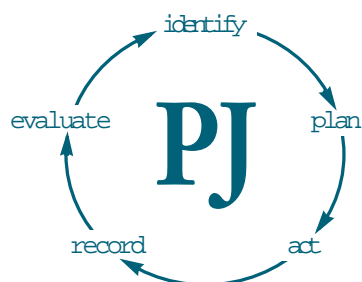


(6) COMPLEMENTARY THERAPIES IN PREGNANCY

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This article, the last in a series on pregnancy, discusses the evidence for the efficacy and safety of some European herbal medicines and complementary therapies used in pregnancy and available through pharmacies



identify gaps in your knowledge

1. What evidence is there for using ginger for nausea and vomiting in pregnancy?
2. What is raspberry leaf traditionally used for in pregnancy?
3. Can acupressure bands be recommended to pregnant women?

This article relates to the Royal Pharmaceutical Society's core competency of "appropriate advice, referral or selection of treatment" (see "Medicines, ethics and practice — a guide for pharmacists", number 26, July 2002, pp105–6). You should consider how it will be of value to your practice.

Pregnant women can experience various pregnancy-related complaints or other conditions, such as coughs and colds, for which herbal medicines and complementary therapies may present an attractive treatment option. However, the efficacy of most of these treatments has not been proven in clinical trials and there is little reliable information on their safety if used during pregnancy. The latter is particularly pertinent to herbal medicines. Pharmacists are encouraged to report suspected adverse reactions (including congenital abnormalities) associated with maternal use of herbal or complementary medicines to the Committee on Safety of Medicines using the yellow card scheme.

EXTENT OF USE

The extent of use of herbal medicines and complementary therapies before and during pregnancy has not been fully explored in the United Kingdom but several relevant studies have been carried out in other developed countries. One study involving 211 women interviewed at an antenatal clinic in south Australia reported that 62 per cent used both a vitamin or mineral preparation and a herbal product, most commonly ginger and raspberry leaf, before they conceived and during pregnancy.¹ In many cases, decisions to use herbal preparations were mainly based on advice from friends or relatives. A similar finding was reported following a questionnaire survey of pregnant women (n=70) in north America who contacted a hospital telephone helpline providing advice on nausea and vomiting.² It was found that 61 per cent used complementary therapies, most commonly ginger preparations and acupressure.

The use of herbal medicines and complementary therapies during pregnancy is not limited to self-treatment. In a cross-sectional survey, a questionnaire was sent to a sample (n = 500) of members of the American College of Nurse-Midwives and 52 per cent of the 172 respondents disclosed that they used herbal preparations to stimulate labour in their patients.³ Most commonly, castor oil (from *Ricinus communis* seeds), blue cohosh, raspberry leaf, evening primrose

oil and black cohosh were used. However, the sample was not obtained randomly and no follow-up questionnaires were sent to non-responders. A higher response rate (68.3 per cent) was achieved in a similar survey of all 120 licensed certified nurse-midwives in North Carolina, United States.⁴ In total, 94 per cent of respondents reported recommending a complementary therapy to pregnant women in their care and, of these, 60 respondents reported recommending herbal medicines for pregnancy-related conditions, including nausea or vomiting and labour induction.

It is likely that there are several reasons why pregnant women choose to use such health care approaches. These may include the belief that herbal medicines and complementary therapies are effective, perhaps based on anecdote or knowledge of traditional use, and the perception that herbal medicines, since they are from natural sources, and complementary therapies are safe, or at least safer than conventional medicines.

HERBAL MEDICINES

Efficacy and safety Because of their known constituents or pharmacological activities, many herbal medicines clearly should be avoided or used only with caution during pregnancy. Some, such as feverfew (*Tanacetum parthenium*), golden seal (*Hydrastis canadensis*), juniper (*Juniperus communis*) and sage (*Salvia officinalis*) are reputed abortifacients, and certain others (eg, pennyroyal, *Mentha pulegium*) are documented as such. Several, including aloes (*Aloe barbadensis*; dried leaf juice), cascara (*Rhamnus purshiana*), frangula (*R frangula*) and senna (*Cassia senna*, *C angustifolia*) contain anthraquinones, and unstandardised preparations should be avoided. Pharmacists are encouraged to consult reference texts for further guidance.⁵

As with other medicines, herbal products should be used during pregnancy only if the expected benefits outweigh the possible risks. Currently, for many herbal medicines definitive evidence of efficacy from methodologically rigorous randomised clinical trials is limited and reliable information on safety aspects, particularly when used during pregnancy, is lacking; for some, phytochemical constituents and pharmacological properties need further investigation. This does not mean that herbal medicines lack efficacy or are unsafe, but at present it is prudent to advise that pregnant women avoid taking herbal preparations. It is also relevant to consider the variability that exists in the constituent profile of different marketed herbal medicinal products

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(HMPs) originating from the same plant species, as well as the pharmaceutical quality (including the possibility of contamination) of unlicensed HMPs.

Ginger Ginger (*Zingiber officinale* Roscoe) has a long history of use for various conditions, but modern-day interest is partly focused on its use to treat and prevent nausea or vomiting. The part used medicinally is the rhizome (often referred to as ginger root). Important constituents include the essential oil (with β -bisabolene and zingiberene as major constituents) and the oleoresin, which contains gingerols and shogaols (degradation products of gingerols).⁵

The effects of ginger root in treating and preventing pregnancy-associated nausea or vomiting have been tested in three randomised controlled trials (RCTs) but there is still insufficient evidence to recommend ginger root routinely as a treatment. One randomised, double-blind, placebo-controlled, cross-over trial involving 30 women with hyperemesis gravidarum (defined as vomiting severe enough to require admission to hospital before the 20th week of pregnancy) assessed the effects of capsules containing powdered ginger root 250mg taken four times daily for four days.⁶ Symptom relief was reported to be significantly greater during treatment with ginger than with the lactose placebo ($P=0.035$), but the study had methodological flaws, eg, no checks on the success of blinding.

In another double-blind RCT, 70 women with pregnancy-related nausea received capsules containing baked, powdered fresh ginger root 250mg, or placebo, four times daily for four days. The median change in nausea scores was reported to be significantly greater in ginger recipients than in placebo recipients ($P=0.014$). However, when an intention-to-treat analysis was carried out to include three study withdrawals from the placebo group, the difference was statistically significant only on the last day of treatment.⁷ After four days' treatment, the proportion of women experiencing vomiting was significantly lower in the ginger group, compared with the placebo group (37.5 vs 65.7 per cent; $P=0.21$). A more recent double-blind RCT involving 26 women in the first three months of pregnancy assessed the effects of one tablespoon of 250mg ginger root in syrup four times daily over a two-week period.⁸ Some beneficial effects on the duration and severity of nausea and vomiting were reported for the ginger group, although the sample size used is too small to allow meaningful conclusions to be drawn.

The safety of ginger root preparations in pregnancy is not clear. It is recommended that doses much exceeding amounts used in foods should not be taken during pregnancy.⁵ One case of spontaneous abortion occurred in a woman in the 12th week of pregnancy who received ginger in the first RCT described above,⁶ although in the second RCT, three such cases were reported in the placebo group, compared with one in the ginger group ($P=0.615$).⁷ The trials reported that all infants were born without deformities or recognised congenital anomalies. However, given the small number of participants studied, it is unlikely that any differences in risk would have been detected.

Reproductive toxicity studies involving small numbers of pregnant rats have suggested that administration of ginger tea over days six to 15 of pregnancy does not induce gross malformations in fetuses, but there was evidence of greater embryo loss in ginger-treated rats, compared with control rats ($P<0.05$).⁹ Surviving fetuses were heavier with maternal administration of the lower, but not higher, concentration ginger tea (grated ginger rhizome 20g/L or 50g/L, respectively), compared with controls ($P<0.01$). *In vitro* studies have indicated that different constituents of ginger have mutagenic and antimutagenic activity⁵ but the clinical relevance of these findings is unclear.

Raspberry Raspberry (*Rubus idaeus* L) has a long history of use in pregnancy. It is recommended by some for pregnancy-related nausea and vomiting and, when taken continuously after the first trimester and/or during labour, to aid birth.¹⁰ The leaf is the part used medicinally, but little is known about its phytochemical constituents. Tannins and flavonoids have been documented.⁵

Clinical investigation of the effects of raspberry leaf in pregnancy is limited. There has been no clinical investigation of raspberry leaf in pregnancy-related nausea and vomiting. The effects of raspberry leaf in labour, however, have been explored in a randomised, double-blind trial involving 240 nulliparous women

who had experienced a healthy pregnancy and who received tablets containing raspberry leaf extract 1.2g or placebo, at a dosage of one tablet twice daily from 32 weeks' gestation until commencement of regular contractions.¹¹ Data for the 192 women (96 per group) who completed the trial did not show any statistically significant differences between the two groups in length of labour (stages I, II and III), need for medical augmentation or induction of labour, mode of birth and neonatal outcome. In short, the study did not demonstrate that taking a raspberry leaf preparation shortened labour, or that it was associated with adverse outcomes. However, the study had several methodological limitations, including a small sample size, failure to conduct an intention-to-treat analysis and its reporting of statistically non-significant results as "clinically significant". Older experimental work documented that raspberry leaf infusion caused contractions when applied to strips of uterus obtained from women at 10 to 16 weeks of pregnancy, but not strips from non-pregnant women.⁵

Due to the lack of definitive evidence of efficacy or potential uteroactivity and safety data, it is recommended that raspberry leaf should not be used during pregnancy⁵ or labour.

Black cohosh and blue cohosh Black cohosh (*Cimicifuga racemosa* Nutt) and blue cohosh (*Caulophyllum thalictroides* L) have both been used traditionally as emmenagogues (induce menstruation), although such use was probably to induce abortion.¹⁰ Modern use of black cohosh focuses on the treatment of menopausal symptoms, but blue cohosh is still recommended by some as a uterine stimulant. The root and rhizome from both are used medicinally. Black cohosh contains triterpene glycosides, blue cohosh contains saponins (eg, caulosaponin), and both contain quinolizidine-type alkaloids, as well as other phytochemical constituents.⁵

The efficacy and safety of black cohosh and blue cohosh during pregnancy have not been investigated. There is an isolated report of a child born without spontaneous breathing and who subsequently experienced brain hypoxia and seizures following the oral administration of black cohosh and blue cohosh by a midwife in an attempt to induce labour in a woman who otherwise had had an uneventful pregnancy. The report has been criticised, however, because it did not provide details of the dose or formulation of the herbs.⁵ Another isolated report describes a 21-year old woman who developed tachycardia, heavy perspiration, abdominal pain, vomiting, muscle weakness and fasciculations after taking blue cohosh tincture in an attempt to induce an abortion.¹² The symptoms resolved within 24 hours and the woman was discharged from hospital. Causality in these cases has not been established.

The following information comes from experimental studies but its clinical relevance is unclear:

- Components of a methanolic extract of black cohosh bound to oestrogen receptors in isolated rat uterus
- There are conflicting data on the oestrogenic activity of black cohosh extracts and their isolated constituents
- There are conflicting data from *in vitro* and *in vivo* (animal) studies regarding the uterine stimulant effects of blue cohosh extracts and certain isolated constituents
- *In vitro* teratogenic activity (assessed using the rat embryo culture method) of N-methylcytisine from an extract of blue cohosh rhizomes; N-methylcytisine is also found in black cohosh rhizome^{5,13}

In view of the above, black cohosh and blue cohosh should not be taken during pregnancy.^{5,10}

Echinacea The benefits of specific echinacea preparations for the prevention and treatment of the common cold and other upper respiratory tract infections (URTIs) have not been definitively established (P7, 16 November 2002, pp716–8).

A prospective, controlled, cohort study explored pregnancy outcome in women who had taken echinacea products for URTIs during pregnancy and who had contacted a teratogen information service at a hospital (n=206).¹⁴ The control group comprised 206 disease- (URTI) and age-matched women who had also contacted the information service but who subsequently did not use echinacea products. Of the women who had used echinacea, 54 per cent had

action : practice points

1. Speak to your local midwife and find out what he or she thinks about the use of herbal or complementary therapies in pregnancy.
2. Visit the Cochrane library (www.update-software.com/cochrane/) and have a look at what relevant trials/systematic reviews there are on complementary therapies.
3. Think about the last time you advised a pregnant woman about complementary therapies. Has reading this article changed the advice you would give?

have a look at what relevant trials/systematic reviews there are.

evaluate

How could your learning have been more effective?
What will you do now and how will this be achieved?

done so in the first trimester, and 8 per cent were exposed in all three trimesters. Most women used products containing *E. angustifolia* or *E. purpurea* continuously for five to seven days. No statistically significant differences were seen between the echinacea and control groups in pregnancy outcome, delivery method, maternal weight gain, gestational age, birth weight, fetal distress and frequency of major malformations ($P > 0.1$ for all). Six different major malformations occurred in the echinacea group (four where echinacea was taken during the first trimester) and seven in the control group; relative risk and 95 per cent confidence intervals were not specifically reported. The study has several important limitations, including the broad definition of exposure (any echinacea product use). In particular, the sample size was not large enough to allow detection of a doubling of even the overall rate of birth defects.

HOMOEOPATHIC MEDICINES

The use of homoeopathic medicines is recommended by some as a safe and effective option for pregnancy-related ailments and other symptoms that may arise during pregnancy. However, there has been little rigorous clinical investigation of homoeopathy as a treatment approach in pregnancy. Furthermore, data from high-quality RCTs in various conditions have not provided convincing evidence that individualised homoeopathy has effects superior to those of placebo.

A Cochrane systematic review of RCTs of homoeopathy used for third trimester cervical ripening or induction of labour identified only one study.¹⁵ The double-blind trial (insufficient information was provided on randomisation) included 40 women who (contrary to standard homoeopathic practice) all received *Caulophyllum D4* (a homoeopathic preparation of blue cohosh), or placebo, taken every seven hours or until initiation of labour. There were no statistically significant differences in outcomes between the two groups.

The safety of homoeopathic medicines administered during pregnancy and labour has not been investigated, although it is unlikely that highly dilute homoeopathic medicines would cause adverse effects in either the mother or fetus. However, homoeopathic medicines at lower dilutions, say, less than 3C (three sequential steps of one in 100 dilution) or 6X (D6; six sequential steps of one in 10 dilution), still contain reasonable quantities of starting material and if that material is toxic or highly pharmacologically active, then adverse effects are possible. For this reason, some homoeopathic medicines, such as aconite, arsenicum (arsenic) salts, prednisolone and vaccine derivatives below 3C or 6X, are prescription only medicines and are used rarely.

ACUPRESSURE

Several clinical trials have investigated the effects of acupressure on the acupoint P6 (pericardium 6, PC6; a point above the wrist on the palmar side, stimulation of which is believed by acupuncturists to have effects on the upper gastrointestinal tract). A systematic review of controlled trials of P6 stimulation as a treatment for nausea and

vomiting of various causes included seven trials of manual pressure, acupressure wrist bands or TENS (transcutaneous electrical nerve stimulation) used for pregnancy-related nausea and vomiting.¹⁶ Six of the trials reported statistically significant outcomes, such as relief of nausea and change in nausea scores in the intervention group. All three studies that were deemed to be of higher methodological quality reported statistically significant results for the intervention, compared with the control group. These three trials are also part of a Cochrane systematic review and meta-analysis.

Several new trials of acupressure in pregnancy-related nausea and vomiting have been conducted, but these have not yet been subject to systematic review. On balance, most controlled trials of P6 acupressure report significant effects, but several studies have methodological limitations, so benefits have not been definitively established.

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