



## GALACTOGOGUES: EFFECTIVENESS AND SAFETY

### Key Points:

- Medications should never replace adequate support, education and assessment of breastfeeding technique to increase milk production.
- Current evidence does not support the efficacy or safety of galactogogues in women wishing to initiate lactation.
- There is little evidence to support galactogogue use to maintain adequate milk supplies and should be used as a last resort, after lactation counseling of proper technique.
- No medications, prescription or herbal, have been approved for use as a galactogogue by Health Canada
- If medications are recommended, 10 mg PO TID of either metoclopramide or domperidone may be used; most studies were 7-10 days in duration.

### Breastfeeding:

Breastfeeding has been the primary source of nutrition for a newly born baby for centuries.<sup>1</sup> It is a natural, effective and healthy way for the baby to get adequate nutrition required to grow and thrive. Short and long term benefits have been associated with breastfeeding including: reduced sudden infant death syndrome, positive immunological effects; reductions in the risks of otitis media, severe lower respiratory tract infections, and type 1 and 2 diabetes.<sup>2</sup> Proper breastfeeding techniques such as frequent feeding sessions, regular and complete milk removal, and proper latching, need to be taught and practiced by new mothers in order to achieve adequate milk removal and therefore adequate milk production<sup>3</sup> Breastfeeding is not recommended for HIV positive mothers in developed countries in order to reduce mother to infant transmission.

### What is a Galactogogue?

Galactogogues are medications or other substances believed to assist initiation, maintenance, or augmentation of the rate of maternal milk synthesis.<sup>4</sup> The theory behind pharmaceutical galactogogues is that dopamine antagonists increase prolactin secretion and subsequently increase the overall rate of milk synthesis. However, studies show no correlation exists between serum prolactin and increased milk volume.<sup>4-7</sup> Galactogogues have been prescribed to increase the amount of milk production. They are commonly used in

mothers with infants in the neonatal intensive care unit, adoptive mothers wanting to breastfeed, or for re-lactation in mothers who have weaned their infant and would like to re-establish breastfeeding.<sup>4</sup> Prescription medications such as domperidone and metoclopramide are two galactogogues that have been prescribed for breastfeeding mothers. Over twenty herbal products, e.g. Fenugreek, goats rue, and milk thistle also claim to have some galactogogue activity.

### Metoclopramide:

Metoclopramide is a selective dopamine antagonist. It is thought to block dopamine receptors at the pituitary and adrenocortical cellular level therefore causing an increase in prolactin levels. It has been used off-label as a galactogogue since 1975.<sup>8</sup> It is the most-studied galactogogue to date with 15 clinical trials published.<sup>9-23</sup> A major limitation to most of these studies was lack of education given to subjects on proper breastfeeding techniques.<sup>8</sup> However, four double-blinded, randomized control trials (RCT) met current standards and were of value when evaluating its efficacy.<sup>13,18,21,23</sup> Of the four trials, none found a statistically significant difference in milk volume or duration of breastfeeding between metoclopramide and the placebo group. Two of these studies did however find optimal counseling on breastfeeding to have a positive association with a statistically significant increase in infant weight gain.<sup>4</sup>

One double-blind RCT looked at mothers of premature infants.<sup>13</sup> They were randomized into a treatment group: metoclopramide 10 mg three times a day or a placebo group. All mothers received standard instructions from a lactation consultant. Milk volumes were measured daily for 17 days. No differences were found in volumes between the two groups. One major flaw of this study is that no selection was made for mothers expressing difficulties producing breastmilk, however, this study does demonstrate the importance of breastfeeding education.

#### **Domperidone:**

Domperidone is another dopamine antagonist, which selectively blocks D2 receptors in the pituitary and adrenocortical cellular level. Domperidone has been used in lactating mothers who perceive a low production of breast milk for many years although this is not a Health Canada approved indication. Although not as extensively studied, domperidone has been an attractive alternative to metoclopramide because it does not cross the blood brain barrier.<sup>24</sup> The evidence behind the use of domperidone as a galactagogue is severely lacking. There have been no studies to date to prove its efficacy in the use in adoptive mothers or mothers looking to establish re-lactation.

However, a number of small studies have looked at domperidone and its use in mothers with premature infants.<sup>8</sup> A recent Cochrane review concluded there were modest improvements in the volume of expressed breast milk short-term when domperidone 10 mg three times daily is used short-term (7–14 days) after preterm delivery.<sup>25</sup>

One study by Wan et al looked at response rates with different doses of domperidone on milk production in mothers with preterm infants. He concluded if no response was seen with domperidone 10mg three times a day, no additional benefit to increase the dose to 20mg was seen, however, it was associated with more side effects.<sup>26, 27</sup>

#### **Safety:**

Safety and long term effects of domperidone and metoclopramide as they pertain to lactogenesis have not been well studied. Both drugs have been associated with abdominal cramping, diarrhea or constipation, drowsiness, dizziness, anxiety, and skin rash.<sup>24</sup>

Metoclopramide is also associated with an increased risk of depression with suicide ideation. In July 2011, Health Canada issued a warning regarding tardive dyskinesia associated with metoclopramide use, and cautioned against long term use (>12 weeks).<sup>28</sup> As of

March 2012, Health Canada has also issued an advisory on domperidone, stating doses greater than 30mg a day are associated with an increased risk of QT prolongation, and should be avoided in patients on other drugs known to prolong the QT interval.<sup>29</sup> Both drugs cross into the breast milk; however, the dose of each drug the baby would receive is lower than that used anecdotally to treat gastric reflux in infants. Since long term safety has not been adequately studied in infants, caution should be exercised when considering these medications.

#### **Herbal Products:**

There are many herbal products out there all claiming to have some lactogenic properties. Fenugreek, goats rue, fennel, and milk thistle have been used for the stimulation of milk production in breastfeeding mothers, though no evidence is available for any of these herbs. Two case reports of breastfed infants and mothers using fennel showed symptoms of neurotoxicity.<sup>30</sup> Some references state milk thistle, goat's rue, and fenugreek are contraindicated during breastfeeding.<sup>2</sup> Products that are not approved by Health Canada may lack standardization, and/or contain potential contaminants. For these reasons and the lack of evidence, herbal products should be avoided whenever possible.<sup>4</sup> If a mother is determined to use a natural galactagogue a product with a Natural Product Number (NPN) should be recommended.

#### **Where is the Evidence?**

Currently all the research for galactagogue use has been conducted in lactating women with or without established lactation problems; this research has not been able to establish efficacy. The most effective method to stimulate milk production is still proper breastfeeding. Galactagogue use may be of benefit in adoptive mothers looking to breastfeed, mothers with infants in the neonatal intensive care unit, or for mothers looking to re-establish breastfeeding after weaning.<sup>4,25</sup> With all medications, prescription or herbal, there are always safety concerns that need to be considered. However, if galactagogues are to be recommended in these situations more studies need to be conducted in non-lactating mothers to establish the role of galactagogues in this population.

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