# **CASE REPORT**

# Induction of lactation in the intended mother of a surrogate pregnancy

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A case of a successful induction of lactation in a commissioning mother of a surrogate pregnancy is reported. Induction of lactation was achieved with oral metoclopramide which was well tolerated. Alternative methods to induce lactation are reviewed. The advantages of breast-feeding and the relative ease with which lactation can be induced after a surrogate pregnancy would suggest that this could be offered to all commissioning mothers.

Key words: induction of lactation/metoclopramide/surrogacy

# Introduction

In the UK, surrogacy is a well accepted option of treatment for a minority of infertile women with certain clearly defined medical disorders, and the reported perinatal outcome of IVF surrogate pregnancies is reassuring (Parkinson *et al.*, 1998). However, the neonate is usually deprived of the advantages of breast-feeding, which include improved cognitive development (Rogan and Gladen, 1993; Anderson *et al.*, 1999) and protection against infection and allergy (Haller and Simpser, 1999). Ideally this may be overcome with induced lactation. Furthermore, breast-feeding allows close skin and eye contact which might be beneficial in achieving a mother–infant relationship after a surrogate pregnancy.

# **Case report**

A 27 year old woman was diagnosed with congenital absence of the uterus. As both her ovaries were present, she underwent ovulation induction using a standard protocol. Following oocyte retrieval and IVF using her husband's spermatozoa, two embryos were transferred to a surrogate host, resulting in a singleton pregnancy.

When the surrogate host was 26 weeks pregnant, the commissioning mother expressed the wish to breast-feed the baby. To induce hyperprolactinaemia in the absence of a preceding pregnancy, she was treated with oral metoclopramide 10 mg three times daily; this was started when the surrogate host was 28 weeks pregnant and discontinued 1 week before the expected date of delivery. The treatment was well tolerated and its effect was assessed initially by measuring serum prolactin and oestradiol concentrations, which were 1195 mU/l (reference values:

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0–550 mU/l) and 367 pmol/l (reference values: 150–1150 pmol/ l) respectively. In addition to drug therapy, nipple stimulation was performed with an electric breast pump.

Following the delivery of the surrogate host, the commissioning mother confirmed that lactation had been successfully induced; she reported that breast milk was produced quite easily but in insufficient quantities to breast-feed the baby exclusively and therefore the feeding was supplemented with formula milk. The commissioning mother enjoyed the close contact of breast-feeding and this seemed to comfort the baby. She discontinued breast-feeding after 3 months and was very satisfied with the induced lactation experience.

We believe that this is the first report of successful induction of lactation after surrogate pregnancy, although there have been several reports on breast-feeding after adoption.

## Induced lactation

Breast-feeding is physiologically and hormonally linked to pregnancy. The breast is prepared by oestrogen and progesterone, which cause proliferation of the ductal and alveolar system throughout pregnancy in anticipation of the time when lactation will begin. These hormones work in association with an increase in serum prolactin levels. The importance of prolactin in lactation may be seen by the failure of lactation following post-partum pituitary necrosis in Sheehan's syndrome.

Induced lactation is the process by which a non-puerperal woman is stimulated to lactate. Historically the motivation for this has been to provide nourishment for an infant whose mother had either died in childbirth or was unable to breastfeed. Recently, the interest in induced lactation stems from a desire on the part of an adopting mother to nurture an adopted

Table I. Drugs used	l clinically to	induce or augment	lactation
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Drug	Dosage	Side-effects	Reference	Action
Domperidone	10 mg three times daily	Well tolerated	Petraglia et al., 1985	Blockage of pituitary dopamine receptors
Thyrotrophin-releasing hormone	Nasal spray; 1 mg four times daily	Well tolerated, no clinical signs of hyperthyroidism	Peters et al., 1991	Direct stimulation of adenohypophyseal lactotrophs
Metoclopramide	10 mg three times daily 10 mg four times daily	Well tolerated; fewer side-effects	Banapurmath <i>et al.</i> , 1993; Nemba, 1994; Hallbauer, 1997	Blocks dopamine mediated inhibition of prolactin secretion
Sulpiride	50 mg three times daily	Extrapyramidal symptoms, drowsiness	Hallbauer, 1997	Blocks dopamine mediated inhibition of prolactin secretion
Chlorpromazine	25–100 mg three times daily	Extrapyramidal symptoms, drowsiness	Brown, 1977; Nemba, 1994	Blocks dopamine mediated inhibition of prolactin secretion

child at the breast. Several methods and pharmacological agents have been used to induce or augment lactation.

# Traditional methods

Herbal teas are used as galactagogues in some cultures (Lawrence, 1994), while much of the success of induced lactation in New Guinea has been attributed to the ingestion of coconut milk (Mead, 1963).

# Oestrogens and progestogens

Oestrogens and progesterone stimulate the proliferation of the alveolar and ductal systems throughout pregnancy, working in association with an increase in prolactin production. After delivery has occurred and the placenta has been removed, there is a marked fall in oestrogen and progesterone, and prolactin initiates milk production. Efforts to simulate this hormonal response have had variable success (Lawrence, 1994). A single priming dose of 100 mg of medroxyprogesterone 1 week prior to chlorpromazine or metoclopramide (Nemba, 1994), ethinyloestradiol 50  $\mu$ g three times daily (Kramer, 1995) or a combination of oestrogens and progestogens long-term (Thearle and Weissenberger, 1984) have been used successfully to induce adoptive breast-feeding

# Prolactin secretion increasing drugs (Table I)

Several drugs have been used to increase prolactin secretion. An increased basal prolactin concentration and milk production was seen after the use of thyrotrophin-releasing hormone nasal spray in women with inadequate lactation after giving birth (Peters et al., 1991). Metoclopramide increases prolactin release, regardless of the route of administration (McNeilly et al., 1974; Harrington et al., 1983) and this has been used successfully to induce lactation after adoption (Banapurmath et al., 1993; Nemba, 1994). Domperidone has been used to increase prolactin levels but after prolonged treatment a diminished response is seen (Brouwers et al., 1980). As it does not cross the blood-brain barrier it does not provoke extra pyramidal effects (Laduron and Leysen, 1979). Domperidone has been used clinically to induce lactogenesis in puerperal women (Petraglia et al., 1985) but has not been used in non-puerperal women to induce lactation. Sulpiride, an antipsychotic neuroleptic, also increases prolactin levels but few data are available to recommend its use for the

improvement or induction of lactation, and possible extrapyramidal side-effects are cause for concern (Hallbauer, 1997). An increase in prolactin secretion is seen after chlorpromazine and this may enhance lactation (Lawrence, 1994). It has been used clinically to induce lactation (Nemba, 1994) but its sedative properties make it less suitable. Cimetidine increases prolactin level after i.v. administration but this effect was not seen after an oral dosage (Cavallini *et al.*, 1979) and no data are available on its use to induce lactation.

No documented trials are available to establish which pharmacological agent is most effective and it has been suggested that these agents might be of mainly psychological benefit (Waterston, 1995).

# Oxytocin

Oxytocin nasal spray has been used in early lactation with some success in enhancing let-down (Newton and Egli, 1958), although it has no effect on the secretion of prolactin. Therefore it could be considered once lactation has been initiated. It has been associated with an easier establishment of breast-feeding and an improvement of milk production in puerperal women (Huntingford, 1961). Women using oxytocin nasal spray for induction of lactation were divided on the efficacy of its use, but often reported that the milk ejection response was more likely to occur if it was used in conjunction with nipple stimulation (Auerbach and Avery, 1981).

To induce lactation it has been suggested that the woman should begin systematically to express the breast manually and stimulate the nipples for up to 2 months prior to the arrival of the infant (Lawrence, 1994). The most important factor promoting continued breast-milk production is regular stimulation of the nipples, correct suckling and regular emptying of the breast. It has been stated (Jeliffe and Jeliffe, 1972) that a basic factor for continued milk production is stimulation of the nipple and areola.

As the onset of lactation varies in time, provision for additional nourishment during the period of establishing milk production is most important. This can be provided by bottle-feeding, but an alternative is the Lact-Aid Nursing Trainer System<sup>®</sup>. This system consists of a flexible tube attached to a bag containing formula milk. It is positioned near the mother's

Psychological factors can influence the prolactin and oxytocin reflexes and it has been suggested that confidence and a strong desire to lactate are important components of success (Lawrence, 1994; Nemba, 1994). Support from her partner, family and friends for the mother in her attempt to breast-feed is essential (Lawrence, 1994). This should be supplemented by professional support but unfortunately most clinicians are not familiar with the principles of induced lactation. Professional help is however available from qualified lactation consultants (International Board of Certified Lactation Consultants).

### Success rate

A study of induction of lactation after adoption with chlorpromazine or metoclopramide in non-puerperal women in New Guinea showed an 89% success rate (Nemba, 1994). The success rate was similar in women who had never lactated as compared with women who had lactated previously, although a higher success rate had been reported previously in the latter group (Auerbach and Avery, 1981). Induction of lactation after adoption by a combination of nipple stimulation, the drop and drip method and metoclopramide 10 mg 8 hourly showed a 50% success rate (Banapurmath *et al.*, 1993). It has also been suggested that if the pleasurable experience in the mother is taken as an index of success, induced lactation is associated with good results (Thearle and Weissenberger, 1984).

#### Discussion

A case of induction of lactation after a surrogate pregnancy is described and the different methods with which this can be achieved are reviewed above.

The main reasons for the wish of the commissioning mother to breast-feed were to achieve a mother–infant relationship and the nutritional benefits of breast-milk as compared to formula milk. These reasons were also important features in the studies of non-puerperal lactation of adoptive children (Auerbach and Avery, 1981; Elia, 1994; Lawrence, 1994).

A fundamental difference of breast-feeding after adoption in comparison to surrogacy is that adoptive mothers are given a very short notice when to expect the child and therefore are unable to induce lactation before the baby arrives. Breastfeeding after a surrogate pregnancy allows a longer period of preparation and treatment with a galactogogue and is commenced sooner after delivery and therefore potentially has a better chance of success. Metoclopramide was chosen in this case because of the success reported in previous studies. Furthermore, it is a well tolerated preparation.

A commissioning mother who is interested in inducing lactation requires sympathetic counselling in order to appreciate that she may not be able to feed completely the infant by her milk alone without supplementation. The need to supplement the infant's intake while the milk supply is being developed and the availability of supplemental nursing systems needs to be addressed. It should be stressed that the inability to exclusively breast-feed the baby should not be seen as a failure; the definition of success is more related to the mother's feeling about her breast-feeding experience than to the quantity of milk she produces or how long she breastfeeds (Cheales-Siebenaler, 1999).

Induced lactation after a surrogate pregnancy offers many advantages. At present the possibility and its relative ease of success are not widely appreciated and may not be discussed with the patient. However it should be offered to all commissioning mothers.

#### References

- Anderson, J.W., Johnstone, B.M. and Remley, D.T. (1999) Breast-feeding and cognitive development: a meta-analysis. Am. J. Clin. Nutr., 70, 525–535.
- Auerbach, K.G. and Avery, J.L. (1981) Induced lactation: a study of adoptive nursing by 240 women. Am. J. Dis. Child., 135, 340–343.
- Banapurmath, C.R., Banapurmath, S. and Kesaree, N. (1993) Successful lactation in surrogate mothers. *Indian J. Paediat.*, **60**, 693–743.
- Brouwers, J.R.B.J., Assies, J., Wiersinga, W.M. *et al.* (1980) Plasma prolactin levels after acute and subchronic oral administration of domperidone and of metoclopramide: a cross-over study in healthy volunteers. *Clin. Endocrinol.*, **12**, 435–440.
- Brown, R.E. (1977) Relactation: an overview. Pediatrics, 60, 116-120.
- Cavallini, G., Cascio, V., Angelini, G. *et al.* (1979) Serum prolactin response to acute and chronic cimitidine administration in man. *Acta Hepato*gastroenterol., 7, 627–629.
- Cheales-Siebenaler, N.J. (1999) Induced lactation in an adoptive mother. *J. Hum. Lact.*, **15**, 41–43.
- Elia, I. (1994) Adoptive breastfeeding. Nurs. Stan., 8, 20-21.
- Hallbauer, U. (1997) Sulpiride (Eglonyl) use to stimulate lactation. S. Afric. Med. J., 87, 774–775.
- Haller, C.A. and Simpser, E. (1999) Breastfeeding: 1999 perspective. Curr. Opin. Pediatr., 11, 379–383.
- Harrington, R.A., Hamilton, C.W., Brogden, R.N. et al. (1983) Metoclopramide: an updated review of its pharmacological properties and clinical use. Drugs, 25, 451–494.
- Huntingford, P.J.H. (1961) Intranasal use of synthetic oxytocin in management of breast-feeding. Br. Med. J., 243, 709–711.
- Jeliffe, D.B. and Patrice Jeliffe, E.F. (1972) Non-puerperal induced lactation. *Pediatrics*, **50**, 170–171.

Kramer, P. (1995) Breast feeding of adopted infants. Br. Med. J., 311, 188-189.

- Laduron, P. and Leysen, J. (1979) Domperidone: a specific *in vitro* dopamineantagonist devoid of *in vivo* central dopaminergic activity. *Biochem. Pharmacol.*, **12**, 2161–2167.
- Lawrence, R.A. (1994) *Breastfeeding: A Guide for the Medical Profession*, 4th edn, Ch. 17. Mosby Year Book, St Louis.
- McNeilly, A.S., Thorner, M.O., Volans, G. et al. (1974) Metoclopramide and prolactin. Br. Med. J., 2, 729.
- Mead, M. (1963) Sex and Temperament in Three Primitive Societies. Dell Publishing, New York.
- Nemba, K. (1994) Induced lactation: a study of 37 non-puerperal mothers. *J. Trop. Paediat.*, **40**, 240–242.
- Newton, M. and Egli, G.E. (1958) The effect of intranasal administration of oxytocin on the let-down of milk in lactating women. *Am. J. Obstet. Gynaecol.*, **1958**, 103.
- Parkinson, J., Tran, C., Tan, T. et al. (1998) Perinatal outcome after in-vitro fertilization surrogacy. Hum. Reprod., 14, 671–676.
- Peters, F., Schulaze-Tollert, J. and Schuth, W. (1991) Thyrotrophin-releasing hormone: a lactation promoting agent? Br. J. Obstet. Gynaecol., 98, 880–885.
- Petraglia, F., De Leo, V., Sardelli, S. et al. (1985) Domperidone in defective and insufficient lactation. Eur. J. Obstet. Gynaecol. Reprod. Biol., 19, 281–287.
- Rogan, W.J. and Gladen, B.C. (1993) Breast-feeding and cognitive development. *Early Hum. Dev.*, **31**, 181–193.
- Thearle, M.J. and Weissenberger, R. (1984) Induced lactation in adoptive mothers. Aust. NZ. J. Obstet. Gynaecol., 24, 283–286.
- Waterston, T. (1995) Breast feeding of adopted infants. Author's reply. Br. Med. J., 311, 189.

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