

## **(A) EVENING PRIMROSE OIL FOR MENORRHAGIA**

### **Scientific background**

Menorrhagia (Heavy Menstrual Bleeding (HMB) has a major impact on a woman's quality of life and accounts for about 10 % of consultations in Primary Care. Eighty percent of women with HMB have no anatomical pathology, which makes medical therapy, rather than surgery, the preferred treatment option, especially for women desiring to preserve their child-bearing potential. Several pharmacological agents have been shown to be effective in reducing HMB, though all carry a risk of adverse reactions. Evening Primrose Oil (*Oenothera biennis* L), being rich in gamma linoleic acid (GLA) is believed to inhibit the release of uterine prostaglandin E<sub>2</sub> and F<sub>2</sub>, high levels of which contributes to HMB. If found clinically effective, Evening Primrose Oil could offer a more natural and acceptable treatment option.

### **Aim of the investigation**

To assess the effectiveness of Evening Primrose Oil in the treatment of menorrhagia.

### **Method**

All GPs in a South London Primary Care Trust will be invited to refer patients with a history of at least 6 months of HMB to the local Gynae Outpatients Department. There, patients will receive detailed information about the trial, and those interested in joining will provide a full gynaecological history and undergo physical (pelvic) examination and Ultrasound Scan to exclude pelvic pathology. Entry criteria require patients to be aged 18 – 45 years, currently not on medication for HMB, and free of pelvic pathology (eg fibroids). After obtaining informed consent, patients will be taught to complete diary record cards, documenting the dates and severity of menstrual bleeding, based on the woman's daily requirement for sanitary protection. They will then be randomised to receive either Evening Primrose Oil or placebo capsules, and advised to take two capsules per day for two menstrual cycles, starting on the first day of their next, and ending on the last day of their third menstrual period following study entry. They will record use of any concomitant medication and avoid any that might affect the volume of blood loss. Patient will not know if they are on active treatment or placebo. At the end of treatment, a research nurse will check patients' diary cards, enquire about possible adverse events, and record patients' perceptions regards treatment benefit, based on a scale of 0 – 10, where 0 means 'no improvement' and 10 'marked improvement'. Reasons for dropout will be documented. Recruitment will cease after 50 patients have joined.

### **Analysis and interpretation**

The research nurse, who is aware of which treatment a patient received, will abstract the data on amount of sanitary protection required from the diary cards, calculate the mean for the last two periods for each patient, and the data for the active and placebo groups will then be subjected to statistical testing.

## **(B) GINGER FOR PREGNANCY-RELATED NAUSEA AND VOMITING**

### **Scientific background**

Nausea and Vomiting (N+V) in early pregnancy is common, with prevalence rates of 50 – 80% for nausea and 50% for vomiting reported in the literature. Symptoms can occur at any time of day and diminish after the first trimester. The precise cause is not yet known, though number of previous pregnancies and conditions with high levels of human chorionic gonadotrophin seem to increase the risk. The condition causes considerable physical and psychological distress. Women are usually given dietary advice and offered pharmaceutical interventions. Concern about possible adverse effects on the foetus, has led women and healthcare providers to look to complementary and alternative therapies, including herbal remedies, eg ginger, the efficacy and safety of which still requires rigorous assessment.

### **Aim**

This trial aims to assess the effectiveness of Ginger (*Zingiber officinale*) in the treatment of nausea and vomiting in early pregnancy.

### **Method**

Women with a current history of pregnancy-related N+V, and attending the antenatal clinic of two large Teaching Hospitals in the Midlands, will be invited to join. They need to be aged 18 – 45 years, with a singleton pregnancy of less than 20 weeks gestation. Following verbal and written information about the trial by a research midwife, volunteers will provide a full medical and obstetric history and complete the 'Rhodes Index of Nausea, Vomiting and Retching', (which measures physical symptoms of and distress caused by them). This will serve as a baseline against which on-treatment experience will be compared. Patients will receive a supply of capsules, each containing 125 mg Ginger extract, equivalent to 1.5 g of dried Ginger. They are then advised to take one capsule four times a day for the next four weeks, starting from the day of recruitment. Follow-up will be at 2 and 4 weeks, when patients will again complete the 'Rhodes Index', and report any adverse events and any concomitant medication, including other herbal substances, taken. Reasons for drop-out will be documented.

### **Analysis and interpretation**

The data will be analysed on an intent-to-treat basis. The 'Rhodes Index' measurements scores (ranging from 8 – 40, with the latter representing maximal symptoms), obtained at 2 weeks and 4 weeks will be meaned and then compared with those obtained at baseline for each patient.

## (C) ORTHOTICS FOR FLAT FEET IN PRIMARY SCHOOL CHILDREN

### Scientific background

At birth the sole of a baby's foot is flat, but by the age of 6 years a muscular arch has normally developed. In about 10% of children this plantar arch does not develop properly, causing the condition of *pes planus* or flat feet. This can cause serious pain in the calf and even arthritis in the ankle. There is serious dispute about the most effective treatment. Some paediatricians believe that an insole in the shoe sculpted to support the fallen arch is highly effective, but very expensive. Others believe the cure rate with the sculpted insole is no greater, or even less, than an inexpensive flat sole in the shoe.

A proponent of the sculpted sole has offered to fund a trial to find out if the extra cost of the sculpted "orthotic" sole is justified by the better development in the plantar arch after six months compared with that observed in a control group offered an inexpensive flat insert.

**Aim** To find out if the extra expense of an orthotic sole (about £50 per child for six months treatment) is justified by the greater efficacy in treatment of *pes planus* compared with a standard flat shoe insert.

### Method

The protocol of the trial has been approved by the ethics committee of an NHS hospital trust in north-west London. Children aged 6 to 8 years old referred to the orthopaedic clinic with flat feet will be invited to enter the trial. The criterion of entry will be a ratio of more than 0.5 in the width at the narrowest part of a "wet footprint" compared with the width at the widest part at the base of the toes. A leaflet explaining the trial will be given to the child and guardian at the first visit to the clinic. To those who agree to join, a second appointment will be made for two weeks later, at which any questions will be answered and written consent obtained. An orthotic technician will take a plaster cast of the soles of the child's feet, the child will be registered at the trial office and given an identifying code number. Recruitment will stop when 40 children have been enrolled.

The plaster casts will be taken to the orthotic centre where an insert will be prepared and stamped with the code number. The insert will be either sculpted to fit the contours of the cast, or have a flat upper surface, depending on a randomised table issued by the trial office. The inserts will be returned to the clinic and fitted into the child's shoes at the next clinic, and follow-up wet footprints (identified only by the code number of the child) will be taken after three and six months.

### Analysis and interpretation

The minimum to maximum width in each wet footprint will be measured and entered into a table by a technician who is blind to the type of insert worn by the child. The code is then broken and the relative improvement in the plantar arch in sculpted and flat inserts can be tested for statistical significance.

## **(D) DESENSITISATION OF FOOD ALLERGIES IN WEANLING CHILDREN**

### **Scientific background**

Allergy to foods is an important cause of illness in children and adolescents. It often begins with intolerance to the first solid foods that the child is given, indicated by colic and fretful behaviour in the child. Often things get worse as allergies develop to other foods including staple foods such as eggs, wheat flour and milk, so it becomes very difficult to provide the growing child with an adequate balanced nutritional diet.

We have observed that if the infant is desensitised to the initial weaning foods his or her subsequent life is free from future troublesome food allergies. This desensitisation can be safely achieved if the baby showing intolerance to a new weaning food is taken off that food and returned to milk only for two weeks, during which time a homeopathic extract of the weaning food is given in very low dosage with the milk three times a day. After two weeks of desensitisation the weaning food can usually be returned to the diet without causing allergy.

**Aim** To show that, if babies with early signs of allergy to weaning foods are given two weeks of desensitisation, this can cure the immediate allergy and protect the child from developing more allergies in childhood and adolescence.

**Method** The rationale of early desensitisation of allergy to weaning foods will be explained to the mother or guardian of the baby, and permission sought to enter the baby into a controlled trial. If informed consent is given the baby will be treated for the present allergy, and monitored at monthly visits to the clinic to detect, and if necessary treat further allergies by homeopathic desensitisation. This monitoring will be continued until the child enters primary school. When that happens a detailed account of the allergy history of the child will be sent to the school doctor so the menu at school can avoid known allergens.

In the event that the mother or guardian declines to give consent to the research plan, the child will serve as a control. He/she will be offered exactly the same monitoring at monthly visits to the clinic, but episodes of allergy will not be treated with homeopathic desensitisation. The difference between the incidence of food allergies in children in the research programme who received homeopathic desensitisation, and that in the control group who had exactly the same treatment but without the homeopathic desensitisation, will illustrate the value of early desensitisation in the prevention of childhood food allergy.

The clinical reaction to any antigen will be reported on the Heptor scale (0 to 10) which takes note of both the severity and duration of the response. Every 4 weeks the sum of the responses in each child to any allergen will be sent to a statistician who does not know whether a child is in the treated or control group. If a child fails to attend the clinic, a value equal to the mean of that child's previous scores will be entered. Observations end when the child enters primary school, when a final score is calculated..

### **Analysis and interpretation**

When all the scores are available, the statistician will be informed about which group a child belongs to, and the data will then be subjected to statistical testing.