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Original Article

Role of newer drug cabergolin in lactation suppression as compared to estrogen-androgen combination

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Abstract

Objectives: To compare the efficacy of newer drug cabergoline with estrogen-androgen combination in lactation inhibition and suppression. *Methods:* In a tertiary care teaching hospital, 196 postpartum women in need of inhibition or suppression of lactation were randomly divided into Group A (100 women who were given tablet cabergoline orally) and Group B (96 women who were given estrogen-androgen combination intramuscularly). Both groups were followed till complete cessation of milk expulsion. Number of days and extra doses of drug required were recorded and statistically analyzed on SPSS version 10 of windows 2000. *Results:* The mean number of days required was significantly less (0.73±0.963) in Group A, (p value=0.001). Extra doses of drug were needed less often in Group A (p value=0.017). *Conclusion:* Cabergoline is more effective drug for prevention and suppression of lactation with added advantage of oral route and easy dosage schedule.

Key words: cabergoline, lactation suppression, lactation inhibition, stillbirth puerperium

Introduction

Lactation is a physiological process in postpartum women essential for feeding of the baby. Inhibition or prevention of lactation is needed if the baby is born dead or the mother is not able to feed the baby due to medical or personal reasons. Suppression of lactation is needed once lactation is established and baby dies or the mother cannot continue breast-feeding for personal reasons. With the increasing number of working mothers, 50% of the parturients need lactation inhibition or suppression.

Drugs used conventionally for the inhibition and suppression of puerperal lactation are estrogens alone, estrogen-androgen combination, pyridoxine and bromocriptine. All these drugs show variable efficacy, high incidence of rebound lactation and various side effects. These drugs also have poor patient compliance due to parenteral route or oral therapy for long durations. Cabergoline is a newer drug introduced for prevention and suppression of lactation. It is a synthetic ergoline that shows high specificity and affinity for dopamine D2 receptors (dopamine agonist). It is a potent and long acting drug for inhibition of prolactin secretion and thus for inhibition and suppression of lactation. Cabergoline has better patient compliance than other drugs due to its oral route of administration and easy dosage schedule.

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Lactation inhibition or suppression when required in Indian women is most commonly achieved with estrogen-androgen combination. This study was done to compare cabergoline with estrogen-androgen combination for inhibition and suppression of lactation.

Methods

A randomized control trial was performed from March 2004 to September 2005 in 196 postpartum women admitted in the department of Obstetrics and Gynecology of King George Medical University, Lucknow. Institutional ethics committee approval was taken before starting the study. These women either needed inhibition of lactation due to stillbirth or suppression of lactation due to neonatal death. They were randomly divided into two groups (group A and group B) after taking written informed consent in their hospital records. A total of 200 opaque white envelopes were sealed, mixed and put in a box. One hundred of these contained an instruction for cabergoline and another 100 for estrogen-androgen combination. Each woman was asked to open one envelope and recruited in one of the two groups as per instructions inside the envelope.

Group A consisted of 100 postpartum women who were given tablet cabergoline orally. The dose for lactation inhibition in women without any milk output at the time of inclusion was 1.0mg stat. The dose of cabergoline for suppression of lactation in those with presence of milk output at the time of inclusion was 0.25mg twice daily for two days. Group B consisted of another 96 postpartum women who were given single injection of estrogen-androgen combination intramuscularly. The preparation contained estradiol benzoate (1mg), estradiol phenyl propionate (4mg), testosterone propionate (20mg), testosterone phenyl propionate (40mg) and isocaproate (40mg). It was repeated for a maximum of three doses if milk expression persisted after one injection. In both groups treatment was started within 24 hours of delivery or neonatal death.

Both groups were followed daily with breast examination to see the presence or absence of milk expression till there was no milk expression even on pressing the breast. Results were analyzed by noting the number of days required for complete inhibition or suppression of lactation, number of women requiring extra doses of drug and side effects observed. Statistical analysis was done using SSPS 10.0 of windows 2000.

The procedures of the study received ethical approval from he institutional committee responsible for human experimentation.

Results

Table 1 shows the baseline characteristics of the two groups. These were comparable in the two groups as the differences were not statistically significant.

Table 1. Distribution of women according to baseline characteristics.

Characteristics	Group A N=100	Group B N=96	Statistical analysis
Mean age (years)	26.65±4.825	25.97±4.846	p value=0.326
Parity Primipara	41 (41%)	43 (44.79%)	
Multipara	59 (59%)	53 (55.21%)	p value=0.592
Period of gestation			
<28 weeks	8 (8%)	5 (5.21%)	
28-36 weeks	41 (41%)	38 (39.58%)	p value=0.683
>36 weeks	51 (51%)	53 (55.21%)	
Drug usage			
Lactation inhibition	54 (54%)	48 (50%)	
Lactation suppression	46 (46%)	48 (50%)	p value=0.575

Table 2 shows that the mean number of days required for inhibition of lactation were less in group A than group B. The difference was statistically significant (0.73±0.963 days vs 1.81±1.81 days; p value=0.001, t=3.881). The mean number of days required for suppression of lactation was comparable in the two groups.

Table 2. Mean number of days required for inhibition and suppression of lactation.

	Inhibition (mean no. of days)	Suppression (mean no. of days)
Group A	0.73±0.963	3.29±2.59
Group B	1.81±1.81	3.96±2.81
't'	3.881	1.172
P value	0.001	0.244

Table 3 shows that the need for extra doses was less in group A as compared to that in group B. The difference was statistically significant for suppression of lactation (p value=0.017).

In group A, both women who needed extra doses were of term gestational age. In group B, out of 11 women who needed extra doses, 4 women were of preterm gestational age and 7 women were of term gestational age. On statistical analysis it was found that gestational age at the time of delivery does not have any affect on the efficacy of the two drugs

.

Conclusion

Cabergoline is a more effective drug for inhibition and suppression of lactation than estrogen-androgen combination with added advantage of oral route of administration and easy dosage schedule.

Table 3. Comparative efficacy of the two drugs in terms of extra doses.

	Preventive efficacy With single dose	Suppressive efficacy With extra doses	With single dose	With extra doses
Group A	54 (100%)	-	44 (95.65%)	2 (4.35%)
Group B	47 (97.92%)	1 (2.08%)	38 (79.17%)	10 (20.83%)
X2	1.136		5.73	
P value	0.286		0.017	

Discussion

Lactation is established by a complex mechanism [1,2]. High levels of prolactin, estrogen and progesterone during pregnancy promote the anatomical development of breast. Prolactin causes lactose synthesis in breast but estrogen and progesterone inhibit this effect during pregnancy. The sudden fall in the latter hormones after delivery allows prolactin to initiate lactation. The posterior lobe of pituitary gland produces oxytocin in a pulsatile fashion which contracts the myoepithelial cells lining the alveolar ducts for milk ejection. Milk ejection is also produced in response to suckling by the infant.

About 50% of the parturients need lactation inhibition or suppression due to stillborn baby, neonatal death and inability to feed for medical (HIV) or personal reasons[3].

Various natural methods are known for lactation suppression. IBCLC4 recommends the use of tight breast support, ice packs, sage tea and cabbage leaf compresses for this purpose. These methods are useful in cases of engorged breasts but do not bring about complete lactation suppression.

Due to the known inhibitory effect of estrogen in vivo, its commercial preparations with androgens in injectable form have been used for lactation suppression since a long time. This combination was found to be associated with high serum testosterone levels that persisted up to five times the normal level after six weeks of usage[5].

Pyridoxine is safe oral drug for lactation suppression but needs to be given for two to the weeks.

Bromocriptine, a dopaminergic receptor stimulant inhibits prolactin secretion from pituitary. It has been used for both inhibition and suppression of lactation in oral tablet form taken for two weeks. In 1980 Stehlin[6]

reported brain related side effects, which led to its withdrawal from the market. It is contraindicated in PET patients due to increased risk of postpartum hypertension[7].

Cabergoline is another dopaminergic receptor stimulant that inhibits prolactin secretion. It has been authorized for marketing in India since 2002. It needs to be given as a stat dose of 1mg for lactation inhibition and 0.25 mg twice daily for two days for lactation suppression. Complete lactation inhibition was reported in 90% of the patients when 1.0mg dose was compared with 0.75 mg, 0.5 mg and placebo group[8,9]. In our study, complete inhibition was achieved in all (100%) patients without the need of an extra dose. Complete lactation suppression was achieved in 95.6% with single course.

Comparative study of cabergoline and bromocriptine shows similar efficacy without any rebound activity[10]. Cabergoline still has the advantage of easy dosage schedule as compared to bromocriptine. We compared cabergoline with combined estrogen-androgen injections for lactation inhibition and suppression. Efficacy of the two drugs was similar (p value=0.286) for lactation inhibition. The mean number of days required for complete inhibition were significantly less (p value=0.001) with cabergoline. Cabergoline was also found to be significantly better (p value=0.017) for lactation suppression as 20.8% patients of the estrogen-androgen group needed extra doses to achieve complete suppression.

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Reference

1. Ganong WF, The Gonads: Development and functioning of reproductive system. In, Review of Medical Physiology. 19th ed. Barnes DA, Ransom J, Roche J. (Eds). *Stamford, Connecticut, Appelton and Lange. 1999;430-2.*
2. Cunninghan FG, Gant NF, Leveno KG. The Puerperium. In, Williams Obstetrics. 21st ed. Seil A, Noujaim SR. Davis K (Eds) *New York, McGraw Hill, 2001;410-2.*
3. Kochenour NK. Lactation suppression. *Clin Obstet Gynecol 1980;23:1045-59.*
4. Smith, A. Lactation suppression. http://www.storknet.com/cubbies/breast/AS-lacsuppression.htm (accessed on 8th November 2008)
5. Lev-Gur M, Rodriguez LJ, Smith KD et al. Serum hormone changes in parturients given steroid preparations to suppress lactation. *Int J Fertil 1990;35:95-99.*
6. Moore DB, Catlin A. Lactation suppression: forgotten aspect of care for the mother of a dying child. *Pediatr Nurs 2003;29:383-4.*
7. Watson DL, Bhatia RK, Norman GS et al. Bromocriptine mesylate for lactation suppression: a risk for postpartum hypertension. *Obstet Gynecol 1989;74:573-6.*
8. Caballero-Gordo A, Lopez-Nazareno N, Calderay M et al. Oral cabergoline. Single dose inhibition of puerperal lactation. *J Reprod Med 1991;36:717-21.*
9. Melis GB, Mais V, Paoletti AM et al. Prevention of puerperal lactation by a single oral administration of the new prolactin inhibiting drug, cabergoline. *Obstet Gynecol 1988;71:311-14.*
10. Single dose cabergoline vs bromocriptine in inhibition of puerperal lactation: randomized double blind, multicentre study. European Multicentre Study Group for Cabergoline in lactation inhibition. *BMG 1991;302:1367-71.*