

## **A) *CROCUS SATIVUS L. (SAFFRON)* IN THE TREATMENT OF PREMENSTRUAL DYSPHORIC DISORDER (PMDD)**

### **Background**

PMDD is a sub-type of premenstrual syndrome that is characterised by severe mood and behavioural changes in the luteal phase. It affects 3 - 8% of women of reproductive age. The aetiology of the disorder is multifactorial and not completely understood. The symptoms of PMDD have been suggested to be associated with disturbed serotonin metabolism. Saffron (dried stigma of *Crocus sativus L.*) is effective in mild to moderate depression, a disorder also related to serotonin abnormalities.

### **Aim**

The aim of this study is to investigate if saffron can relieve the symptoms of PMDD.

### **Method**

Women will be recruited through advertisement in the national press and women's magazines. All will have PMDD diagnosed by a gynaecologist according to the criteria of the American College of Obstetrics and Gynecology, and will have experienced symptoms for at least 6 months. The volunteers will be aged 20 – 45 years and have regular menstrual cycles. The following exclusion criteria will apply: pregnancy or lactation, menstrual cycle shorter than 26 or longer than 33 days, major psychiatric disorder, use of mood altering drugs, medication for PMS or PMDD, hormonal medication in the last 6 months, history of substance abuse.

All women who express interest in the study and who fulfil the entry criteria on the screening interview by telephone will be sent an information pack and, with documented verbal agreement, will be asked to keep a daily symptom record for two months. This record is a checklist of 8 premenstrual symptoms rated on a score of 1 – 4 according to their severity throughout the menstrual cycle. A provisional diagnosis of PMDD will be made if the total daily symptom rating score over the 6 days prior to menstruation is at least 25 and 20% higher than the total post menstrual score on days 5 – 10 (day 1= 1<sup>st</sup> day of menstruation). These women will be invited to an interview with a psychiatrist who will confirm the diagnosis of PMDD and exclude major physical or psychiatric illness. Those invited to participate will be counselled, sign consent and enter the study.

100 women will be randomised to saffron or control in a 1:1 ratio using a computer generated code. The randomisation will be performed by the investigator, who will not be involved in the clinical supervision of the women. Women will take saffron (30 mg) or placebo twice daily for six months. Daily symptom ratings will be completed throughout the six month duration of the trial. Women will be reviewed in the luteal phase of cycle 3 and 6 when diary cards will be checked and compliance with medication discussed with a physician unaware of the treatment allocation. Ethics committee approval will be granted prior to the start of the study.

### **Analysis**

A 25% improvement in the premenstrual score is clinically significant.

A two way repeated measures analysis of variance will be used to compare treated women with controls, and between control and treatment/placebo cycles.

## **B) MOXIBUSTION FOR BREECH PRESENTATION**

### **Background**

Breech presentation (head up) is common in the mid trimester of pregnancy. At 28 weeks the prevalence is 20%. Spontaneous version is common and at term only 3 – 4% of singleton pregnancies present as breech. It is standard practice to offer women with a singleton breech presentation at 36 weeks an External Cephalic Version (ECV). This is successful in 30 – 80 % of cases. ECV is not suitable for, or acceptable in, all cases, hence treatment options that facilitate spontaneous version are being explored. These include postural exercises, and moxibustion, a type of acupuncture that involves the application of heat to specific acupuncture points, generated by the burning of specific herbs (moxa), a technique favoured in China. If moxibustion can be shown to be effective, women would avoid the need for CS, with its inherent risks.

### **Aim**

To determine whether moxibustion is effective in producing spontaneous version of breech presentation in late pregnancy.

### **Method**

The trial will take place at five London hospitals. Healthy women with a singleton pregnancy attending ante-natal clinics, who are found to have a breech presentation on physical examination by a midwife or obstetrician at 34 – 35 weeks gestation, will be invited to take part. They will receive verbal and written information about the aim and procedures of the study. Exclusion criteria include pelvic abnormalities; previous uterine surgery; fetal or uterine abnormality or other pregnancy complications. Recruitment will cease after 120 women are enrolled.

Consent having been obtained, participants will be seen by midwives, who have been specially trained in the administration of moxibustion. They will perform the first treatment on the day of study entry. This involves identifying the location of the acupuncture point BL 67 (tip of the fifth toe) and burning sticks of the herb *Artemisia vulgaris* next to BL 67, to induce a warming sensation. Participants will then be taught the technique and advised to carry it out at home, for 30 minutes (15 minutes per side) twice a day for seven days, choosing a time of day conducive to tranquillity and absence of interruptions. All participants will be required to complete a form to count 'Active Fetal Movements' (AFM) twice a day for seven days, with the number of AFM counted in an hour. If, after one week of treatment, breech presentation persists (demonstrated on physical examination by the midwife), the same treatment is to be continued for another week, and the patient will be examined again. Thereafter, women in whom the treatment is unsuccessful, will be offered ECV.

The primary outcome measure is the number of spontaneous versions after two weeks of treatment, based on physical examination. Secondary outcome measures comprise treatment compliance and fetal motor activity (AFM count).

### **Analysis and Interpretation**

The number of spontaneous versions following treatment with moxibustion will be compared with historical controls. If 15% of patients experience spontaneous version after one or two weeks of treatment, moxibustion will be considered to be successful.

## **C) SUPPORT TIGHTS FOR VARICOSE VEINS**

### **Background**

Varicose veins are common. Apart from being unsightly, many sufferers complain of aching limbs and skin discolouration. Surgical support tights have been previously shown to help relieve the symptoms of ache in the legs. It has been suggested that they may improve the appearance of the veins and help prevent skin discolouration. If this can be demonstrated, a considerable amount of money will be saved by sufferers not requiring surgery to remove the veins.

Riverbank Primary Care Trust has had its budget cut in 2010 – 2011 and is trying to make savings without affecting patient care. They are financing this study to see if support tights work.

### **Aim**

The aim of the study was to see if wearing support tights improves the cosmetic appearance of varicose veins and lessens skin discolouration.

### **Methods**

All patients who present to their GP in Riverbank PCT complaining of varicose veins will be encouraged to join the study. Support tights will be worn daily for six months. Each patient will see their GP prior to the study when their veins will be assessed and any skin discoloration noted. At the end of the six month study period each patient will be reviewed by the same GP who will comment if the veins have improved in appearance and will note any skin discoloration and whether it has worsened during the six month study period.

The practice nurse will phone every patient participating in the study from their practice monthly. They will answer any questions and document compliance with the wearing of support tights.

The study participants will keep a diary card and document any change in appearance of the veins or skin reactions.

Ethics committee approval has been granted.

### **Statistics**

Each practice will submit their data to the PCT at the end of the six month study period. The data will show how many patients have found an improvement in the appearance of the veins and skin discoloration after 6 months of wearing support tights. If a significant number of patients have found that the tights have improved the appearance of veins and lessened skin discolouration the commissioners will suggest that all new patients complaining of varicose veins are treated with support tights rather than surgery.

## **D) COCOA BUTTER LOTION FOR THE PREVENTION OF STRIAE GRAVIDARUM IN PREGNANCY.**

### **Background**

Striae gravidarum (stretch marks) are a common cosmetic concern. They usually appear on the abdomen and breasts, less commonly on the hips, buttocks and thighs. Initially they are pink/purple bands which eventually mature to become pale, atrophic, wrinkled lines. Prevalence varies according to the population studied but is reported as 50 – 90%. Although not detrimental to health, stretch marks affect a woman's self esteem. Many preparations are claimed to prevent their appearance with little evidence to support their efficacy.

Cocoa butter is a natural fat derived from cocoa beans, which has moisturising properties and is used in many private centres to prevent stretch marks.

### **Aim**

The aim of the study is to investigate if cocoa butter prevents stretch marks

### **Methods**

200 nulliparous women, with singleton pregnancies who present to either St Giles Maternity Unit, or St Jude's Maternity Unit, in their first trimester in 2011 will be invited to participate in this study. Women with a known hypersensitivity to cocoa butter or any of the components of the lotion will be excluded from the study. Eligible women will be invited by their obstetrician to participate. If they agree, those at St Giles will be given cocoa butter, and those at St Jude's placebo. Consent will be obtained just prior to giving the first bottle of lotion. The placebo lotion is made to look, smell and feel exactly like the cocoa butter. Ethics committee approval has been granted by both hospital Trusts.

Women will be instructed to apply the lotion (administered by pumps) to the abdomen (2 pumps) breasts and thighs (1 pump each) from 12 weeks gestation until delivery.

One midwife at each hospital will assess the women throughout the study. She will have been trained to assess the severity of the stretch marks on a scale previously validated. The scale accounts for the density and width of the stretch marks to estimate the surface area of the body part affected.

Initial assessment will be just prior to 12 weeks. Each woman will be telephoned monthly to check compliance and ensure she is not developing skin reactions. After delivery each woman will be seen within two weeks and the development and severity of the stretch marks will be noted. Severity at each site will be rated as mild moderate or severe and scored 1, 2 and 3 respectively. Each woman will have a total score for stretch marks.

### **Statistics**

The total "stretch mark score" for all the women using cocoa butter or placebo will be calculated. If it is significantly lower for those women using cocoa butter it will suggest that cocoa butter helps prevent stretch marks.