Q&A 254.3

Management of depression in breastfeeding mothers – Are St. John's Wort and other complementary therapies safe?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals

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Background

Mood disorders, including depression, are one of the leading indications for the use of complementary and alternative medicines (1). These include herbal remedies such as St.John's Wort (SJW), gingko biloba and valerian (2) and nutritional supplements such as tryptophan and S-adenosyl methionine (SAMe) (1). Use of these products is often perceived by patients to be a safer or more natural alternative to conventional antidepressants. Of these complementary remedies, the strongest evidence base for benefit in depression exists for St. John's Wort (2, 3). A recent Cochrane systematic review concluded that the available evidence suggests that the hypericum (SJW) extracts tested in the included trials (3):

a) Are superior to placebo in patients with major depression.
b) Are similarly effective as standard antidepressants;
c) Have fewer side effects than standard antidepressants.

The association of country of origin and trial precision with effects complicates the interpretation (3).

However, although there is evidence that SJW may be of benefit in treating mild to moderate depression, advice from the National Institute for Health and Clinical Excellence (NICE) is that it should not be prescribed or recommended for use by patients because of uncertainty about appropriate doses, persistence of effect, variation in the nature of preparations and potential serious interactions with other drugs such as oral contraceptives, anticoagulants and anticonvulsants (4). In the UK, the MHRA has granted marketing authorisations for a small number of preparations derived from SJW (5-9). No clinical efficacy data are required for registration of traditional herbal medicinal products.

Answer

Herbal medicines

Breastfeeding mothers should be advised not to self medicate with herbal products during lactation because of the lack of data to support safe use at this time (10).

The safety of herbal medicines in breastfeeding women has been reviewed recently in the UKMi Q&A, "Is it safe for breast feeding women to take herbal medicines?" (11). A systematic review of 32 studies of the use of herbal medicines in lactation was published in 2012 , which concluded that it is difficult to develop accurate information on the safety and efficacy of specific herbs during breastfeeding based on the available literature (12).

St John's Wort

SJW (H*ypericum perforatum*) has many biologically active constituents. The two major components initially thought to be responsible for its antidepressant activity are hypericin and hyperforin but researchers now think that the effect is due to a combination of constituents (13,14). When taken orally, SJW is usually well tolerated but side effects can include insomnia, restlessness, anxiety, agitation, gastrointestinal discomfort, dizziness and headache. Hypoglycaemia has also been documented (13).

Experience of the use of SJW in breastfeeding mothers is very limited. A prospective observational cohort study was conducted on 33 breastfeeding mothers who were taking SLW and 101 matched controls (15). In the group of infants whose mothers were taking SJW, there were two cases of colic, two cases of drowsiness and one case of lethargy. No specific treatments were required for any of the infants. No significant difference was observed between the two groups for frequency of maternal reports of decreased milk production or infant weight in the first year of life (15). In a second study in a single patient treated with 3 daily doses of Jarsin® 300 (a brand of SJW), milk hypericin levels were

below the limit of detection (0.2 nanograms/ml) whilst hyperforin levels ranged from 0.58 – 18.2 nanograms/ml. Neither component was detectable in infant plasma over the 18 hour study period (16).
Five breastfeeding mothers taking SJW (Jarsin®) 300 mg three times a day were studied to measure levels of hyperforin in maternal and infant plasma and breast milk and to estimate infant daily intake (17). Other active components of SJW were not assessed. Samples were taken between 10 and 22 weeks post partum. Breast milk concentrations were measured in two infants and were found to be at the limit of quantification (0.1 nanograms/ml). Milk/plasma ratios ranged from 0.04 to 0.13 and the mean relative dose received by the infant was estimated at 0.9 – 2.5% of the weight adjusted maternal dose. These figures are similar to those reported for other antidepressants. No adverse effects were reported in any of the infants (17).

Two small volunteer studies suggested that higher doses of Hypericum perforatum may inhibit prolactin production (18,19). This effect seems to be inconsistent (20).

A systematic review published in 2006 concluded that there is only weak scientific evidence that SJW use in lactation does not affect milk production nor affect infant weight but, in a few cases, may cause colic, drowsiness or lethargy (21). Caution is warranted when using SJW in lactation until further good quality data are available. (21).The potential for drug interactions should be borne in mind.

Breastfeeding mothers should be advised not to self-medicate with SJW. Although NICE guidance states that SJW should not be prescribed or recommended for use in depression, it is sometimes used under medical supervision. Any infant exposed to the active constituents of SJW via breast milk should be monitored for sedation, poor feeding or any other untoward effects. Its use in breastfeeding mothers of premature infants or those with morbidity should be avoided.

Gingko biloba
Gingko biloba has been used for cognitive disorders secondary to depression (22). Side effects include gastrointestinal upset, headache, dizziness and constipation. Reports of spontaneous bleeding are of concern (22). No data exist on the passage of the active ingredients into breast milk and its use in breastfeeding women is not recommended (22).

Valerian
Valerian root is most commonly used as a sedative/hypnotic and may be used to treat insomnia associated with depression but has also been used for mood disorders such as depression (23). Reported adverse effects include headache, gastric discomfort, morning drowsiness, insomnia, cardiac disturbances and vivid dreams (23). There is no experience on its use in breastfeeding women or data on the transfer of the active constituents into breast milk. Use in lactation is not recommended (23,24).

Nutritional Supplements

Tryptophan
L-tryptophan is licensed as adjunctive therapy for depression resistant to standard antidepressants. It has been associated with eosinophilia-myalgia syndrome. Other side effects include drowsiness, nausea, headache, light-headedness and suicidal behaviour. Tryptophan should be initiated under specialist supervision (25).

Tryptophan is a normal constituent of human milk (26). In the newborn, tryptophan and its metabolites are essential for brain maturation (27). It is not known whether exogenous tryptophan affects milk concentrations.

As a result of the occurrence of eosinophilia-myalgia syndrome in people taking dietary supplements containing tryptophan in the US and UK, the Tryptophan In Foods (England) Regulations 2005 states that the recommended daily dose for food supplements should not exceed 220 mg of L-tryptophan daily28). The recommended dose for the treatment of depression is 1g tryptophan three times daily, up to a maximum of 6g daily (25).

Because of the lack of data to support safe use during lactation, tryptophan supplements are best avoided in lactation.

S-adenosyl methionine
S-adenosylmethionine (SAMe) is involved in numerous biochemical methyl donation reactions, including reactions forming monoamine neurotransmitters (29). The mechanism for the antidepressant effect is unknown, but is thought to be associated with increased serotonin turnover and elevated dopamine and noradrenaline levels (30). A systematic review of SAMe as a treatment for depression concluded from an analysis of 11 studies which met the inclusion criteria that there appears to be a role for SAMe in the treatment of major depression in adults but all studies were short term, making application to the clinical setting difficult. Further data are needed about the mechanism of action, bioavailability and absorption of SAMe (31). No data are available regarding the passage of SAMe into breast milk. Use of SAMe is best avoided in lactation (30).

Summary

- The National Institute for Health and Clinical Excellence advises that St John's Wort preparations should not be prescribed or recommended for use by patients because of uncertainty about appropriate doses, variation in the nature of preparations and potential serious interactions with other drugs such as oral contraceptives, anticoagulants and anticonvulsants.

- Women who are breastfeeding should be advised not to self-medicate with herbal preparations or nutritional supplements for depression.

- Some evidence exists to support the safe use of St John's Wort during breastfeeding but further data are needed to confirm these preliminary findings. For the time being, it is recommended that St.John's Wort is avoided in breastfeeding mothers.

- Published experience of the use of complementary medicines in lactation is confined to St John's Wort and this is very limited. Minor side effects – colic, drowsiness and lethargy – have been described in breastfed infants whose mothers were taking St. John's Wort. Breastfed infants exposed to the active constituents of St John's Wort via milk should be monitored for sedation, poor feeding or any other untoward effects.

- Because of the lack of data to support safe use in lactation, tryptophan and SAMe are best avoided in breastfeeding mothers.

Limitations

Data on the use of herbal and nutritional supplements for the management of depression in lactation are very limited. The above outline is provided for general guidance only. Many decisions as to the safety of antidepressant regimens in breastfeeding mothers will need to be taken on a case-by-case basis, particularly if there are unusual circumstances e.g. infant morbidity, requirements for high doses, concurrent medication etc. In these instances, further advice can be sought from the UK Drugs in Lactation Advisory Service (UKDILAS).

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Search strategy

- UK Drugs in Lactation Advisory Service – in-house data-base
- Medline and Embase: Standard UKDILAS search pattern found at http://www.ukmi.nhs.uk/activities/specialistServices/default.asp?pageRef=2

HERBAL MEDICINE, PHYTOTHERAPY OR PLANTS,MEDICINAL,DEPRESSION

- AMED search

DEPRESSION, MILK,BREAST FEEDING, LACTATIONDISORDERS,HYPERICUM PERFORATUM, DRUG THERAPY, PLANTS MEDICINAL, GINKGO BILOBA, TRYPTOPHAN, DIET THERAPY

- Medications and Mothers' Milk Online (Medilact): Gingko Biloba ,St.John's Wort and Valerian Officinalis monographs)
- US National Library of Medicine Lactmed database
- Clinical Knowledge Service (antenatal and postnatal depression)
- SIGN website (postnatal depression and puerperal psychosis)
- National Institute for Health and Clinical Excellence website (antenatal and postnatal mental health and depression guidelines)
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