

Pregnancy and the use of raspberry leaf, and blue cohosh. 78

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pregnancy and herbs

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raspberry

Health care consumers increasingly turn to complementary medicine. In America the estimated use in 1997 by adults was 42% (Eisenberg et al 1998). Herbal medicine is part of many health care systems around the world. The World Health Organisation estimated that 80% of the world's people rely on herbs for their primary health care needs. (Akerlele O 1993)

The World Health Organisation has passed resolutions encouraging governments of member states to promote development of knowledge and use of medicinal plants, and recommends that historic and cultural usage should be combined with modern scientific research when evaluating the quality, safety and efficacy of herbal products. The potential savings in healthcare have also heightened interest in herbal medicine (Akerlele O 1993). A cost analysis of the savings to a health maintenance organisation where herbs were used instead of pharmaceuticals, where appropriate, was made. This centre spent nearly \$1 million annually on selective serotonin reuptake inhibitors (Prozac) (Kincheloe 1997). The researchers concluded that if Hypericum were effective for 25% of these patients, a conservative estimate of saving would be \$250,000 a year (Kincheloe 1997).

Many herbal remedies have been used for centuries in various parts of the world. In most European countries the traditional use of a herbal remedy is considered to be valid evidence of the safety and efficacy of the herb (Tyler 1994). Although the use of herbs has quadrupled in the last 20 years, reports of toxicity related to herbs or plant have remained low. (Herbs Research Foundation. Herb safety report. Boulder (C) O: Herb Research Foundation).

The use of herbs in pregnancy;

The use of herbal medicine by pregnant women raises additional questions about safety for the foetus, alongside the safety to the women themselves. Use of herbal medicine by pregnant women is high, the following table is a summary of research done in America, Canada and Europe on the frequency of use of herbs by pregnant women.

Midwifery and herbalism share historic links; herbs have been used for centuries to aid in pregnancy and childbirth.

Surveys of midwives and midwifery education programs in America (McFarlin et al 1999) has indicated that the recommendation of herbs to pregnant women is prevalent; about half of those who replied used herbal preparation in labour, the most frequently used preparations were: Blue Cohosh (64%), Black Cohosh (45%), Raspberry leaf (63%). Of the educational centres 64% of nurse midwifery education programs reported formal inclusion of teaching of herbal

preparations for cervical ripening, augmenting or inducing labour. Whereas 92% of the educational centres indicated the use of herbal preparation to stimulate labour being informally discussed. Most commonly discussed herbs were blue and black cohosh, and red raspberry leaf. The adverse effects attributed to blue and black cohosh were nausea, increased meconium-stained fluid, and transient foetal tachycardiac; no adverse effects were reported from raspberry leaf (McFarlin et al 1999).

A survey of North Carolina Certified Nurse–Midwives (Allaire et al 2000) indicated that of the 57.3% who reported recommending complementary and alternative medicine, 73.2% recommended herbal treatment. The most common indications would be nausea and vomiting, labour stimulation, perineal discomfort, lactation disorders, postpartum depression, preterm labour, postpartum haemorrhage, labour analgesia, and malpresentation of the foetus. In this survey 37% of nurse midwives offered herbal treatments before allopathic medicine, and 30% believe that they are safer than orthodox medicine.

Consumers as well as the health professionals are driving herbal medicine into the mainstream of medicine. Herbal medicine has become a reality and health professionals are recommending herbal products.

Pregnant women will use herbal medicine, health professionals will recommend herbal medicine, assuming that anything natural is, as a consequence, safe. However we suffer an information vacuum regarding the reproductive safety of herbs, and lack of objective information allows artificial assessment to gain some credibility. Traditional information is valuable but not often accepted by authorities. One way to address this problem is to combine information on traditional use with observational studies, since many herbs have already been used by humans, pregnant or not, it is ethical and relevant to observe the safety outcomes of using these herbs. One such study was conducted in Hong Kong, where 88 women who took Panax ginseng during their pregnancy were compared with 88 matched controls, 8 patients in the control group had pre-eclampsia, but only one patient taking ginseng suffered this condition ($p < 0.02$). There were no other significant differences between the 2 groups (Chin 1991).

Another was done in relation to the use of Echinacea, a prospective controlled study, where it was found that gestational use of Echinacea during pregnancy is not associated with increased risk of major malformation (Gallo et al 2000).

To illustrate the importance of traditional use, plus up to date information to draw conclusions about what is safe, I will look close into 2 examples of frequent used herbs as *partus praeparator* (used to prepare the uterus for labour) in pregnancy, Raspberry leaf and Blue Cohosh.

Raspberry leaf;

Traditional usage can at least date back to the sixth century, referred to in many old herbals as an aid in maternity (Beckett et al 1954). The leaf has been used in Europe for nourishment during pregnancy and preparation for delivery since ancient times (Gerard 1597). It was used during labour (Neil 1889), it is still mentioned for these purposes today in North America in the folk medicine of the Amish (McGrath 1985), and of the Hispanic Southwest (Moore 1990). The Chippewa, Cherokee, Iroquois, Kwakiutl and Quinalt tribes have all used raspberry during pregnancy and labour (Beckstrom-Sternberg et al 1995).

It is thought that the use of raspberry leaf tea throughout pregnancy and labour strengthens the uterus and tones it, assisting contractions and checking any haemorrhage during labour. The active constituents of raspberry leaves seem to possess contradictory effects, on the one hand relaxing the uterine muscle and on the other initiating contractions, this has puzzled the researchers, but confirmed herbalists belief that raspberry leaves are an uterine tonic.

Studies with raspberry leaf are just a few; three of them animal studies, one experimented on first trimester uteri after removal from the body (Bamford et al 1970). There are three studies on women, one on postpartum women (Whitehouse 1941), one a retrospective observational study conducted (Parsons et al 1999), and one double-blind, randomised placebo controlled trial (Simpsons et al 2001).

A research by J.H.Burn (Burn et al 1941), a professor of pharmacology at Oxford University, was published in The Lancet 1941, inspired by the traditional use of plant for female complaints, identifying antispasmodic and uterine sedative properties in various extracts of raspberry leaf for cats, dogs, guinea pigs and rabbits. They found that an intravenous injection of raspberry leaf had a relaxant effect on the uterine muscle of cats, and it not only reduced the strength and frequency of contractions but also caused tonically contracted muscles to relax. It was found that if the muscle was relaxed the herb induced contraction. (Burn 1941) Contractions were diminished in force and frequency and occurred at evenly spaced intervals, secondary contractions were eliminated (Whitehouse 1941).

Several constituents were isolated from the raspberry leaf, some increased uterine contractions while other relaxed the uterus (Beckett et al 1954).

One study involved postpartum women;

Whitehouse 1941 found that the uterine contraction diminished in frequency and strength and secondary contractions were eliminated in those women given 20-40g of raspberry leaf in the first few days after birth. The relaxant effect of raspberry leaf was later interpreted as producing more coordinated uterine contractions in labour (Bamford et al 1970). Bamford explained that the major problem in obstetrics is in coordination of uterine contraction, and that raspberry could be helpful in these situations. Bamford felt that raspberry is able to produce more coordinated uterine contractions. Contemporary herbalists give raspberry the last one or two trimesters of pregnancy, and benefits on the uterine muscle may partly be due to long term nutritional tonic effect from calcium, magnesium, and potassium. The mild antispasmodic effects relative to the strength of the contractions of labour may normalize erratic and inefficient contraction, which is consistent with the traditional Native American use and European use to reduce pain in Childbirth.

Often the medical profession is opposed to using raspberry leaf, thinking that it may cause miscarriage, or premature labour. However only one reference can be found in the literature to that effect and that was related to contractions initiated in strips of human uteri, after removal from the body and injected with raspberry leaf extract between 10-16 weeks of pregnancy. This is a far cry from the usual way that raspberry leaf is used; raspberry leaf tea is not injected into the uterus (Bamford et al 1970).

The retrospective study (Parsons et al 1999) demonstrated the safety of the raspberry leaf herb for women and their babies when consumed during pregnancy. A sample size of 109 postnatal women primiparous and multiparous were interviewed, 58 consumed raspberry products in tea, tablet or tincture in various dosages, commencing consumption as early as 8 weeks to as late as 39 weeks gestation. A control group of 51 postnatal women who had not taken raspberry were used as a comparison. In this study, it was found that the average length of the first stage of labour for women who took raspberry teas was shorter, where as the average lengths of the second and third stages of labour were similar in both groups. There was one preterm labour and birth in the control group compared to none in the group taking raspberry leaf. The percentage of normal births in the raspberry leaf group (77.2%) was slightly higher than the percentage in the control group (66.7%).

Being retrospective, there was no control on quantity taken, or quality of product nor how long it has been taken for. The women were both primiparous and multiparous, one can draw little conclusive information from this research, apart from the fact that none of the women are reported to have experienced adverse effects.

There is one double blind, placebo, randomised, observational study which was conducted at one hospital in Sydney. (Simpson et al 2001)

The questions explored were whether raspberry had any adverse effects on the mother (increase in blood pressure, or increase in loss of blood at birth) and baby (lower Apgar score at birth and birth weight). Did it affect duration of pregnancy, shorten duration of labour and reduce the likelihood of medical intervention during labour and birth

(medical or surgical augmentation of labour, epidural anaesthesia increased rate of forceps, ventouse or caesarean delivery)?

The sample consisted of 192 low-risk, Nulliparous women. Raspberry tablets were given (2x1.2g per day) from 32 weeks gestation until labour (Dosages recommended by the pharmaceutical Society of Great Britain are 4-8g per day). Between the groups there were no age and weight difference, the only difference between them was that more women in the raspberry leaf group chose to receive their care from a private obstetrician (11.5% compared to the control groups 5.2%).

The aim was to identify the effect and safety of raspberry leaf on labour and birth outcomes.

Length of gestation in days for each group was the same. There was a tendency for the placebo group to need more intervention in the form of artificial rupture of the membranes. 58 Women needed artificial rupture of membranes, of those 54% were in the placebo group, $p=0.35$.

The results showed that there were no adverse effects for mother or baby, and it did not shorten the first stage of labour. However there was a shortening of the second stage of labour (period between full dilation of the cervix and birth of the baby), between the treatment and the control group (19.3%vs. 30.4%). The mean difference was 9.6 minutes, the raspberry group was 12% shorter in time on average than the placebo group.

The two groups were compared on type of birth, excluding those who went for elective caesarean. More women in the raspberry group had normal vaginal birth, 58 (62.4%) in the raspberry leaf group, 45 in the placebo group (50.6%).

A lower rate of forceps deliveries between treatment group and the control group (19.3% versus 30.4%) was seen. Emergency caesarean section was equal in both groups.

There were 21 incidences of blood loss greater than 600ml, 6.1% in the raspberry group, compared to 8.1% in the placebo. Maternal blood loss was measured in 148 women (44 were excluded because of caesarean birth).

The raspberry leaf group had a slightly higher diastolic blood pressure, in early pregnancy $M=64.4\text{mmHg}$, and at 32 weeks 71.1mmHg compared to the placebo group $M=64$, $M=69$. Of the 240 recruited 4.2 % of the raspberry group, and 2.1% placebo developed pregnancy-induced hypertension.

The above study found raspberry leaf to be safe, and may have some benefit for the women and babies during labour. The average length of gestation was similar, indicating that raspberry leaf is unlikely to cause or facilitate preterm labour and birth. The second stage of labour was found to be shorter in the raspberry group ($M=9.6\text{minutes}$) and coincided with decrease in instrumental deliveries. Overall it seemed that the raspberry leaf group was more likely to deliver their babies vaginally and unassisted, and less likely to need the use of forceps compared to the control group. More women in the raspberry leaf group experienced spontaneous rupture of the membranes, and were therefore less likely to receive artificial rupture of membranes.

An overall lower newborn Apgar score was affected five vaginal breech births in the raspberry leaf group compared to the only one in the placebo group. Breech and forceps deliveries have higher respiratory distress (Towner et al 1999).

As a side effect, constipation was unique to raspberry leaf, which is probably due to the astringent action of the leaf. However, this could also be due to pregnancy. The low dose was enough to have a beneficial effect, and it would be interesting to see a study done on the traditional recommended dosages.

Conclusion:

Raspberry leaf has been used traditionally over many hundreds of years for ease of labour. Clinical trials have shown it might be of benefit, although doses used were smaller than is usually recommended. No adverse effects have been reported traditionally, as well as in the clinical study. Given the frequent use by pregnant women today and no reports of adverse effects, one can assume that raspberry leaf is safe, and can possibly aid labour with the result of need of less intervention.

Optimal dosage needs to be found as dosages used in this trial were lower than the recommended dosages than is traditionally used.

Caulophyllum thalictroides; Blue cohosh.

Blue cohosh is frequently used as a *partus praeparator* as seen in the survey above.

Early research showed that the extract of the whole herb increased the uterine tone, but decreased the rate and amplitude of contractions (Pilcher 1916). The saponins fraction seems to increase the amplitude of the contraction and cause a small increase in rate (Ferguson et al 1954).

Several adverse events have been associated with the use of blue cohosh in pregnancy and profound neonatal congestive heart failure was linked to maternal consumption of blue cohosh tablets. Three incidences have been recorded in the literature. A newborn infant whose mother ingested blue cohosh to promote uterine contraction presented with acute myocardial infarction associated with profound congestive heart failure and shock. The infant remained critically ill for several weeks although he eventually recovered. The labour was also precipitous, coming on suddenly and lasting only one hour (Jones and Lawson 1998). The mother was taking three tablets a day, but had been advised to take only one tablet per day. The powder was used, and contained all the alcohol-soluble constituents of the plant, and would require only very low doses, 5-10 mg, and a dose of even 1 capsule of powder could be an overdose by a factor of 30-60 times. The child after 2 years is well but on digoxin therapy.

A similar case had appeared previously in the scientific literature. In one case report, a midwife in New Zealand used blue and black cohosh (Gun and Wright 1996) in a pregnant woman after 41 weeks and 6 days gestation. She was given the herbs to induce labour. After a normal birth of 3840g infant with Apgar scores of 1 at 1 minute, 4 at 5 minutes, and 5 at 10 minutes. After the birth, the baby was not able to breathe spontaneously and was administered cardiac massage and oxygen. The infant was resuscitated, had seizures, renal failure and required mechanical ventilation.

The child sustained CNS hypoxic-ischaemic damage which may have been related to myocardial toxicity (Wright 1999).

The third report was of a baby who had a stroke, possibly because its mother drank blue cohosh tea to induce labour. On recommendation of her obstetrician, she did so and went into labour. The baby looked initially healthy, but then started to have seizures, caused by stroke confirmed by a CT scan, they were not able to positively link blue cohosh to the stroke but they suspect it played a role (Finkel 2004).

Caulosaponin causes coronary blood vessel constriction and direct myocardial toxicity (Baillie et al 1997). Information on doses is lacking, and cardiotoxic effects are due to much greater doses than would be found in doses commonly used in labour.

The negative effects of blue cohosh has been disputed on the grounds that the toxic effects suggested would only occur if much higher doses than reported were consumed (Baille 1997).

One survey of midwives in America has shown that 75% recommended herbal treatment for pregnant and postpartum patients (Allierre et al 2000). The most common herb used was *Caulophyllum thalictroides* for women past their due date, and one must ask if it is indeed used as frequently as that, why are there not more adverse events being reported?

The McFarlin study found that in those midwives who prescribed herbs, 64% used blue cohosh, although 21% of these reported resulting complications such as nausea, meconium stained liquor, transient foetal tachycardia.

Attempts have been made to understand these adverse events in terms of the constituents, and four known alkaloids and one new alkaloid were discovered which were tested in vitro (JB Lippincott 1992)..

The plant contains several glycosides, caulosaponins and caulophyllosaponin, quinolizidine alkaloids (Sparteine) which have oxytocic properties (JB Lippincott 1992). Studies performed on excised uteri of guinea pigs, initiated contraction in non-active strips of uterine tissue, but also increased tone with cessation of contraction, which the authors described as tetanus (Pilcher 1916).

A decrease in blood pressure of 30-50mm with a fairly prompt return to normal was observed when blue cohosh was administered to dogs in these large doses, and a subsequent in vivo study on dogs indicated no effect on the uterus when blue cohosh was administered in high doses (Pilcher 1918). An eclectic pharmacist states in 1898 that blue cohosh partially yields its virtues to hot water and glycerine and fully to alcohol, which was confirmed in 1998 by Jones and Lawson suggesting that the constituents responsible may have been the alkaloid methylcystine, soluble in alcohol, that has vasoconstrictive effects or the saponins caulosaponins and caulophyllosaponin, which are uterine stimulants, and may also cause coronary vasoconstriction. (Jones and Lawson 1998)

The presence of quinolizidine alkaloids including sparteine in blue cohosh could explain both its oxytocic activity and its occasional toxicity. Sparteine was once widely used as an oxytocic drug but is not used anymore since the uterine spasm that occurred in women who were unable to metabolise the alkaloid effectively. About 5% of males and females studied were unable to metabolise sparteine by N-oxidation (Eichelbaum et al 1979) and this defect appears to be genetic. (Vinks et al 1982).

N-methylcystine, the proposed teratogenic compound is a quinolizidine alkaloids with a structure closely related to sparteine and perhaps like sparteine a percentage are unable to metabolise this alkaloid and possibly others in blue cohosh.

This could explain that while widespread use of blue cohosh is apparent, as seen in the surveys, we have not come across more adverse effects reported.

In contrast to the present day midwives, blue cohosh was only used on rare occasions traditionally. Cook, 1869, says it was used it was rarely used in the form of a powder. One traditional herbal warns that blue cohosh can cause precipitous labour when used alone, and it can affect foetal heart tone during delivery (Weed S 1985). References to traditional use of blue cohosh are rare; one most frequent quoted source goes back to a medical botanist Constanie (Rafinesque in 1828) who quoted a doctor Peter Smith. Peter Smith was called an Indian Doctor, the name used to describe someone using Native North American Herbs, he had been selling a commercial preparation of blue cohosh and had created an commercial pamphlet in 1813, but he had not necessarily been trained by or had observed the American Indians. So the statement can hardly be used primary evidence of use of blue cohosh by Native Americans. Of the ten tribes listed which used blue cohosh, only 2 ethnobotanical studies found blue cohosh used as a childbirth aid and in these it is not clear for which they were used as preparation for childbirth or for stalled labour (Moerman 1998). Overall, the use of blue cohosh was not universal among tribes, and the major source for taking it, as partus praeparator, is from Peter Smith. The use during labour to promote delivery was more common, and only occasional

use has been found of the plant given in preparation for childbirth (1970Vogel).

Between 1882-1905 it was listed in the United States Pharmacopoeia as a labour inducer (Lippincot 1992).

Thomsonsonian herbalism was the primary health care system in America between 1820-1850 and, by the 1830s, Blue Cohosh was included in a Mothers cordial formula and has been used since in America as a preparation for childbirth, in the form of a tincture (Bergner 2001). It was never used as a single herb. William Cook mainly used the herb as a decoction and rarely as a powder and, although any other herbs he used in quite high doses, with blue cohosh he used only very small doses in conjunction with other herbs (Bergner 2001).

So the widespread use indicates safety in most cases, however high infant mortality might have masked adverse effects of the blue cohosh. In the early 20thC it was widely used by all schools for stalled labour. When used in tincture, doses were very low, and never on its own. When used as a decoction, doses were higher

Traditionally, therefore, as a tincture, the herb would have been used in either very small doses, or larger doses as a decoction, and would not have been used on its own. The case reported by Jones and Lawson, stated that the woman took three times the recommended dose. The powder in the tablets contains all the alcohol-soluble constituents of the plant and, if used, would require very low doses; 5-10 mg for instance. The use of blue cohosh in this form is not supported by historical herbal use and the precipitous labour and cardio toxicity are consistent with pre-existing warnings in contemporary herbal literature.

Conclusion;

Blue cohosh was not traditionally used as a partus praeparator, if used, only in those experiencing a difficult labour, not for weeks up to labour. The high use in the United States by midwives indicates that most of the time blue cohosh probably will not give a problem but, occasionally, individuals will respond negatively. Though most of the time the use of blue cohosh does not cause a problem, traditional use does not support the general use of blue cohosh partus praeparator. And, with the incidence of adverse affects to blue cohosh by the new born, it should not be recommended in pregnancy.

The above herbs illustrate the importance of accurate information on traditional use, and linking it with up-to-date information. Concerning raspberry leaf we can go back a long time in its use as a labour preparation. Blue cohosh has not that tradition. Raspberry leaf is safe and possibly can help in labour. Blue cohosh can, occasionally, lead to negative effects and therefore should not be used as a preparatory herb for labour.

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