The Combined Oral Contraceptive Pill Versus Bromocriptine to Suppress Lactation in Puerperium : A Randomized Double Blind Study

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A randomised double blind comparative study of 230 HIV infected mothers who had a normal delivery at 37-42 weeks' gestation were divided into two groups; 116 combined pill users and 114 bromocriptine users to suppress lactation. There were 33 cases (28.5%) of combined pills users and 29 cases (25.4%) of bromocriptine users who had breast engorgement without statistical difference. All of them had mild breast engorgement without any treatment except one case (0.9%) in the bromocriptine group had severe breast engorgement with puerperal fever and needed an analgesic drug. There were no side effects of the drugs. This study showed that combined pills were beneficial to suppress lactation in HIV infected mothers to prevent postnatal mother-to-child transmission because of low risk and low cost.

Keywords : *Suppress lactation, Combined pills, Bromocriptine, HIV infected mother, Breast engorgement*

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Rationale

Transmission of Human Immunodeficiency Virus (HIV) from mother to child is a large problem in obstetrics. Vertrical transmission during pregnancy and labour has been reported at 24% - 38.5%[1-4]. There are many reports of postnatal transmission during breast feeding[5-7]. Breast milk transmission of HIV-1 can occur at any time during the entire duration of breastfeeding. The risk of late postnatal transmission (after 2.5 months of age) is 3.2 per 100 child/years of breastfeeding[8]. Mastitis, an inflammation of the breast, has recently been linked to a higher human immunodeficiency virus load in breast milk[9]. Avoidance of breastfeeding can prevent postnatal transmission to a child who may not be infected. However, countries where the risk of death in the first year of life is 50% from diarrhea and other diseases (excluding AIDS) breastfeeding is still the feeding method of choice. Clemen[10] reported that infants in whom breastfeeding was initiated early had a 20% lower rate of diarrhea than in those initiated late. In Thailand, our national policy is to avoid breast-feeding to prevent postnatal transmission from HIV infected mother so that suppression of lactation in the puerperal is needed.

Prolactin level is high during the early postpartum period. Prolactin will stimulate milk production within 3-4 days of delivery so that breast engorgement will last about 48-72 hours[11]. Mothers with breast engorgement usually experience pain and fever so suppression of lactation can prevent these symptoms.

There are many methods to suppress lactation. Breast binding can decrease stimulation of the nipple and the milk ejection reflex but 60% of lactating mother still had breast engorgement from day 3-5 postpartum[12]. High dose estrogen reduces lactation in 86% [13] but increses the risk of postpartum thromboembolism by three times that of postpartum thromboembolism[14]. Bromocriptine has been used worldwide since 1980 for the prevention of breast engorgement in the puerperium[15]. A comparative study between high dose estrogen and bromcriptine showed that bormocriptine had a better outcome[12]. Many reports[15-17] showed that using bromocriptine

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during the puerperium increases the risk of vasospasm especially in those with pregnancy induced hypertension. At present, the use of prophylactic antiretroviral treatments has brought about a dramatic decrease in the risk of transmission[18] but have shower progress in ablactation.

Objective

To compare the effect outcome of bromocriptine and a combined oral contraceptive pill containing 50 micrograms ethinyl estradiol in the supression of lactation in the puerperium.

Material and Method

A randomised double blind comparative study of 230 asymptomatic HIV infected mothers aged between 18-35 years. All subjects had a normal delivery at 37-42 weeks' gestation and were willing to participate in this study and signed the consent form. The subjects were randomised by computer to either bromocriptine or a combined pill containing 50 micrograms of ethinyl estradiol two tablets twice a day for 5 days. Both drugs were put into the same type of capsule so that both patient and doctor were "blind" to the treadment. The first dose of drug was given within 12 hours of delivery. Signs and symptoms of breast engorgement and any side-effects of the drugs were recorded daily by a different group of doctors and nurses until 12 hours after the last dose. The degree of breast engorgement was identified as mild or severe. Mild breast engorgement was defined as generalized tenderness and/or generalized swelling with heat of the breast. Severe breast engorgement was defined as generalized tenderness and/or generalized swelling with heat plus puerperal fever.

The exclusion criteria were

1. Subjects at high risk for taking a combined pill with a high dose of estrogen were those more than 35 years old, overweight or with a past history of a thromboembolic episode.

2. Subjects at high risk for taking bromocriptine were those with pregnancy-induced hypertension, seizure, stroke or myocardial infarction.

Results

From January 1997 to December 1998 there were 230 HIV infected mothers who delivered and were willing to paticipate in this study. The subjects were divided into two groups; 116 subjects took the combined oral contraceptive pill and 114 subjects took bromocriptine in order to suppress lactation. The clinical and demographic characteristics of both groups were similar (Table 1). The average age was 23.2 $\pm$ 4.6 years in combined pill users and 24.3 $\pm$ 5.1 in bromocriptine users. Body mass indices were 25.1 $\pm$ 4.7 and 24.9 $\pm$ 4.0 kg/m^2 respectively. The obstetric histories of both groups were also similar; The majority were primigravida and, the gestational age of the pregnancy was 39.4 $\pm$ 1.6 and 38.8 $\pm$ 1.5 weeks in the combined pill group and the bromocriptine group respectively. There were 33 cases (28.5%) of breast engorgement in the combined pill users and 29 cases (25.4%) in the bromocriptine users (Table 2). In the combined pill group, there were 0.9%, 3.4%, 10.3%, 9.5% and 4.3% who had breast engorgement on the first day, second day, third day, fourth day and fifth day after delivery respectively. In the bromocriptine group, there were 1.8%, 4.4%, 7.9%, 7.9% and 3.5% who had breast engorgement on the first day, second day, third day, fourth day and fifth day respectively. All of them had mild breast engorgement except one in the bromocriptine group who had severe breast engorgement and needed analgesics (Table 3). There were no side effects of the drugs seen in this study.

Table 1. Characteristics of women in the study according to type of medication. Received figures are percentage

Characteristic	Combined pills N = 116	Bromocriptine N = 114
Age (year)	23.2 $\pm$ 4.7	24.3 $\pm$ 5.1
BMI (Kg/m^2)	25.1 $\pm$ 4.7	24.9 $\pm$ 4.0
Gestational age (week)	39.4 $\pm$ 1.6	38.8 $\pm$ 1.5
Abortion	0.7 $\pm$ 0.4	0.7 $\pm$ 0.5
Gravida	1.7 $\pm$ 0.9	1.8 $\pm$ 0.9

Table 2. Day that breast engorgement commenced according to the drug used to suppress lactation

	Combined pill (n = 116)		Bromocriptine (n = 114)	
	No.	%	No.	%
First day	1	0.9	2	1.8
Second day	4	3.4	5	4.4
Third day	12	10.3	9	7.9
Fourth day	11	9.5	9	7.9
Fifth day	5	4.3	4	3.5
Total	33	28.5	29	25.4

Table 3. Severity of breast engorgement according to drug used to suppress lactation

Breast endorgement	Combined pills		Bromocriptine	
	No.	%	No.	%
Severe	0	0	1	0.9
Mild	33	28.5	28	24.6
None	83	71.6	85	74.6
Total	116	100.1	114	100.1

Discussion

Precautions for antepartum, peripartum, and postpartum care of infected mothers and infants are important. In management during pregnancy, a number of investigations have shown that a combination of nucleoside analogs given along with a protease inhibitor is highly effective in suppression of HIV-RNA levels[19]. Wade et al colleague[20] reported that perinatal transmission rate was 8% if zidovudine was begun in the prenatal period, 10% if given only intrapartum, and 9% if given to the newborn within the first 48 hours. Stiehm et al[21] reported that zidovudine prophylaxis is also highly effective in reducing perinatal transmission in women with advanced disease.

Breast milk increases the risk of neonatal transmission. It has been estimated that one to two thirds of maternal transmission in breast-fed-intants is from breast milk[22]. In general, breastfeeding is not recommended in HIV-positive women. Suppressing lactation is needed to prevent breast engorgement. The figures for mild and severe breast engorgement in both combined pill users and those taking bromocriptine were very low in the present study compared with the study of Almeida and Kitay[23]. They found an incidence of puerperal fever from breast engorgement of 13.3% in mothers using bromocriptine to suppress lactation.

These was no statistical difference in the severity of breast engorgement between the combined pill and bromocripine users. This shows that both combined pills and bromocriptine can suppress lactation to a similar degree. There were no side effects or risk from either drug used in the present. Chumnijarakij[24] reported that postpartum thromboembolism in Thai women is very rare when compared with European women. This supports the benefit of a combined oral contraceptive pill to suppress lactation as it has low cost and has a low risk.

The authors concluded that combined oral contraceptive pill is beneficial to suppress lactation in postpartum women such as HIV infected mothers, because action of a combined pill similar to bromocriptine but the cost of a combined pill was lower and the side effects of a combined pill in Thai women were very low.

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ศึกษาเปรียบเทียบการยับยั้งการหลั่งน้ำนมของยาเม็ดคุมกำเนิดและ Bromocriptine

(ขาดชื่อผู้แต่งภาษาไทย)

การศึกษาเปรียบเทียบโดยวิธี randomised double blind ผลของยาเม็ดคุมกำเนิด (combined pill) และ bromocriptine ในการยับยั้งการหลั่งน้ำนมในมารดาที่ติดเชื้อเอดส์ ที่คลอดปกติทางช่องคลอดเมื่ออายุครรภ์ 37-42 สัปดาห์ จำนวน 230 ราย โดยแบ่งผู้ป่วยเป็น 2 กลุ่มโดย 116 รายใช้ยาเม็ดคุมกำเนิด และ 114 รายใช้ bromocriptine ในการยับยั้งการหลั่งน้ำนม จากผลการศึกษาพบว่า ร้อยละ 28.5 ในกลุ่มที่ใช้ยาเม็ดคุมกำเนิด และร้อยละ 25.4 ในกลุ่มที่ใช้ bromocriptine ยังมีอาการนมคัดผลที่ได้ไม่แตกต่างกันทางสถิติ อาการนมคัดส่วนใหญ่มีอาการไม่มาก ยกเว้นหนึ่งรายคิดเป็น ร้อยละ 0.9 ในกลุ่มที่ใช้ bromocriptine มีอาการนมคัดมากจนต้องใช้ยาแก้ปวด และจากผลการศึกษาไม่พบอาการแทรกซ้อนของยา แสดงให้เห็นว่ายาเม็ดคุมกำเนิดสามารถยับยั้งการหลั่งน้ำนมได้ดีอย่างน้อยเท่า bromocriptine แต่มีข้อดีกว่าเพราะยาเม็ดคุมกำเนิดราคาถูกและหาได้ง่ายกว่า