

## Case Report

# A Successful Induction of Lactation in Surrogate Pregnancy with Metoclopramide and Review of Lactation Induction

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### Abstract

In surrogate pregnancies genetic parents have little opportunity for early bonding with their infants, either prenatally (in utero) or during the immediate postnatal period. Procedures commonly used to induce lactation include both pharmacologic and nonpharmacologic methods, often in combination. Studies reporting induced lactation are sparse, due to the rarity of augmented lactation. Here we report a case of lactation induction following a surrogate pregnancy. Other methods that can be used to augment lactation are described below. We used metoclopramide in this case due to the success rates reported in previous studies and case reports. Additionally, it is a well tolerated and safe agent.

**Keywords:** Surrogate, Pregnancy, Lactation, Metoclopramide

### Introduction

Infertility is emotionally painful and draining, particularly if the couple has been trying for a number of years with several failed infertility treatment cycles. Choosing adoption or surrogacy can be a positive experience for some couples (1). However, this route is not ideal due to the remorse of not being able to experience pregnancy, give birth nor enjoy the bond and closeness experienced with breastfeeding. In this way, the neonate is deprived of the advantages of breastfeeding, which include improved nutritional, emotional and cognitive development (2, 3) as well as vaccination against infections and allergies (4). Induction of lactation is a good option to overcome this problem, unfortunately not enough milk is produced to exclusively breastfeed the infant, but women find satisfaction in this rigorous process because of the maternal-infant bonding it promotes (5). Procedures commonly used to induce lactation include both pharmacologic and non-pharmacologic methods, often in combination (6). Few studies exist regarding induced lactation, because the practice of augmented lactation is uncommon. Bryant, in a recent review of induced lactation, reported no large studies or randomized controlled trials regarding the use of domperidone and metoclopramide in induced lactation (7). In March 2001, the first case of a mother breastfeeding her baby born via a surrogate host was reported (1). Other recent studies have reported the use of metoclopramide as a galactagogue

(7-9). Use of this drug may be warranted when risks versus benefits are considered. Controversy exists, however, surrounding the use of domperidone and metoclopramide for induced lactation. We present the process of lactation induction with metoclopramide in combination with nipple stimulation for an Iranian woman who was the commissioning mother in a surrogate pregnancy.

### Case report

A 36 year-old woman presented with a 14 year history of secondary infertility from Polycystic ovarian syndrome (PCOS) and repeated assisted reproductive technology (ART) failures (two tubal ectopic pregnancies, and two, eight week pregnancies without fetal heart) in Royan Institute, where she requested the use of a surrogate host in this centre. She underwent ovulation induction using a standard protocol. Following 17 oocyte retrievals and intra cytoplasmic sperm injection (ICSI) performed with the use of her husband's spermatozoa, there were six embryos which underwent a preimplantation genetic diagnosis (PGD) program due to the patient's history of abortions and repeated ART failures. Two high quality male embryos were transferred to the surrogate host who was her sister-in-law, which resulted in a singleton pregnancy. Routine prenatal care was performed for the surrogate host. At 28 weeks of pregnancy, according to Biervliet et al. oral metoclopramide therapy

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at a dose of 10 mg twice daily was initiated in the commissioning mother (1). The commissioning mother was followed by phone contact to assess for any potential adverse drug effects. After a one week period, due to the absence of adverse drug effects, the dosage was increased to eight tablets daily and continued until one week prior to the expected delivery date. The treatment was well tolerated with no metoclopramide side effects reported. In addition to metoclopramide therapy, mechanical stimulation of the nipples was performed. Following cesarean section of the surrogate host on June 16, 2009, the commissioning mother was unable to feed her baby due to absorbed nipples. However, after encouragement and continued twice daily metoclopramide therapy combined with nipple stimulation by an electric breast pump; lactation was successfully induced. The commissioning mother was able to feed her baby and thus enjoy the close contact of breast-feeding, which seemed to satisfy both the mother and baby. After two months, the metoclopramide dosage was decreased to one-half tablet daily. She successfully continued breast-feeding until three months, although milk production and secretion were present, it was inadequate for the infant and therefore, the feedings were supplemented with formula.

### **Induced Lactation**

Normal lactation is maintained by a balance of various hormones in combination with frequent and regular stimulation of the breasts. Estrogen and progesterone prepare the breast by proliferation of both the ductal and alveolar systems during pregnancy, in anticipation of the time when lactation will start (7). Since prolactin is the essential hormone during lactation; therefore attempts to induce lactation are largely based on increasing prolactin levels. Induction of lactation is the process by which a nonpregnant woman who is not currently breastfeeding another child is stimulated to lactate (6, 7). Initially, augmentation of lactation has been used to provide nourishment for infants of mothers who are either unable to breast-feed or who died during childbirth. Currently this process is used for adoptive mothers desiring to breastfeed their adopted infants. Several methods (pharmacological and non-pharmacological) have been implemented to augment lactation (6).

### ***Non-pharmacological methods***

Nipple stimulation, by hand or electric breast pump, mimics the sucking of a newborn infant and the suggested time period to commence nipple stimulation techniques is at least two months prior to the arrival of

the adopted infant (10-12). Other non-pharmacological methods such as dietary aids and breast massage with warm compresses, remain controversial (6).

### ***Pharmacological methods***

Galactogogues are medications that aid in initiating and maintaining adequate milk production. The most common agents are listed in Table 1.

Metoclopramide antagonizes the release of dopamine, which in turn inhibits the effect of prolactin-inhibitory factor (PIF) on the pituitary. Metoclopramide blocks the effects of dopamine, which consequently increases prolactin production and therefore milk production. Prolactin may reach 3-8 times the normal levels within one hour of metoclopramide administration and remain elevated for up to eight hours (13). This drug is also being evaluated in commissioning mothers who desire to breastfeed after their infants are delivered by surrogate mothers (1). Lastly, metoclopramide has been successfully used by adopting mothers to stimulate milk production (7-9). The general dose of metoclopramide for induction of lactation is 10-15 mg, three times daily for a period of 7-15 days. Because metoclopramide crosses the blood-brain barrier, its use can be limited by significant central nervous system (CNS) side effects (13). Sedation is the most common side effect, occurring in approximately 10% of users. Depression occurs less frequently. Extra-pyramidal side effects, such as tardive dyskinesia (1%), can occur and are more common in women and children (9, 13). Although the medical literature reports a low incidence of depression, it is a widely held belief among women seeking to induce lactation that depression is a very significant and common side effect (7). Metoclopramide remains the galactogogue of choice due to its documented record of efficacy and safety in women and infants (9). Domperidone, like metoclopramide, is a dopamine antagonist which crosses the blood brain barrier and enters the breast milk to a lesser extent than metoclopramide; thus decreasing the risk of toxicity to both mother and infant, making it an attractive alternative (7-9, 11, 14). Traditional antipsychotics, sulpiride (6-9, 15) and chlorpromazine (7, 9, 16), have been evaluated however adverse events limit their use. Human growth hormone (9), thyrotrophin-releasing hormone (17), and oxytocin (1, 9) have also been studied. Finally, herbal medications have traditionally been used as galactagogues in some cultures. For example, fenugreek and blessed thistle have not been adequately studied, as objective data have been obtained from women already lactating (7-9). Numerous other herbs such as milk thistle, fennel, alfalfa, oats, and marshmallow root are reported to

**Table 1: Galactagogue agents clinically used to augment lactation**

Agent	Mechanism of Action	Recommended Dosage	Adverse Effects	Hale's Lactation Risk Category*	References
<b>Metoclopramide</b>	Blockage of pituitary dopamine receptors; crosses blood-brain barrier	Oral: 10-15 mg, 3 times per day	Well tolerated. Diarrhea, sedation, depression, tremor, bradykinesia	L2	Biervliet et al., 2001; Bryant, 2006; Gabay, 2002; Hale, 2006
<b>Domperidone**</b>	Peripheral dopamine antagonist; minimally crosses blood-brain barrier	Oral: 10-20 mg, 3-4 times per day	Well tolerated. Dry mouth, skin rash or itching, headache, gastrointestinal disturbance	L1	Bryant, 2006; da Silva & Knoppert, 2004; Gabay, 2002; Hale, 2006; Riordan, 2005
<b>Sulpiride</b>	Selective dopamine antagonist	Oral: 50 mg, 2 times per day	Tremor, bradykinesia, acute dystonic reactions, sedation	L2	Emery, 1996; Gabay, 2002; Hale, 2006
<b>Chlorpromazine</b>	Central nervous system tranquilizer; blocks dopamine receptors	Oral: 25 mg, 4 times per day reported; use not recommended because of associated adverse reactions	Sedation, lethargy, tremor, bradykinesia, weight gain	L3	Gabay, 2002; Hale, 2006; Nemba, 1994
<b>Thyrotrophin-releasing hormone</b>	Direct stimulation of adenohypophyseal lactotrophs	Nasal spray: 1mg four times daily	Well tolerated. No clinical signs of hyperthyroidism	-	Peters et al., 1991
<b>Fenugreek</b>	Herbal supplement; reputation as a galactagogue, but mechanism of action unknown	Oral: 2-3 capsules, 3 times per day; variable	Maple syrup odor in urine and sweat, diarrhea, hypoglycemia, dyspnea	L3	Bryant, 2006; Hale, 2006
<b>Blessed Thistle</b>	Herbal supplement; reputation as a galactagogue, but no data support its use	Unknown	None	L3	Bryant, 2006; Hale, 2006

\*Hale's Lactation Risk Categories are as follows: L1 (Safest) = The drug is not orally bioavailable in the infant, or no increase in adverse effects to the infant have been noted in controlled studies or observed with a large number of breastfeeding mothers; L2 (Safer) = A limited number of studies of this drug have shown no increase in adverse effects to the infant and/or little evidence exists of risk to the breastfeeding infant; L3 (Moderately Safe) = No controlled studies by breastfeeding women exist, but risk of untoward effects to infant is possible. Therefore a risk benefit assessment should be made (6).

aid in lactation, however research is scant (7). Most women who succeed in inducing lactation require supplementation in order to provide an adequate amount of nutrition for their infants. Since frequent nursing encourages milk production, it is desirable to keep the infant at the breast for all feelings. The best way to achieve both goals is to use a supplemental feeding device worn at the breast that delivers formula (or stored breast milk). Two common devices are the SNS by Medela and the Lact-Aid Nursing Training system (7). The mother who chooses to augment lactation will need more support and encouragement from her partner, family and health clinician in her efforts to induce lactation. Emotional and psychological factors can influence prolactin and oxytocin secretions, therefore self-confidence and a strong desire to succeed are important factors of success (16, 18).

## Discussion

A case of lactation induction after a surrogate pregnancy is reported. Other methods that can be used for augmenting lactation are described above. We have used metoclopramide in this case because of the success rates reported in both previous studies and case reports. Additionally, it is a well tolerated and safe agent.

Most recommendations in the area of induced lactation are based on anecdotal experience because the few studies that exist are either small, short-term studies or case reports (1,10,19,20). Placebo-controlled trials of metoclopramide have demonstrated doses of 10 to 15 mg three times a day to be effective in increasing prolactin and milk production in women with lactation problems (7). Another placebo-controlled study of domperidone, 10 mg three times a day, reported increases in prolactin levels

and milk production in women who were pumping milk for their newborns in the neonatal intensive care unit (NICU) (7). In a comparison study, single doses of 5 and 10 mg of metoclopramide and 10 mg of domperidone were administered to nonpregnant women. Prolactin levels were then measured at various time intervals. The results of this study showed that nulliparous women had a greater response (percentage of elevation above baseline) to both medications, with the greatest response to metoclopramide (10 mg). Multiparous women had similar responses to all medication doses (21). Several studies previously evaluated the efficacy of medications on lactation in puerperal women or adoptive mothers. Our case was the second commissioning mother that succeeded in breast-feeding, the first case was reported by Biervliet et al. An important reason for the increased success in commissioning mothers when compared with adoptive mothers is that surrogate mothers have a longer preparation period and galactagogue treatment can be started sooner after delivery. However, in adoptive mothers, the timing of the adoption is rarely specific and it is frequently a great challenge for a mother to initiate preparation for lactation induction in an adequate amount of time.

For many mothers, the primary goal of lactation induction is not milk production but rather establishing an emotional bond with their infants. The purpose of most adoptive and commissioning mothers interested in lactation induction is to achieve the enhanced mother–infant bonding that breastfeeding promotes, rather than the nutritional benefits it brings. Therefore, it is necessary for both clinicians and nurses to give them sympathetic counseling and adequate information to enable them to achieve high success rates (1,6). The success rates for lactation induction amongst adopting women have ranged from 50–90% (1).

Few studies exist on lactation induction, and those that are available are small and primarily have studied women who completed their pregnancies. Additionally, even less is known about the mechanisms of action that herbal supplements use to increase lactation. In our case, metoclopramide therapy appears to be safe, well tolerated and effective in induced lactation in a surrogate pregnancy. Hence, we suggest that this preparation can be used for all commissioning mothers. However, a need for more well-designed studies in order to consider the risks versus benefits of this drug exists.

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