

Drugs affecting milk supply during lactation

SUMMARY

There are morbidity and mortality benefits for infants who are breastfed for longer periods. Occasionally, drugs are used to improve the milk supply.

Maternal perception of an insufficient milk supply is the commonest reason for ceasing breastfeeding. Maternal stress or pain can also reduce milk supply.

Galactagogues to improve milk supply are more likely to be effective if commenced within three weeks of delivery. The adverse effects of metoclopramide and domperidone must be weighed against the benefits of breastfeeding.

Dopamine agonists have been used to suppress lactation. They have significant adverse effects and bromocriptine should not be used because of an association with maternal deaths.

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Introduction

Breast milk is a complex, living nutritional fluid that contains antibodies, enzymes, nutrients and hormones. Breastfeeding has many benefits for babies such as fewer infections, increased intelligence, probable protection against overweight and diabetes and, for mothers, cancer prevention.¹ The World Health Organization recommends mothers breastfeed exclusively for six months postpartum.

Breastfeeding is influenced by many complex physiological and psychosocial factors. While most women have a desire to breastfeed, some do not. In high-income countries such as Australia the duration of breastfeeding is shorter than in low- and middle-income countries. A 2011 Australian Institute of Health and Welfare survey estimated that only 56% of infants younger than six months were exclusively breastfed, and by 12 months this dropped to 30%. While breastfeeding should be encouraged, a woman's right to choose not to breastfeed should be respected. By understanding the reasons for their decision, strategies can be offered to support their choice.

Physiology of lactation

Milk production begins between 10 and 22 weeks gestation. Within 48 hours of delivery, the mother produces a small amount of milk, mainly colostrum. However, it is not until serum progesterone decreases sufficiently, up to four days postpartum, that milk supply becomes more plentiful. Lactogenesis may be delayed if the baby is premature.

Milk production is controlled by a complex interplay of hormones and neurotransmitters. Prolactin is secreted by the anterior pituitary in response to

nipple stimulation. Its release is inhibited by dopamine from the hypothalamus. Within a month of delivery, basal prolactin returns to pre-pregnant levels in non-breastfeeding mothers. It remains elevated in nursing mothers, with peaks in response to infant suckling. Drugs that act on dopamine can affect lactation.

In response to suckling, oxytocin is released from the posterior pituitary to enable the breast to let down milk. Oxytocin release is inhibited by catecholamines produced if the mother is stressed or experiencing pain.

The feedback inhibitor of lactation is a peptide found in breast milk. If the milk is not removed, the inhibitor will stop milk production. When the baby cannot suckle, expressing the milk will remove the inhibitor and encourage more production.

Milk supply

A maternal perception of insufficient milk is the commonest reason for ceasing breastfeeding. Some women have difficulty producing sufficient breast milk after a difficult labour, delayed initiation of breastfeeding, separation due to the baby being preterm, formula substitution, cracked nipples or maternal illness.

Support and reassurance are as important as determining the cause of the problem, before recommending infant formula. Simple strategies can restore confidence and assist in increasing milk supply. Encourage the mother to 'hang in a bit longer' as babies have adequate nutrient stores to cover the first postpartum week. Make sure she is well hydrated, has adequate nutrient intake and home support, and reassure her that a crying baby is not necessarily a hungry baby. Increase the frequency of feeding or

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offer the baby both breasts at each feed. Check the baby's suckling patterns, ensure adequate but not excessive hydration and avoid the use of a dummy.

Where feeding problems persist, referral to a lactation consultant is an appropriate option.

Maintaining the milk supply may also be problematic as the baby grows. An infant typically requires about 150 mL/kg/day. So, to feed a 9 kg versus 3 kg baby daily (1350 mL vs 450 mL) can be a physiological challenge for some women.

Galactagogues

Antipsychotic drugs can increase pituitary prolactin secretion and breast milk production through dopamine antagonism, but the gastrointestinal motility drugs metoclopramide and domperidone are most commonly used off label as galactagogues. Metoclopramide and domperidone block dopamine D₂ receptors in the anterior pituitary and, in a limited number of clinical trials, they have had modest efficacy over placebo in initiating and maintaining lactation.² The best chance for efficacy is if the galactagogue is started within three weeks of delivery.³

The safe duration of galactagogue therapy is controversial. Although increased prolactin can be detected within eight hours of the first dose, about two weeks is required for the breast changes required to sustain milk production. Current recommendations of 10–14 days are based on a limited number of controlled studies and the limited number of longer term controlled clinical trials.

Metoclopramide

Metoclopramide is a centrally acting drug. It can increase milk supply by 66–100% within 2–5 days in total daily doses of 30–45 mg. While the relative dose in milk ranges from 4.7–14.3%, adverse outcomes in infants have not been reported.⁴ However:

- effects are dose dependent, with a threshold of 10 mg
- doses need to be administered regularly three times a day
- only 50–85% of women with low milk supply will respond
- maternal adverse effects include diarrhoea and depression
- there is a theoretical risk of extrapyramidal adverse effects in the baby
- if metoclopramide is discontinued rapidly, there can be a significant rebound decline in milk supply.

Domperidone

Domperidone is a peripheral dopamine antagonist. At doses of 10–20 mg three times daily it has comparable efficacy to metoclopramide.⁴ Little domperidone passes into milk (relative infant dose 0.01–0.04%), so the risk of extrapyramidal effects in the baby is less than with metoclopramide.⁴

In 2004, the US Food and Drug Administration (FDA) issued an alert that domperidone could cause cardiac arrhythmias. This was in response to its illegal importation into the USA by breastfeeding mothers. The data related to historical cases of high-dose, intravenous use in sick patients receiving cancer chemotherapy. Two case control studies using oral domperidone in a general population supported this rare association. However, only three probable case reports in lactating women have been received by the FDA in postmarketing surveillance.⁵ Concomitant use of moderate or strong inhibitors of cytochrome P450 3A4 such as ketoconazole can increase plasma concentrations of domperidone and therefore the risk of QT prolongation.

In 2013, the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency recommended that the daily oral dose be restricted to a maximum of 30 mg and that domperidone not be used for longer than one week. It is therefore important that women being offered domperidone as a galactagogue have tried non-pharmacological strategies first. They need to be aware of the very low risk of QT prolongation and weigh this against the benefits of breastfeeding.

Complementary medicines

Herb-derived galactagogues have been used for centuries in folk medicine to augment lactation. These plants contain lipophilic, pharmacologically active constituents which, if taken in sufficient quantity, can pass into the breast milk. While there are generally few adverse effects (Table), there is limited evidence of efficacy. Most of the supporting evidence is based on case reports, or historical use.

Lactation suppression

Some women may require lactation suppression after miscarriage, stillbirth, maternal illness or when they do not wish to breastfeed. While breast stimulation should be avoided, there is a risk of engorgement if the breasts are not drained.

Pharmacological options all have significant adverse effects. The dopamine agonist bromocriptine was associated with maternal deaths from myocardial infarction and is no longer

recommended. It has been replaced by a single 1 mg dose of long-acting cabergoline, ideally taken on the first postpartum day. The common adverse effects are nausea, headache and dizziness. If the woman changes her mind, it can be difficult to restore milk production.

Other drugs no longer used include large doses of pyridoxine and diuretics. Oestrogen is avoided because of the risk of thromboembolism.

Conclusion

Breast feeding is a natural process with benefits for both mother and baby. Some women find it difficult to breastfeed, but many problems can be overcome with reassurance and support.

Occasionally, non-drug approaches may not increase the supply of milk. There is limited evidence for the off-label use of domperidone and metoclopramide. However, if a drug is considered for increasing milk supply, discuss with the mother a trial of an agreed dose, for a maximum agreed duration beginning as soon as feasible postpartum. Also discuss the potential for adverse effects.

There are few indications for using drugs to suppress lactation. Cabergoline has been used, but bromocriptine should be avoided because of maternal deaths. <

Conflict of interest: none declared

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FURTHER READING

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Table Adverse effects of herbs used as galactagogues

Herb	Adverse effects
Alfalfa <i>Medicago sativa</i>	Dose-related bleeding
Blessed thistle <i>Cnicus benedictus</i>	Gastric irritation and potential allergies, as it is part of the ragweed family
Chaste tree <i>Vitex agnus-castus</i>	Nausea, vomiting, irritation, pruritus, rash, headache, increased menstruation
Dill <i>Anethum graveolens</i>	Alterations in sodium balance
Fennel <i>Foeniculum vulgare</i>	Allergic reactions, dermatitis (photo and contact)
Fenugreek seed <i>Trigonella foenum-graecum</i>	Hypoglycaemia, hypertension, diarrhoea and maple syrup body odour in mother Allergy potential as part of the peanut family
Goat's rue <i>Galega officinalis</i>	Hypoglycaemia, hypotension, coughing, dose-related toxicity
Milk thistle (silymarin) <i>Silybum marianum</i>	Allergic reactions, diarrhoea
Malunggay <i>Moringa oleifera</i>	Hypoglycaemia, sedation
Raspberry leaf <i>Rubus idaeus</i>	Hypersensitivity reactions, changes in blood glucose
Shatavari <i>Asparagus racemosus</i>	Possible teratogenicity – avoid in pregnancy
Damiana <i>Turnera diffusa</i>	Hepatotoxicity, confusion and hallucinations with high-dose <i>Turnera</i>