 cycles, each patient received either EGb761 or placebo from the 16th day of the first cycle to the 5th day of the next cycle.

A double-evaluation of the symptoms was realized by the patient using a daily rating scale and by the practitioner during the visits at the premenstrual phase before and after the two cycle's treatment. From 165 patients included, 143 observations were available. With good acceptability Egb761 was effective against the congestive symptoms of PMS. The extract was particularly good against congestive breast symptoms with a statistical significance between Egb761 and placebo. The neurophysiological symptoms were also improved. (Tamborini and Taurelle, 1993)

Oleson and Flocco (1993) conducted a randomized controlled study of PMS symptoms treated with ear, hand and foot reflexology. The objective was to

determine whether reflexology therapy could significantly reduce premenstrual symptoms compared to placebo treatment. Thirty-five women who complained of previous premenstrual distress were randomly assigned to be treated by ear, hand and foot reflexology or to receive foot reflexology. All the participants completed a daily diary, which monitored 38 premenstrual symptoms on a four-point scale.

Somatic and psychological indicators of premenstrual distress were recorded every day for two months before treatment, for the two months during reflexology and for two months afterward. The reflexology sessions for both groups were conducted by a trained reflexologist once a week for eight weeks and lasted thirty minutes each. Analysis of variance for repeated measures demonstrated a significantly greater decrease in premenstrual symptoms for the women who were given the true reflexology treatment than for those women in the placebo group. (Oleson and Flocco, 1993)

Most of the homeopathic research on premenstrual syndrome has centered on the use of Folliculinum. Martinez conducted a double-blind placebo-controlled trial using Folliculinum in potencies 9c and 15c in 32 patients. A questionnaire was given to all the patients' prescribed Folliculinum at their first consultation, to be collected at the subsequent consultation. The duration of treatment was two to four months. Of all the patients, 88% showed a satisfactory response to the treatment according to the questionnaire.

Most of the patients (61%) noted an improvement from the second cycle after having started the treatment. 93% of the patients felt that the treatment had physiological effects while only 7% felt that the effect might be due to the placebo effect. The most marked effects on particular symptoms were on breast swelling, metrorrhagia and menstrual irregularities. One of the recommendations of the researchers was that a double-blind study of the effect of Folliculinum in PMS be carried out. (Martinez, 1990)

However, the statistical methods used to arrive at the above percentages are not elucidated. Therefore one cannot evaluate the reliability of these results.

Kirtland conducted research in 1995, using Folliculinum 15CH in the treatment of women suffering from PMS. A sample of 31 women were selected and from this sample 16 were treated with Folliculinum and the other 15 received placebo. This was a double-blind study, with a neutral pharmacist having dispensed the medication/ placebo. (Kirtland, 1995: 67.)

Two questionnaires were used to numerically evaluate patients' symptoms- the Moos Menstrual Distress Questionnaire and the Premenstrual Assessment Form. Mann Whitney unpaired tests were used to statistically evaluate the results. It was seen that there was a statistically significant difference in the following symptoms for the treated group: muscle stiffness, loneliness, swollen breasts, irritability, mood swings and depression. (Kirtland, 1995: 67-68.)

Of the treated group 89% improved, 4% remained unchanged and 7% worsened. In the placebo group 7% improved, 4% remained unchanged, while 89% worsened. (Kirtland, 1995: 67.)

However, upon close scrutiny of the statistical procedures used in the trial conducted by Kirtland, some of the methods used are questionable and may result in an inaccurate assessment of the results.

From the above literature it can be seen that steps have been taken to determine the efficacy of complementary therapies in the treatment of PMS, including homeopathy. The present study was different to those of Martinez and Kirtland because it involved the use of an over-the-counter complex, which is freely available in pharmacies and health shops, thus making them more accessible to the general public.

To many consumers, these commercial complexes are representative of homeopathy, and as such, are representative of the efficacy of homeopathy. This shows the need for research of this nature, which would benefit both the public and homeopathy. The inadequacies found in the research conducted by Kirtland also shows the need for properly conducted clinical trials with sound statistical analyses within homeopathy in order to uphold the standard of medical science.

CHAPTER 3

MATERIALS AND METHODS

3.1. Objectives

The objective of this double-blind placebo-controlled study was to determine the efficacy of a homeopathic complex, Premenstron®, in the treatment of premenstrual syndrome in terms of the patient's perception of the effect of the treatment as assessed by the Moos Menstrual Distress Questionnaire (Appendix E).

3.2. Study Design

The sample size was 34. 17 patients were allocated to the treatment group and 17 to the placebo group.

Simple random sampling was used to place each individual in the sample group in the treatment or placebo group. 34 pieces of paper, 17 marked placebo and 17 marked treatment were placed in an envelope, and a neutral party marked a "T" (treatment) or "P" (placebo) on a numbered list up to 34. As each patient came into the trial they were allocated a group according to the corresponding number e.g. patient number 7 would be given the treatment accorded to number 7 on the randomised list.

The trial lasted approximately two months per patient, which effectively started at the first consultation. Thus, after the initial consultation there would be records of two menstrual periods per patient as assessed by the Moos Menstrual Distress Questionnaire (Appendix E).

3.3. Subjects

34 female subjects were included in the study. These were women from the greater Durban area who suffer from PMS. The sample group was obtained by means of convenience sampling i.e. those who responded to advertisements. Patient participation in the trial was voluntary, and each patient had to read the Study Information Sheet (Appendix A) and then sign the required Informed Consent Form (Appendix B).

Patients were asked not to change their lifestyles for the duration of the trial to minimise any variations.

3.3.1. Inclusion Criteria:

3.3.1.1. Those chosen had to meet the diagnostic criteria as outlined by Dalton (Dalton, 1984: 19) (Appendix C).

3.3.1.2. Participants had to be post-menarche by at least one year and pre-menopausal.

3.3.2. Exclusion Criteria

3.3.2.1. Women who were on corticosteroids or those who had been on steroid treatment in the previous month, either topical or oral.

3.3.2.2. Women who were pregnant or planning to fall pregnant during the duration of the trial.

3.4. Ethics

The nature of the study was explained to the patients who qualified for the trial. If they agreed to participate the patient signed an Informed Consent Form (Appendix B).

3.5. Materials

The homeopathic complex Premenstron® was prepared in 24% alcohol according to the German Homeopathic Pharmacopoeia 16.2. (German Homeopathic Pharmacopoeia, 1993) The placebo was 24% alcohol only.

Each patient was given a 50ml bottle at the initial consultation for the duration of the 2 month trial period. The bottles containing the medication and placebo were labelled exactly the same.

3.6. Method

3.6.1. Patients were obtained through advertisements placed in the Highway Mail, Berea Mail and Sunday Tribune newspapers, and from those who responded to posters placed at the campuses of the University of Natal, Technikon Natal, and ML Sultan Technikon.

3.6.2. The researcher assessed the patients according to the exclusion and inclusion criteria to see if they were suitable for the study. If the patient was accepted into the study the researcher continued with the initial consultation.

3.6.2.1. Each patient accepted into the study received a study information sheet, which outlined what the trial entailed (Appendix A).

3.6.2.2. If the patient agreed to participate she signed an Informed Consent Form (Appendix B).

3.6.2.3. The researcher conducted a medical case history.

3.6.2.4. The researcher conducted a complete general physical examination.

3.6.2.5. The patient then filled out the Personal Details Forms (Appendix D) followed by the Menstrual Distress Questionnaire (Appendix E). This was to ensure that a baseline of the patient's symptoms could be obtained.

3.6.3. After the consultation a neutral party who had the randomisation sheet gave the patient the treatment corresponding to their entry number in the trial.

3.6.4. The patients were informed on how to take, handle and store their treatment (Appendix G). Patients were instructed to take the active medication/ placebo 10 days before the onset of their period. Patients were instructed to take no other medication for PMS during the course of the study.

3.6.5. Follow-up consultations took place approximately one month later, depending on the length of their menstrual cycle. At the follow-up consultation the patient's general response to the treatment was reviewed. The patient then completed the Menstrual Distress Questionnaire (Appendix E) once more. The patients were told to continue taking the medication in the prescribed manner.

3.6.6. At the third and final visit, approximately one month later, the patients were reassessed and questioned about their overall experience for the duration of trial. The Menstrual Distress Questionnaire (Appendix E) was completed for the final time. The patients were then told which treatment they had been receiving. If the patient had been on the placebo they were given a bottle of the active medication.

3.7. Statistical Analysis

Four subjects dropped out from the study, so statistical analysis was on the basis of 30 results i.e. 15 placebo and 15 treatment. All the questionnaires were screened and all the symptoms were assigned numerical values, which were entered on spreadsheets. Statistical evaluation of the data was conducted using SPSS Base 9.0 by SPSS Inc. (444 N. Michigan Avenue, Chicago, Illinois, 60611, U.S.A).

3.7.1. Methods of Data Analysis

Non parametric tests were used to perform the analyses, as the sample sizes were small i.e. 15 patients in each group. The Mann Whitney Unpaired test and the Wilcoxon's sign rank tests were the two non-parametric tests used. (Daniel, 1978: 31,82.) The level of significance was set at 5% or 0.05.

3.7.1.1. Procedure 1

Comparison between groups 1 (placebo) and Group 2 (treatment)

Three Mann Whitney Unpaired tests (intergroup comparisons) were used to compare groups 1 and 2. The two groups were treated as being independent of each other. The purpose was to find out whether there was any difference between the two groups with respect to the totals of the premenstrual column in the questionnaire, observed 3 times each (beginning, follow-up and end).

(i) Hypothesis testing

The null hypothesis Ho stated that there was no difference between the two groups with respect to the variable of interest. The alternative hypothesis H1 stated that there was a difference between the two groups.

Ho : there is no difference between the 2 groups
H1 : there is a difference between the 2 groups
$\alpha = 0.05$ = level of significance of the test

(ii) Decision rule

For a two –tailed test,

If $p \leq \alpha/2$ reject Ho

If $p > \alpha/2$ accept Ho

3.7.1.2 Procedure 2

Comparison between Group 1 (placebo) and Group 2 (treatment) for Subscales

24 Mann Whitney Unpaired tests were used to compare Group 1 and 2 with respect to the subscales. The purpose was to find out if there was any difference between the two groups with respect to the eight variables observed three times each (beginning, follow-up and end).

(i) Hypothesis testing

The null hypothesis Ho stated that there was no difference between Groups 1 and 2 with respect to the variables of interest. The alternative hypothesis stated that there was a difference.

Ho : There is no difference between the 2 groups

H1 : There is a difference between the 2 groups

$\alpha = 0.05$ = level of significance if the test

(ii) Decision rule

For a two-tailed test,

If $p \leq \alpha/2$ reject Ho.

If $p > \alpha/2$ accept Ho.

3.7.1.3. Procedure 3

Comparison within group 1 (placebo)

Two Wilcoxon's sign rank tests were used within group 1 to find out whether there was any improvement between consultations 1 and 2 and consultations 1 and 3 (beginning and end).

(i) Hypothesis testing

The null hypothesis Ho stated that there was no improvement between consultations 1 and consultations 3 within group 1 (placebo) with respect to the variable of interest. The alternative hypothesis stated that there was an improvement.

Ho : There is no improvement in patient perception
H1 : There is an improvement in patient perception
$\alpha = 0.05$ = level of significance if the test

(ii) Decision rule:

For a one-tailed test,
If $p \leq \alpha$ reject Ho.
If $p > \alpha$ accept Ho.

3.7.1.4. Procedure 4

Comparison within group 1 (placebo) for subscales

16 Wilcoxon's sign rank tests were used within group 1 to find out whether there was any improvement between consultations 1 and 3 with respect to each of the

eight subscales within the questionnaire i.e. pain, concentration, negative effect, autonomic reactions, arousal, behavioral changes, water retention and control (Appendix F).

(i) Hypothesis testing

The null hypothesis Ho stated that there was no improvement between consultations 1 and consultations 3 within group 1 (placebo) with respect to the variables of interest. The alternative hypothesis stated that there was an improvement.

Ho : There is no improvement in patient perception
H1 : There is an improvement in patient perception
$\alpha = 0.05$ = level of significance if the test

(ii) Decision rule

For a one-tailed test,
If $p \leq \alpha$ reject Ho.
If $p > \alpha$ accept Ho.

3.7.1.5. Procedure 5

Comparison within group 2 (treatment)

2 Wilcoxon's sign rank tests were used within group 2 to find out if the were any improvement between consultations 1 and 2 and between consultations 1 and 3.

(i) Hypothesis testing

The null hypothesis Ho stated that there was no improvement between consultations 1 and consultations 3 within group 2 (treatment) with respect to the variable of interest. The alternative hypothesis stated that there was an improvement.

Ho : There is no improvement in patient perception
H1 : There is an improvement in patient perception
$\alpha = 0.05$ = level of significance if the test

(iii) *Decision rule*

For a one-tailed test,
If $p \leq \alpha$ reject Ho.
If $p > \alpha$ accept Ho.

3.7.1.6. Procedure 6:

Comparison within group 2 for subscales

16 Wilcoxon's sign rank tests were used within group 2 to find out whether there was any improvement between consultations 1 and 3 with respect to each of the eight subscales within the questionnaire (Appendix F).

(i) Hypothesis testing

The null hypothesis Ho stated that there was no improvement between consultations 1 and consultations 3 within group 2 (treatment) with respect to the variables of interest. The alternative hypothesis stated that there was an improvement.

Ho : There is no improvement in patient perception

H1 : There is an improvement in patient perception

$\alpha = 0.05$ = level of significance if the test

(i) Decision rule:

For a one-tailed test,

If $p \leq \alpha$ reject Ho.

If $p > \alpha$ accept Ho.

3.7.1.7. Procedure 7

A barchart will be constructed to present findings of the Moos Menstrual Distress Questionnaire. The barchart will be able to give a visual summary of the results obtained from the comparison of the means of the totals of the questionnaire between Group 1 (placebo) and Group 2 (treatment) for consultations 1, 2 and 3. All barcharts will be made using the Microsoft package Excel.

3.7.1.8. Procedure 8

A barchart will be constructed to give a visual summary of the results obtained from the comparison between consultations 1 and 3 with regards to the means of the eight subscales for Group 1 (placebo).

3.7.1.9. Procedure 9

A barchart will be constructed to give a visual summary of the results obtained from the comparison between consultations 1 and 3 with regards to the means of the eight subscales for Group 2 (treatment).

3.7.1.10. Procedure 10

A barchart will be constructed to give a visual summary of the results obtained from the comparison between Group 1 (placebo) and Group 2 (treatment) with regards to the eight subscales in consultation 3 i.e. the end of treatment.

3.7.1.11. Procedure 11

The percentages of the patients that improved and worsened will be calculated in both groups i.e. placebo and treatment, based on the sample of 30 patients.

CHAPTER 4

RESULTS

4.1. Introduction

This chapter deals with the results obtained from the statistical analysis of the data collected from the Moos Menstrual Distress Questionnaire (Appendix E).

4.2. Criteria for the admissibility of the data

- Only data collected from the trial was accepted.
- The examiner performed all case histories and examinations.
- Only the data collected from the Moos Menstrual Distress Questionnaire was used in the study.

4.3. Table 4.1. Comparison between Group 1 (placebo) and Group 2 (treatment)- using the Mann Whitney unpaired test for the totals of the Moos Menstrual Distress Questionnaire (Appendix E)

$\alpha = 0.05$ = level of significance

$P \leq \alpha/2$: placebo and treatment group are different

$P > \alpha/2$: placebo and treatment group are not different

PLACEBO Vs TEATMENT	PROBABILITY VALUE (P- value)	CONCLUSION
Consultation 1	0.198	No difference
Consultation 2	0.868	No difference
Consultation 3	0.480	No difference

The P-values of the Mann Whitney unpaired tests were calculated and tabulated above. There was no difference between Group 1 (placebo) and Group 2 (treatment) in all three consultations.

- In **consultation 1** the P-value was greater than 0.025. Thus the null hypothesis was accepted at the 5% level of significance. The conclusion drawn was that there was no difference between Group 1 and Group 2 in the first consultation.

- In **consultation 2** the P-value was greater than 0.025. . Thus the null hypothesis was accepted at the 5% level of significance. The conclusion drawn was that there was no difference between Group 1 and Group 2 in the second consultation.

- In **consultation 3** the P-value was greater than 0.025. . Thus the null hypothesis was accepted at the 5% level of significance. The conclusion drawn was that there was no difference between Group 1 and Group 2 in the third consultation.

4.4. Table 4.2.- Comparison between Group 1 (placebo) and Group 2 (treatment)- using the Mann Whitney unpaired test for the eight subscales of the Moos Menstrual Distress Questionnaire (Appendix E) (Appendix F)

$\alpha = 0.05$ = level of significance

$P \leq \alpha/2$: placebo and treatment group are different

$P > \alpha/2$: placebo and treatment group are not different

SUBSCALE	PLACEBO Vs TREATMENT	PROBABILITY VALUE (P- value)	CONCLUSION
PAIN	Consultation 1	0.176	No difference
	Consultation 2	0.119	No difference
	Consultation 3	0.244	No difference
CONCENTRATION	Consultation 1	0.070	No difference
	Consultation 2	0.117	No difference
	Consultation 3	0.091	No difference
BEHAVIOURAL CHANGES	Consultation 1	0.070	No difference
	Consultation 2	0.983	No difference
	Consultation 3	0.950	No difference

SUBSCALE	PLACEBO Vs TREATMENT	PROBABILITY VALUES (P- values)	CONCLUSIONS
AUTONOMIC REACTIONS	Consultation 1	0.386	No difference
	Consultation 2	0.249	No difference
	Consultation 3	0.950	No difference
WATER RETENTION	Consultation 1	0.307	No difference
	Consultation 2	0.037	No difference
	Consultation 3	0.016	Difference
NEGATIVE AFFECT	Consultation 1	0.852	No difference
	Consultation 2	0.835	No difference
	Consultation 3	0.261	No difference
AROUSAL	Consultation 1	0.060	No difference
	Consultation 2	0.078	No difference
	Consultation 3	0.110	No difference
CONTROL	Consultation 1	0.933	No difference
	Consultation 2	0.635	No difference
	Consultation 3	0.818	No difference

- The Mann Whitney unpaired tests revealed that there were no differences between Group 1 (placebo) and Group 2 (treatment) for the eight subscales in the questionnaire in all three consultations, except for that of water retention in the third consultation. The P-value was 0.016, and thus the null hypothesis was rejected at the 5% level of significance with regards to water retention.

4.5. Table 4.3.: Comparison within Group 1 (placebo) using the Wilcoxon's sign rank test for the totals of the Moos Menstrual Distress Questionnaire (Appendix E)

$\alpha = 0.05$ = level of significance

$P \leq \alpha$: Improvement

$P > \alpha$: No improvement

	PROBABILITY VALUES (P- values)	**CONCLUSIONS**
Consultation 1 Vs Consultation 2	0.016	Improvement
Consultation 1 Vs Consultation 3	0.191	No improvement

The Wilcoxon's sign rank tests revealed the following:

- On comparison of Consultation 1 and consultation 2 within the placebo group, the P-value was less than 0.05. Thus the null hypothesis was rejected at the 5% level of significance. This indicated that there was an improvement in the placebo group in the second consultation.

- On comparison of Consultation 2 and consultation 3 within the placebo group, the P-value was greater than 0.05. Thus the null hypothesis was accepted at the 5% level of significance. This indicated that there was no improvement in the placebo group in the third consultation.

4.6. Table 4.4.: Comparison within Group 1 (placebo)- using the Wilcoxon's sign rank test for the subscales of the Moos Menstrual Distress Questionnaire in Consultations 1 and 3 (beginning and end)

$\alpha = 0.05$ = level of significance

$P \leq \alpha$: Improvement

$P > \alpha$: No improvement

SUBSCALE	PROBABILITY VALUES (P- values)	CONCLUSIONS
PAIN	0.208	No improvement
CONCENTRATION	0.636	No improvement
BEHAVIOURAL CHANGE	0.877	No improvement
AUTONOMIC REACTIONS	0.026	Improvement
WATER RETENTION	0.100	No improvement
NEGATIVE AFFECT	0.172	No improvement
AROUSAL	0.053	No improvement
CONTROL	0.370	No improvement

Upon analysis of the results of the Wilcoxon's sign rank tests it was found that there was no significant improvement in consultation 3 within the placebo group in seven of the eight subscales. The only subscale which showed some improvement was that of autonomic reactions. The P-value was 0.026, and the null hypothesis was rejected at the 5% level of significance.

4.7. Table 4.5.: Comparison within Group 2 (treatment)- using the Wilcoxon's sign rank test for the totals of the Moos Menstrual Distress Questionnaire

$\alpha = 0.05$ = level of significance

$P \leq \alpha$: Improvement

$P > \alpha$: No improvement

	PROBABILITY VALUES (P- values)	**CONCLUSIONS**
Consultation 1 Vs Consultation 2	0.061	No improvement
Consultation 1 Vs Consultation 3	0.005	Improvement

The Wilcoxon's sign rank tests revealed the following:

- On comparison of Consultation 1 and consultation 2 within the treatment group, the P-value was greater than 0.05. Thus the null hypothesis was accepted at the 5% level of significance. This indicated that there was no improvement in the treatment group in the second consultation.

- On comparison of Consultation 2 and consultation 3 within the treatment group, the P-value was less than 0.05. Thus the null hypothesis was rejected at the 5% level of significance. This indicated that there was an improvement in the treatment group in the third consultation.

4.8. Table 4.6.: Comparison within Group 2 (treatment)- using the Wilcoxon's sign rank test for the subscales of the Moos Menstrual Distress Questionnaire (Appendix E) in Consultations 1 and 3

$\alpha = 0.05$ = level of significance

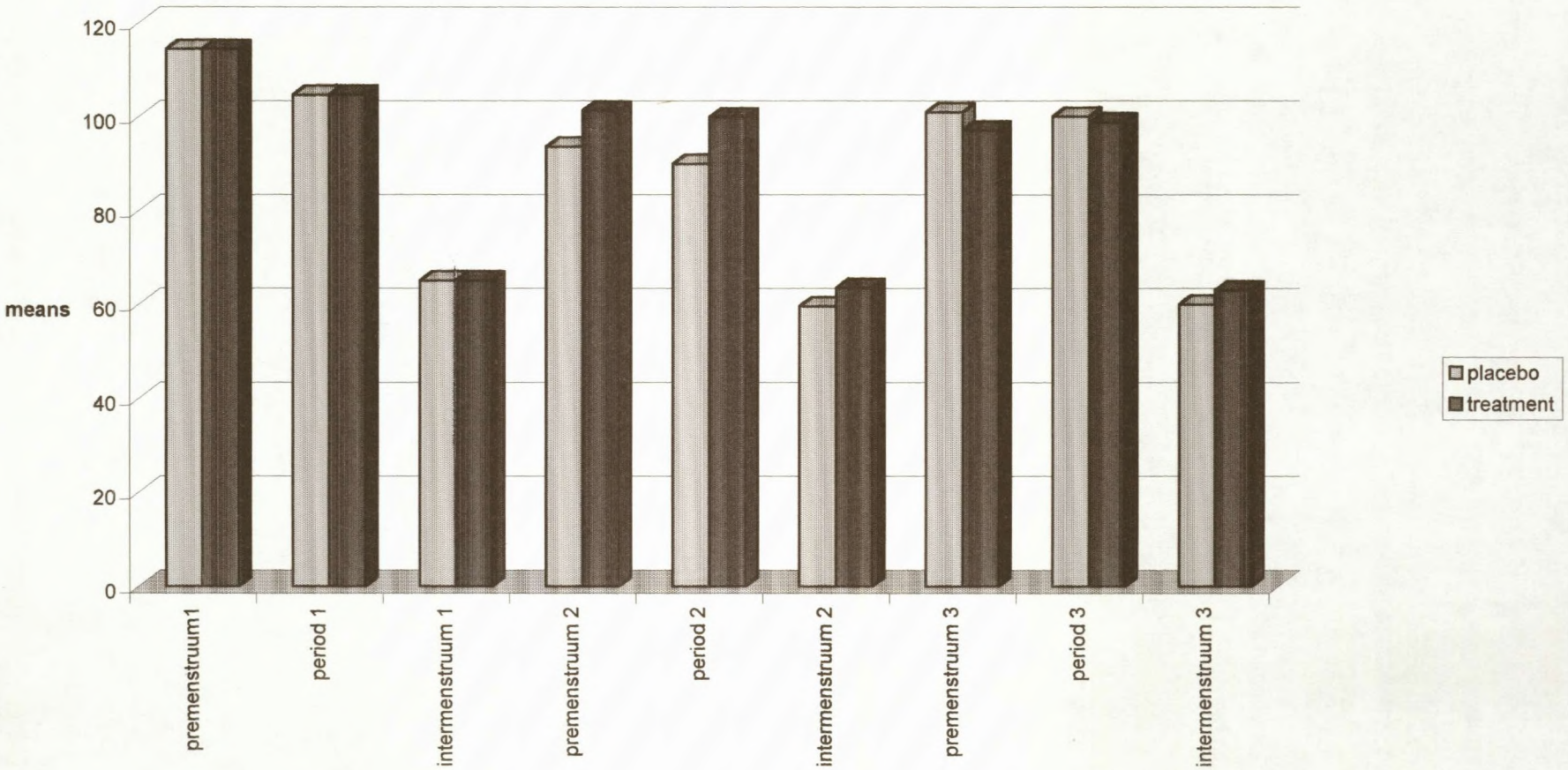
$P \leq \alpha$: Improvement

$P > \alpha$: No improvement

SUBSCALE	**PROBABILITY VALUES (P- values)**	**CONCLUSIONS**
PAIN	0.041	Improvement
CONCENTRATION	0.190	No improvement
BEHAVIOURAL CHANGE	0.181	No improvement
AUTONOMIC REACTIONS	0.296	No improvement
WATER RETENTION	0.023	Improvement
NEGATIVE AFFECT	0.006	Improvement
AROUSAL	0.292	No improvement
CONTROL	0.370	No improvement

Upon analysis of the results of the Wilcoxon's sign rank tests it was found that there was no significant improvement in consultation 3 within the treatment group in five of the eight subscales. The subscales which showed some improvement were those of pain, water retention and negative affect. The P-values were as follows: Pain (0.041) water retention (0.023) and negative affect (0.006). The null hypothesis was rejected at the 5% level of significance for each of these three subscales.

4.9. Figure 4.1. Comparison of totals of questionnaire between Group 1 (placebo) and Group 2 (treatment) for consultations 1, 2 and 3

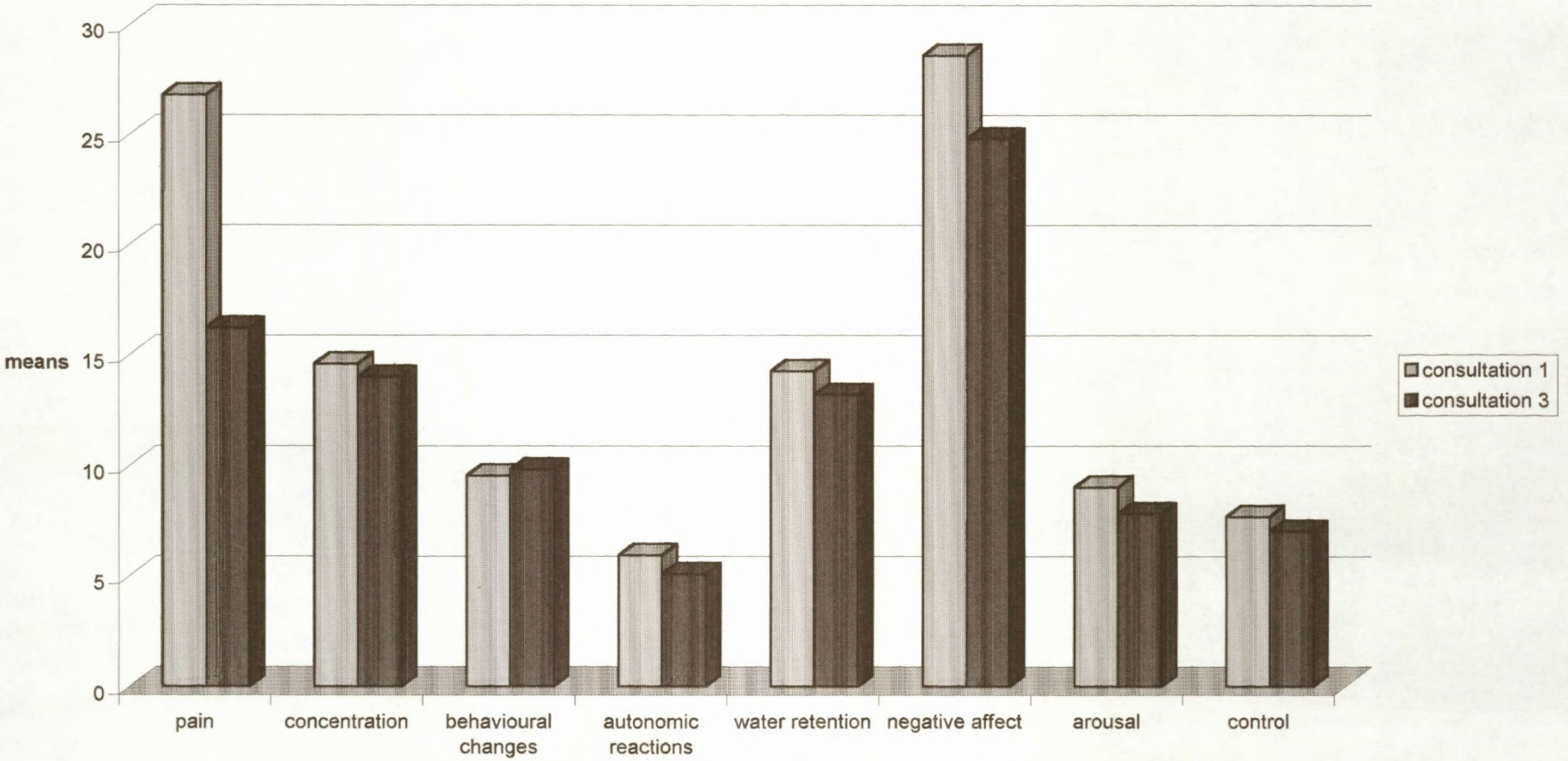


In **Figure 4.1** the bar chart readings for the first three readings i.e. premenstruum 1, period 1 and intermenstruum 1 are the same for both groups. This was done to illustrate a baseline from which to compare further readings, when the actual treatment of both groups had begun.

The latter two premenstrual readings are lower than the first. The comparison of the two groups in the second premenstrual reading revealed that the placebo group showed more of an improvement than the treatment group. However, in the third premenstrual reading the treatment group fared better than the placebo group. In this third reading though, the treatment group did not do better than the placebo group did in the second premenstrual reading.

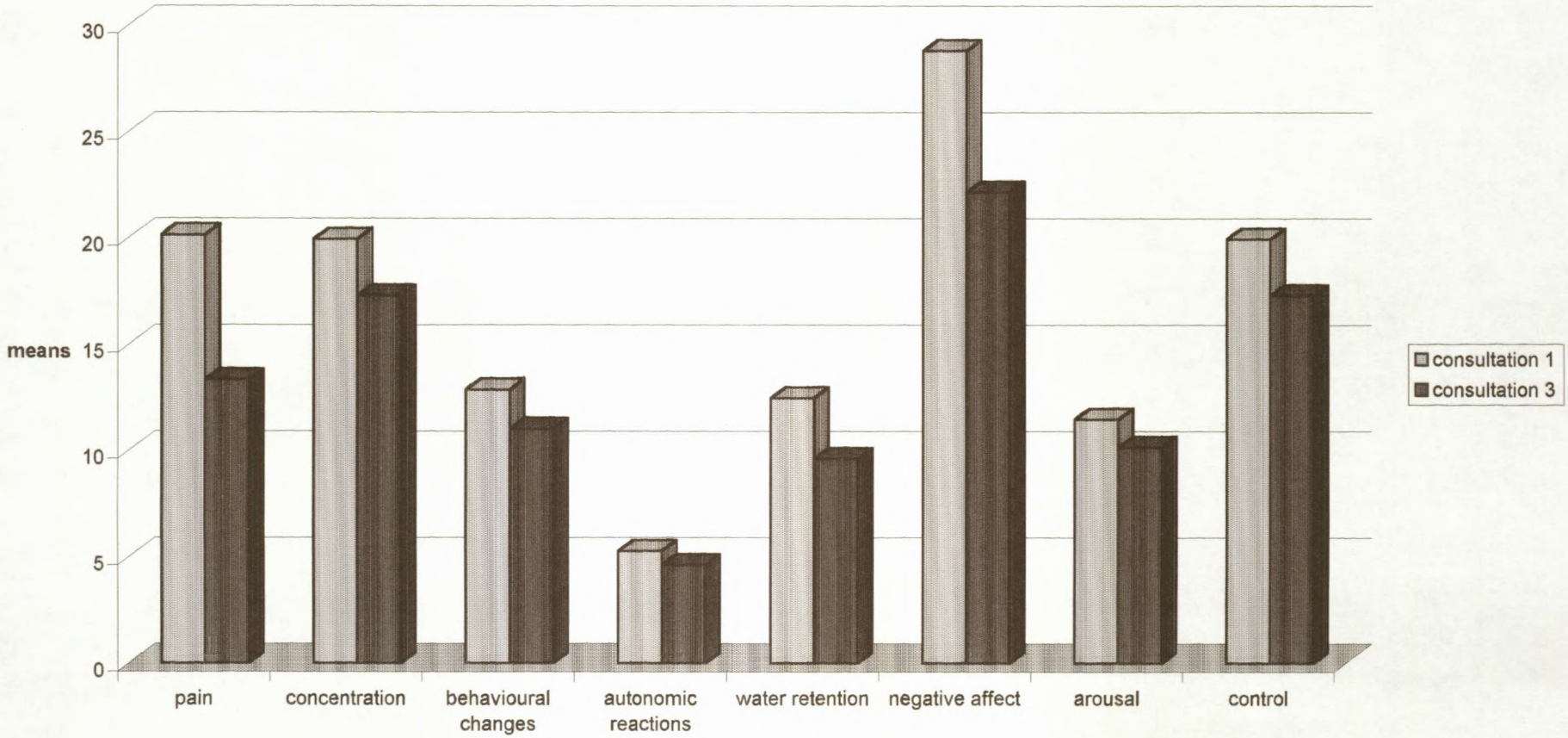
The intermenstrual and period readings were relatively consistent when compared to the baseline, and were only of secondary importance to the premenstrual readings.

4.10. Figure 4.2. Comparison of the means of the 8 subscales between consultations 1 and 3 for Group 1 (placebo)



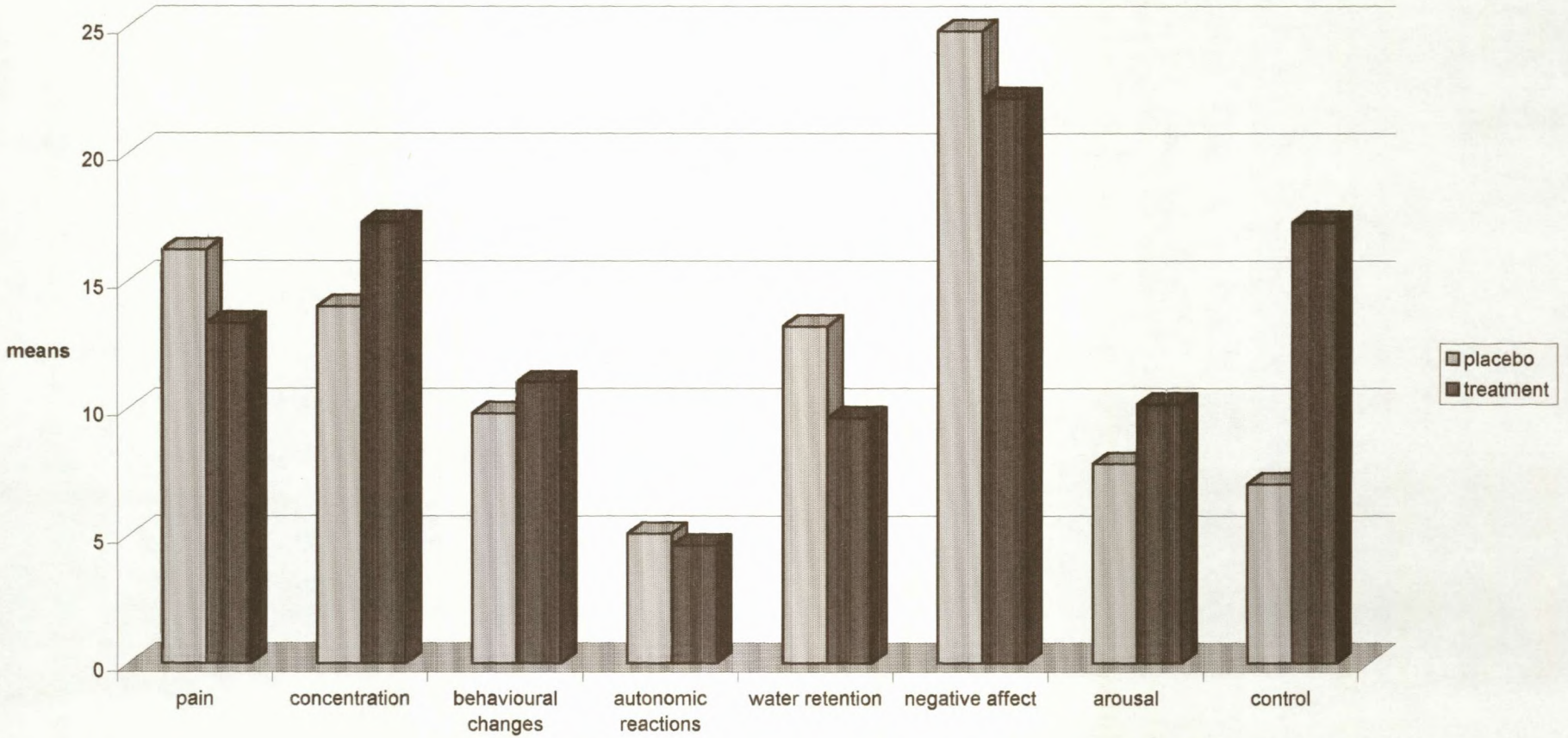
Upon analysis of **Figure 4.2** it was noted that there was an improvement in the placebo group in consultation 3 in seven of the eight subscales. There was no improvement in the subscale of behavioural changes, and in fact it was slightly worse than originally. There was a marked improvement in the pain subscale, with less dramatic improvements in the other subscales.

4.11. Figure 4.3. Comparison of the means of the 8 subscales between consultations 1 and 3 for Group 2 (treatment)



There was an improvement in the treatment group in all of the eight subscales in the third consultation. The subscales of pain and negative affect revealed significant improvements in the final consultation, with slight improvements in the other subscales.

4.12. Figure 4.4. Comparison of the means between Group 1 (placebo) and Group 2 (treatment) with respect to the 8 subscales in consultation 3 (end)



Upon analysis of **Figure 4.4**, the placebo group was found to have fared better in the subscales of concentration, behavioural changes, arousal and control. There was a marked difference between the two groups with respect to the control subscale, in favour of the placebo group. The remaining subscales of pain, water retention, autonomic reactions and negative affect showed a difference between the two groups in favour of the treatment group.

4.13. Percentage calculations for Group 1 (placebo) and Group 2 (treatment)

4.8.1. Group 1 (placebo)

- 53.3% showed an improvement.
- 46.7% worsened.

4.8.2. Group 2 (treatment)

- 86.7% showed an improvement
- 12.3% worsened

However this improvement in the treatment group was not significant enough to verify that the complex was effective when analysed statistically and in comparison with the effects of the placebo.

CHAPTER 5

DISCUSSION

This study was designed to evaluate the efficacy of the homeopathic complex, Premenstron®, in the treatment of PMS with regards to the patient perception of the treatment.

The results of this study showed that there was no overall significant improvement in the patients suffering from PMS who received treatment with the complex compared to those patients who received the placebo.

In order for a drug to be marketed effectively, it should show a significantly better therapeutic effect then the placebo (Krentzman, 2000). This complex did not perform significantly better than the placebo, and in fact, in some aspects the placebo actually outperformed the complex (see Chapter 4).

The placebo effect showed strongly in this trial to the extent that there was an overall improvement in the second consultation amongst the patients receiving the placebo (Table 4.3).

It was Dr. Beecher who first proposed the idea of the placebo effect, claiming that among patients who took a pill with no active ingredients in it, about 35% of these patients would experience improvement in their condition (Carroll, 2000).

The researcher presumes that some of the patient's wishes to please the prescriber would partially account for the placebo effect. Also, a person's beliefs and hopes about a treatment, combined with their suggestibility, may have a significant biochemical effect. There is probably a great deal of truth to the claim that a person's hopeful attitude and beliefs are very important to their physical well being and recovery from injury and illness. (Carroll, 2000.)

Anther theory gaining popularity is that a process of treatment that is showing attention, care, affection etc. to the patients/ subjects, a process that is hopeful and encouraging, may itself trigger physical reactions in the body which promote healing (Carroll, 2000).

It is thought that the touching, the caring, the attention and other interpersonal communication that is part of the controlled study process, along with the hopefulness and encouragement provided by the experimenter, affect the mood of the subject, which in turn triggers physical changes such as the release of substances like endorphins. The process reduces stress by providing hope or reducing the uncertainty about what to take or what the outcome will be. The reduction in stress prevents or slows down further harmful physical damage. (Carroll, 2000.)

This was definitely noted during the trial, with many of the participants grateful that someone actually acknowledged the fact that they had PMS, and also that someone was willing to listen and take their problem seriously.

It was noted that in the last consultations, the patients were more aware of their menstrual cycles, as well as the type and intensity of symptoms they experienced in the premenstruum. This could help explain the increase in the intensity of symptoms of the majority of the placebo patients in the third consultation, resulting in there not being an improvement as there was in the second consultation (Table 4.3). This increased awareness could also reflect directly on there not being a significant improvement within the treatment group (Table 4.6).

Subjectivity was a definite problem in this type of study where the patient's perception is used as a means of measurement. The researcher had to rely on the patients' ability to recall and rate the symptoms indicated in the questionnaire.

This statistical methodology used in the trial were sound, and thus is comparable to other clinical trials which have used or will use similar sample sizes. It is perhaps due to the small sample size of thirty, that no significant overall improvement in the treatment group was found when compared with the placebo group (Table 4.1.). Small trials require huge observed differences in order to be statistically significant (Lewith and Aldridge, 1993: 21).

Taking all the results into account, it can therefore be concluded that this clinical trial showed the homeopathic complex, Premenstron®, to be ineffective in the treatment of PMS with regards to the patients' perception of treatment.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

6.1. CONCLUSIONS

The conclusion reached in this study is that the homeopathic complex Premenstron® is ineffective in the treatment of PMS in terms of the patients' perception of treatment. While the treatment group did improve, it was only at marginal levels. The placebo group showed an equal improvement, and actually performed significantly better in some aspects.

6.2. RECOMMENDATIONS

6.2.1. The sample size of further investigations could be larger to obtain greater statistical accuracy.

6.2.2. The duration of the trial was approximately two months. It is recommended that further investigations might try a longer trial duration.

6.2.3. It is recommended that further investigations use a 'washout' period of one or two months before the randomised trial, wherein which the patients' symptoms are recorded whilst not on any treatment. This will decrease the need for the researchers to rely on the patients' memory of symptoms, will allow for recording of more accurate baseline symptoms, and will allow for greater accuracy for statistical purposes. A 'washout' period after the actual trial could be optional, but

would prove informative as to the long-term effect of the active therapy being tested.

6.2.4. Homeopathic research with regards to using homeopathic simillimum in the treatment of PMS is recommended.

6.2.5. A trial comparing simillimum treatment versus treatment with a complex and a placebo is recommended, to evaluate the efficacy in both types of treatment in PMS as well as providing direct comparisons to assess.

6.2.6. Comparing the homeopathic treatment of PMS (either a complex or simillimum) with another type of complementary medicine treatment e.g. chiropractic, reflexology or acupuncture is recommended.

6.2.7. Since PMS is such a multi-faceted problem, lifestyle changes such as exercise and eating habits should be evaluated together with homeopathic treatment.

6.2.8. The economic viability and effectiveness of homeopathy compared with allopathic treatment e.g. oestrogen, alprazolam, fluoxetine and diuretics, is also recommended for further studies.

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LIST OF APPENDICES

APPENDIX A

STUDY INFORMATION SHEET

PREMENSTRUAL SYNDROME- Study Information Sheet

Premenstrual syndrome is one of the most common problems affecting women. Homoeopathy offers a gentle yet effective treatment for this condition, and can result in an improvement in the quality of life.

This is a double-blind placebo-controlled study, which means that half of the patients will receive the active treatment in the form of Premenstron®, and the other will receive placebo treatment. A placebo is a neutral substance, and provides a comparison for statistical purposes. Neither the researcher nor the patient will know which treatment they are on until the end of the study. If it turns out that you received a placebo treatment during the study, you will be given Premenstron® at the end of the study.

This research project will determine the effectiveness of Premenstron®, an over-the-counter complex on Premenstrual Syndrome in terms of the patients perceptions.

By taking part in the project you are providing invaluable information that is likely to help other women. Thank you for your cooperation.

Shanie Sarawan

Name:_____

Date: _____

APPENDIX B

INFORMED CONSENT FORM

INFORMED CONSENT FORM

(To be completed by patient / subject)

Date :

Title of research project : An evaluation of the efficacy of a homoeopathic complex (Premenstron®) in the treatment of premenstrual syndrome

---

Name of supervisor :

Name of research student : Shanie Sarawan

Please circle the appropriate answer		YES	NO
1.	Have you read the research information sheet?	Yes	No
2.	Have you had an opportunity to ask questions regarding this study?	Yes	No
3.	Have you received satisfactory answers to your questions?	Yes	No
4.	Have you had an opportunity to discuss this study?	Yes	No
5.	Have you received enough information about this study?	Yes	No
6.	Who have you spoken to? _____		
7.	Do you understand the implications of your involvement in this study?	Yes	No
8.	Do you understand that you are free to withdraw from this study?	Yes	No
	a) at any time		
	b) without having to give any a reason for withdrawing, and		
	c) without affecting your future health care.		
9.	Do you agree to voluntarily participate in this study	Yes	No

If you have answered no to any of the above, please obtain the necessary information before signing

Please Print in block letters:

Patient /Subject Name:_____ Signature:_____

Parent/ Guardian:_____ Signature:_____

Witness Name:_____ Signature:_____

Research Student Name:_____ Signature:_____

APPENDIX C

DIAGNOSTIC CRITERIA OF PREMENSTRUAL SYNDROME (Dalton, 1984)

DIAGNOSTIC CRITERIA OF PREMENSTRUAL SYNDROME (Dalton,1984)
(This is the original criteria as developed by Dalton)

The criteria for a diagnosis of Premenstrual syndrome are:

1. Symptoms must occur exclusively during the second half of the menstrual cycle.

   Yes / No

2. Symptoms increase in severity as the cycle progresses.

   Yes / No

3. Symptoms must be relieved by the onset of full menstrual flow.

   Yes / No

4. There must be an absence of symptoms in the postmenstruum.

   Yes / No

5. Symptoms have to be present for at least 2 consecutive cycles.

   Yes / No

If all the above criteria have been met the patient may be accepted into the study.

PATIENT NAME:_____

ENTRY No. :_____

APPENDIX D

PERSONAL DETAILS FORM

PERSONAL DETAILS FORM

Complete the following:

Please print

1. Name:_____

2. Age:_____

3. Marital status:_____

4. Occupation:_____

5. Age at which menstruation began:_____

6. When are you symptoms worse?_____

7. How long do your symptoms last for?_____

8. Do you take any medication to alleviate the symptoms?_____

9. If answered YES, what medication do you use?_____

_____

10. Do you have any children, and if so, how many?_____

11. Present weight: _____

APPENDIX E

MOOS MENSTRUAL DISTRESS QUESTIONNAIRE

MOOS MENSTRUAL DISTRESS QUESTIONNAIRE

(This is the original questionnaire as developed by Moos)

Patient Name:_____

Entry No. :_____

Write the approximate date of your most recent menstrual flow:

A: most recent flow from _____ to _____.
B: week before the most recent flow.
C: other times during the cycle.

Write the date of the menstrual flow that preceded the most recent flow:

D: flow preceding the most recent menstrual flow _____to_____.

On the following pages is list of symptoms that women sometimes experience. Please describe your experience of these symptoms during the three different periods listed below:

COLUMN 1: ***during your most recent menstrual flow (A)***
COLUMN 2: ***one week before the menstrual flow (B)***
COLUMN 3: ***during the remainder of your most recent menstrual cycle(C)***

Note: The answers you put in column 1, 2 and 3 should describe your experience specifically during your ***most recent menstrual cycle***. Please do not report your general symptoms. Please report if the symptoms are related to your menstrual cycle or not.

For each answer choose the category listed below which best describes your experience of each symptom during that particular time. Write the number of that category in the space provided below. If none of the options accurately describe the symptom, please choose an option that is closest to your experience.

CATEGORIES:

1 = no experience of symptoms
2 = barely noticeable
3 = present, mild
4 = present, strong
5 = acute or partially disabling

	Most recent Flow (A)	The week before (B)	Rest of the month (C)
Muscle stiffness			
Headache			
Cramps			
Backache			
Fatigue			
General aches and pains			
Insomnia			
Forgetfulness			
Confusion			
Lowered judgement			
Difficulty concentrating			
Distractible			
Accident prone			
Lowered motor coordination			
Lowered school/work performance			
Take naps; stay in bed			
Stay at home			
Avoid social activities			
Decreased efficiency			
Dizziness, faintness			
Nausea, vomiting			

	(A)	(B)	(C)
Hot flashes			
Weight gain			
Skin disorders			
Painful breasts			
Swelling			
Crying			
Loneliness			
Anxiety			
Restlessness			
Irritability			
Mood swings			
Depression			
Tension			
Affectionate			
Orderliness			
Excitement			
Feelings of well-being			
Bursts of energy, activity			
Feeling of suffocation			
Chest pains			
Ringing in the ears			
Heart pounding			
Blind spots, fuzzy vision			
Change in eating habits			

APPENDIX F

SYMPTOM SCALES OF THE MOOS MENSTRUAL DISTRESS QUESTIONNAIRE

SYMPTOMS SCALES ON THE MOOS MENSTRUAL DISTESS QUESTIONNAIRE

PAIN

Muscle stiffness
Headache
Cramps
Fatigue
General aches and pains

CONCENTRATION

Insomnia
Forgetfulness
Confusion
Lowered judgement
Difficulty concentrating
Distractible
Accident prone
Lowered motor co-ordination

BEHAVIOURAL CHANGE

Lowered school/ work performance
Take naps; stay in bed
Stay at home
Avoid social activities
Decreased efficiency

AUTONOMIC REACTIONS

Dizziness
Nausea, vomiting
Hot flashes

WATER RETENTION

Weight gain
Skin disorders
Painful breasts
Swelling

NEGATIVE AFFECT

Crying
Loneliness
Restlessness
Irritability
Mood swings
Tension

AROUSAL

Affectionate
Orderliness
Excitement
Feelings of well-being
Bursts of energy, activity

CONTROL

Feeling of suffocation
Chest pains
Ringing in the ears
Heart pounding
Blind spots, fuzzy vision

APPENDIX G

HOW TO TAKE THE MEDICATION

HOW TO TAKE THE MEDICATION

- Take the medication three times a day, a half-hour before or after meals.
- Start taking the medication 10 days before the onset of the period, or at the onset of the symptoms.
- Take 10-15 drops in approximately 5ml of water.
- Stop taking the medication at the onset of the period.
- Avoid eating mint before or after taking the medication.
- Do not use any camphor products e.g. Vicks as these destroy the action of the medicine.

RAW DATA

PATIENT LISTING

Patient 1 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	103	91	52	91	97	51	114	99	46
Subscale									
Pain	19	17	6	18	18	6	21	17	6
Concentration	8	8	8	8	8	8	8	11	8
Behavioural changes	15	15	6	14	17	5	20	17	5
Autonomic reactions	6	3	3	4	4	3	5	3	1
Water retention	16	13	4	15	15	4	17	13	4
Negative affect	22	19	8	17	18	8	27	23	8
Arousal	7	7	11	7	9	10	8	8	8
Control	5	5	5	5	5	5	5	5	5
Appetite changes	4	3	1	3	3	2	3	2	1

Patient 2 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	151	111	73	100	64	55	117	97	87
Subscale									
Pain	23	22	16	20	12	10	22	19	16
Concentration	29	20	17	20	16	9	23	19	18
Behavioural changes	13	10	8	9	6	5	6	6	6
Autonomic reactions	14	12	3	9	3	3	9	7	7
Water retention	13	9	6	6	4	4	10	7	5
Negative affect	27	21	8	16	9	9	26	21	18
Arousal	17	11	9	11	8	9	10	10	10
Control	12	5	5	8	5	5	10	7	6
Appetite changes	3	1	1	1	1	1	1	1	1

Patient 3 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	151	161	59	90	85	50	88	84	47
Subscale									
Pain	23	20	8	15	16	6	15	15	6
Concentration	36	35	18	21	18	13	16	14	8
Behavioural changes	20	17	7	13	8	5	6	5	5
Autonomic reactions	5	8	3	4	3	3	5	4	3
Water retention	20	20	4	9	8	4	12	11	4
Negative affect	39	33	8	21	16	8	12	16	8
Arousal	17	13	5	11	9	5	10	9	7
Control	13	9	5	5	6	5	9	8	5
Appetite changes	5	5	1	3	1	1	3	2	1

Patient 4 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	170	140	54	129	134	78	123	127	72
Subscale									
Pain	26	18	8	19	18	10	21	24	11
Concentration	39	27	8	26	29	13	26	30	13
Behavioural changes	25	19	5	17	13	7	17	15	8
Autonomic reactions	6	5	3	3	4	4	4	3	3
Water retention	13	10	4	10	12	7	12	12	9
Negative affect	40	31	8	25	28	15	23	24	11
Arousal	9	13	12	17	18	14	11	11	11
Control	7	7	5	9	19	6	5	5	5
Appetite changes	5	2	1	4	4	3	4	3	1

Patient 5 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	123	114	76	111	100	74	139	117	77
Subscale									
Pain	18	13	12	16	13	11	21	14	10
Concentration	21	14	11	24	19	12	26	17	9
Behavioural changes	6	12	5	11	8	7	15	17	7
Autonomic reactions	8	6	4	3	3	3	6	4	3
Water retention	12	6	4	9	7	6	13	9	6
Negative affect	35	39	18	29	29	15	36	39	18
Arousal	11	11	15	10	7	15	12	8	16
Control	8	9	6	7	7	5	7	9	5
Appetite changes	4	4	1	2	3	1	3	2	1

Patient 6 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	79	115	113	109	135	128	119	97	98
Subscale									
Pain	6	12	12	12	18	18	16	12	12
Concentration	8	15	15	16	24	24	18	16	16
Behavioural changes	10	11	13	11	13	13	14	10	10
Autonomic reactions	6	8	8	6	7	7	7	6	6
Water retention	8	12	12	8	12	12	12	8	8
Negative affect	8	22	22	16	24	24	23	16	16
Arousal	17	14	16	18	19	19	14	17	17
Control	11	14	12	10	15	15	14	12	12
Appetite changes	3	4	3	2	3	3	3	2	2

Patient 7 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	103	105	67	98	98	69	95	98	64
Subscale									
Pain	15	15	15	18	17	17	15	15	17
Concentration	13	13	13	12	12	12	12	12	11
Behavioural changes	5	5	5	5	5	5	5	5	5
Autonomic reactions	3	5	3	3	4	3	3	3	3
Water retention	16	16	4	15	15	4	16	16	4
Negative affect	23	23	13	22	22	15	26	26	11
Arousal	7	7	7	7	7	7	5	5	7
Control	11	11	5	11	11	5	8	11	5
Appetite changes	5	5	1	5	5	1	5	5	1

Patient 8 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	74	74	45	79	87	45	74	82	45
Subscale									
Pain	8	9	6	8	9	6	9	9	6
Concentration	9	10	8	12	12	8	10	12	8
Behavioural changes	7	6	5	8	13	5	5	9	5
Autonomic reactions	3	3	3	3	3	3	3	3	3
Water retention	11	10	5	13	13	5	14	15	5
Negative affect	22	23	8	21	23	8	21	22	8
Arousal	5	5	5	5	5	5	5	5	5
Control	8	8	5	8	8	5	6	6	5
Appetite changes	1	1	1	1	1	1	1	1	1

Patient 9 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	69	74	62	59	65	45	59	67	47
Subscale									
Pain	8	9	6	9	9	6	11	9	6
Concentration	9	9	8	8	8	8	8	8	8
Behavioural changes	7	6	5	6	6	5	5	8	5
Autonomic reactions	3	3	3	3	3	3	3	3	3
Water retention	11	10	4	7	8	4	8	10	5
Negative affect	22	23	8	14	19	8	13	15	9
Arousal	5	5	5	5	5	5	5	5	5
Control	8	8	5	5	5	5	5	6	5
Appetite changes	1	1	1	2	2	1	2	3	1

Patient 10 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	89	115	47	45	45	45	52	51	45
Subscale									
Pain	11	15	6	6	6	6	6	6	6
Concentration	12	20	9	8	8	8	11	12	8
Behavioural changes	5	11	5	5	5	5	9	7	5
Autonomic reactions	3	3	3	3	3	3	3	3	3
Water retention	12	14	4	4	4	4	4	4	5
Negative affect	28	32	9	8	8	8	8	8	8
Arousal	8	10	5	5	5	5	5	5	5
Control	6	6	5	5	5	5	5	5	5
Appetite changes	4	4	1	1	1	1	1	1	1

Patient 11 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	69	104	60	85	74	57	75	76	60
Subscale									
Pain	14	11	9	12	7	6	9	6	6
Concentration	8	16	8	13	10	8	11	12	8
Behavioural changes	5	15	5	10	6	5	6	7	5
Autonomic reactions	3	3	3	3	3	3	3	3	3
Water retention	6	15	4	11	11	4	8	9	4
Negative affect	8	15	8	12	12	8	15	14	8
Arousal	19	15	19	16	16	17	19	19	20
Control	5	5	5	5	5	5	5	5	5
Appetite changes	1	5	1	4	4	1	2	3	1

Patient 12 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	76	94	63	69	74	61	103	85	70
Subscale									
Pain	16	9	7	20	17	8	16	14	9
Concentration	8	15	8	15	20	8	17	12	11
Behavioural changes	12	13	5	10	17	10	18	10	9
Autonomic reactions	4	5	3	3	4	3	4	3	3
Water retention	10	15	4	10	12	5	15	14	5
Negative affect	14	30	10	8	24	14	14	16	14
Arousal	11	9	14	13	9	10	13	8	12
Control	5	6	5	5	7	5	5	5	5
Appetite changes	1	4	1	1	3	1	1	3	2

Patient 13 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	81	106	57	85	113	63	64	64	57
Subscale									
Pain	14	15	8	13	14	8	13	13	8
Concentration	9	10	8	11	11	9	11	11	11
Behavioural changes	5	7	5	5	5	5	5	5	5
Autonomic reactions	3	4	3	4	3	3	3	3	3
Water retention	4	4	4	4	4	4	4	4	4
Negative affect	20	34	10	14	17	12	16	16	14
Arousal	15	12	19	12	14	14	6	6	6
Control	5	7	5	5	5	5	5	5	5
Appetite changes	1	1	1	1	1	1	1	1	1

Patient 14 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	70	103	55	69	65	56	69	83	59
Subscale									
Pain	11	11	6	8	8	6	9	9	6
Concentration	12	22	8	9	12	9	10	14	9
Behavioural changes	7	10	5	5	7	5	6	7	5
Autonomic reactions	3	3	3	4	3	3	3	3	3
Water retention	5	10	4	7	4	4	6	8	4
Negative affect	14	23	8	14	8	8	11	20	8
Arousal	13	11	15	16	15	15	17	14	17
Control	5	5	5	6	5	5	5	5	5
Appetite changes	1	4	1	2	2	1	2	3	2

Patient 15 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	103	144	68	69	127	61	69	126	69
Subscale									
Pain	18	20	7	7	13	6	7	13	6
Concentration	16	30	10	11	21	13	11	21	13
Behavioural changes	6	21	5	10	21	11	10	21	11
Autonomic reactions	7	5	3	3	5	3	3	3	3
Water retention	15	18	8	9	17	5	9	15	7
Negative affect	16	33	10	10	36	14	10	37	15
Arousal	12	6	18	11	6	13	11	8	17
Control	5	6	5	5	5	5	5	5	5
Appetite changes	4	5	2	3	3	1	3	3	2

Patient 16 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	93	94	69	80	86	69	86	80	65
Subscale									
Pain	20	13	8	16	17	11	20	16	9
Concentration	12	12	12	11	12	10	13	11	14
Behavioural changes	6	5	5	5	5	5	5	5	5
Autonomic reactions	4	4	3	4	4	3	6	3	3
Water retention	11	14	4	9	9	4	10	9	4
Negative affect	15	17	9	12	13	10	14	14	9
Arousal	15	18	19	14	15	17	13	13	18
Control	7	7	7	6	7	6	5	5	5
Appetite changes	3	4	2	3	3	1	2	2	1

Patient 17 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	145	150	52	89	93	46	97	99	45
Subscale									
Pain	20	22	6	26	16	6	18	18	6
Concentration	11	17	8	8	8	8	8	8	8
Behavioural changes	8	14	5	8	9	5	9	9	5
Autonomic reactions	9	5	3	5	3	3	5	5	3
Water retention	20	20	5	16	13	5	16	20	4
Negative affect	38	40	11	14	18	8	23	23	8
Arousal	11	14	7	5	12	5	11	10	5
Control	13	13	5	5	7	5	6	5	5
Appetite changes	5	5	1	1	4	1	1	1	1

Patient 18 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	109	104	46	69	65	45	104	80	45
Subscale									
Pain	19	17	6	12	12	6	21	8	6
Concentration	14	14	8	8	8	8	8	8	8
Behavioural changes	5	5	5	5	5	5	7	5	5
Autonomic reactions	9	8	3	3	3	3	6	5	3
Water retention	14	14	5	12	12	4	17	13	4
Negative affect	31	30	8	14	14	8	26	26	8
Arousal	5	5	5	5	5	5	7	7	5
Control	7	6	5	5	5	5	5	5	5
Appetite changes	5	5	1	5	3	1	5	3	3

Patient 19 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	63	116	63	127	150	58	145	138	61
Subscale									
Pain	11	18	8	20	22	7	22	18	7
Concentration	8	15	8	29	29	8	32	28	8
Behavioural changes	12	15	5	21	23	5	23	20	5
Autonomic reactions	4	3	3	3	3	3	6	7	3
Water retention	4	18	4	15	18	4	15	14	4
Negative affect	17	35	11	31	36	8	31	32	8
Arousal	6	7	18	5	7	17	8	9	17
Control	5	5	5	5	7	5	5	5	8
Appetite changes	1	5	1	3	5	1	3	5	1

Patient 20 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	131	124	85	119	117	101	141	131	103
Subscale									
Pain	22	22	12	19	18	13	22	18	13
Concentration	23	23	17	20	19	18	25	22	17
Behavioural changes	8	7	5	8	8	7	8	9	7
Autonomic reactions	10	9	7	9	9	8	10	9	9
Water retention	16	16	9	13	13	8	14	14	9
Negative affect	26	26	11	23	23	16	32	28	17
Arousal	15	15	14	12	12	17	14	15	18
Control	11	11	10	11	11	10	12	12	11
Appetite changes	3	3	2	4	4	2	4	4	2

Patient 21 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	167	102	58	99	72	46	110	74	45
Subscale									
Pain	27	12	6	18	8	5	17	12	6
Concentration	25	17	8	19	9	8	18	13	8
Behavioural changes	23	11	5	13	6	5	13	9	5
Autonomic reactions	11	4	3	4	3	3	5	4	3
Water retention	16	8	4	8	8	5	12	8	4
Negative affect	39	27	8	22	18	8	24	16	8
Arousal	13	16	17	6	10	5	13	5	5
Control	9	6	5	5	7	5	6	5	5
Appetite changes	5	3	2	4	3	2	2	2	1

Patient 22 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	68	95	53	56	46	47	62	45	46
Subscale									
Pain	16	20	7	9	6	6	9	6	6
Concentration	8	8	10	8	8	8	8	8	8
Behavioural changes	6	7	5	5	5	5	5	5	5
Autonomic reactions	7	5	3	3	3	3	3	3	3
Water retention	8	9	5	5	5	4	10	4	5
Negative affect	8	29	10	15	8	10	8	8	8
Arousal	5	8	5	5	5	5	12	5	5
Control	5	5	6	5	5	5	5	5	5
Appetite changes	4	4	1	1	1	1	1	1	1

Patient 23 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	129	147	67	136	149	72	135	151	69
Subscale									
Pain	24	26	10	24	29	12	24	29	11
Concentration	16	17	16	17	18	16	21	20	12
Behavioural changes	15	19	9	15	16	10	18	16	9
Autonomic reactions	8	11	5	10	9	4	8	8	5
Water retention	12	15	5	13	17	5	11	12	7
Negative affect	31	38	8	32	40	8	31	39	14
Arousal	14	12	10	11	8	11	9	10	5
Control	7	7	6	10	7	5	8	12	5
Appetite changes	4	5	1	4	5	1	4	5	1

Patient 24 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	122	136	75	110	117	62	117	126	72
Subscale									
Pain	15	22	13	15	24	11	16	22	14
Concentration	17	17	10	17	17	9	14	16	10
Behavioural changes	10	10	7	11	9	8	11	10	7
Autonomic reactions	8	10	3	9	9	3	9	11	3
Water retention	19	19	7	16	16	4	19	19	6
Negative affect	33	35	17	27	27	11	33	33	12
Arousal	8	10	10	6	6	9	6	6	13
Control	8	8	6	6	6	5	5	5	5
Appetite changes	4	4	2	3	3	2	4	4	2

Patient 25 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	127	183	66	184	194	51	164	168	47
Subscale									
Pain	25	25	8	25	28	10	21	28	6
Concentration	26	36	12	31	37	8	30	28	8
Behavioural changes	13	23	5	16	21	6	23	23	5
Autonomic reactions	5	7	3	11	12	3	9	9	3
Water retention	17	14	4	17	15	4	16	17	4
Negative affect	13	40	8	38	40	8	40	40	8
Arousal	14	15	19	25	25	5	14	15	7
Control	12	16	6	16	16	6	14	14	5
Appetite changes	2	5	1	5	5	1	5	5	1

Patient 26 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	115	109	63	100	96	62	115	112	61
Subscale									
Pain	18	13	10	18	16	10	20	17	11
Concentration	17	17	9	15	15	11	23	23	10
Behavioural changes	16	13	5	15	14	8	16	16	6
Autonomic reactions	8	6	3	7	5	3	7	7	3
Water retention	9	9	4	10	10	4	6	9	4
Negative affect	28	28	16	21	24	14	25	25	12
Arousal	10	10	10	5	5	6	8	8	9
Control	8	8	5	5	6	5	5	5	5
Appetite changes	3	3	1	3	3	1	2	2	1

Patient 27 (treatment)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	103	102	55	137	96	75	89	88	64
Subscale									
Pain	16	16	7	15	15	8	15	12	7
Concentration	23	13	8	23	16	13	17	16	11
Behavioural changes	5	5	5	19	14	12	5	5	5
Autonomic reactions	6	5	3	10	8	5	5	7	4
Water retention	11	11	4	14	5	4	8	8	4
Negative affect	29	24	8	27	21	15	17	18	10
Arousal	18	13	14	12	7	15	11	11	16
Control	13	13	5	17	6	9	9	9	5
Appetite changes	5	5	1	4	3	1	2	2	2

Patient 28 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	76	111	59	66	70	64	72	94	57
Subscale									
Pain	15	7	6	10	9	6	12	10	6
Concentration	17	31	8	14	15	8	12	27	8
Behavioural changes	9	10	5	6	7	5	5	9	5
Autonomic reactions	3	5	3	3	3	3	3	3	3
Water retention	8	13	4	7	7	5	7	9	4
Negative affect	13	33	10	10	11	11	13	22	8
Arousal	5	5	17	9	12	16	13	7	16
Control	5	5	5	5	5	5	5	5	5
Appetite changes	1	1	1	2	3	4	2	2	2

Patient 29 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	96	107	68	104	114	49	99	121	58
Subscale									
Pain	23	21	14	21	21	6	22	20	7
Concentration	8	8	8	8	12	8	8	12	8
Behavioural changes	5	5	5	6	10	6	6	13	6
Autonomic reactions	7	7	3	7	7	3	7	7	3
Water retention	16	17	8	18	18	6	14	16	7
Negative affect	25	30	13	25	27	8	26	31	11
Arousal	5	5	9	5	5	5	5	5	9
Control	9	9	6	9	9	5	6	12	5
Appetite changes	5	5	2	5	5	2	5	5	2

Patient 30 (placebo)

	CONSULTATION 1			CONSULTATION 2			CONSULTATION 3		
	A	B	C	A	B	C	A	B	C
Total	88	101	61	85	96	51	96	112	54
Subscale									
Pain	21	19	14	20	18	8	24	24	6
Concentration	8	9	8	8	8	8	9	8	8
Behavioural changes	5	9	5	5	9	5	8	9	5
Autonomic reactions	3	3	3	3	3	3	3	3	3
Water retention	13	14	5	12	14	5	16	15	6
Negative affect	29	28	9	24	30	11	22	36	15
Arousal	5	5	10	5	5	5	5	5	5
Control	5	6	5	5	5	5	5	7	5
Appetite changes	3	4	1	3	4	1	4	5	1

NOTE: The symptom Appetite changes is not a recognized subscale in the Moos Menstrual Distress Questionnaire, but for the sake of accuracy was included in the raw data.

Key:
Subscales:
Pain
Concentration
Behavioural changes
Autonomic reactions
Water retention
Negative affect
Arousal
Control
Appetite

Columns:
A= period
B= premenstruum
C= rest of month/ intermenstruum