

Impact of Injectable Progestogen Contraception in Early Puerperium on Lactation and Infant Health

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ABSTRACT

Introduction: Unmet need for family planning approaches 40% or higher and many women are at risk of unintended pregnancy. Progesterone contraception after birth is frequently recommended, but concern remain of inhibition of lactation or effects on infant health. In present study we aimed to evaluate impact of short term use of injectable depot medroxy progesterone acetate (DMPA) if given in early post partum period on infant health and breast feeding performance.

Material and Methods: A prospective case control study was conducted and 250 women immediately after delivery were recruited in the study. 150 women who were recruited as study group received Inj. DMPA 150 mg intra muscularly after initiation of lactation before discharge from hospital (Day 2-Day 10 of their delivery). 100 post partum women, not using hormonal contraception were taken as controls. All the subjects were followed to complete a full 6 months follow up. Duration and frequency of lactation, gain in weight, gain in height and any illness spells in the infant were noted at 6 weeks, 3 months and 6 months follow up. In the study group 100 subjects completed

6 months follow-up. The statistical analysis was carried out by using SPSS software version 7. The statistical technique used was z score (significance shown by z score > 1.96) and repeated measure analysis (two way Anova technique).

Results: Hundred percent of primigravidas in the study group and 95% in the control group were satisfied with their lactation amount. The average gain in height was comparable in both study and control group {4.36±0.56 vs 4.33±0.54 (z score 0.38) at 6 weeks, 12.44±0.73 vs 12.40±0.71 (z score 0.39) at 3 months 17.30±0.91 vs 17.28±0.83 (z score 0.16) at 6 months}. Similarly average gain in weight was also not significantly different in two groups {0.89±0.11 vs 0.93±0.10 (z score 0.71) at 6 weeks, 1.77±0.17 vs 1.78±0.16 (z score 1.07) at 3 months and 3.53±0.30 vs 3.46±0.33 (z score 1.19) at 6 months}. The results were comparable with other studies.

Conclusion: Injectable DMPA use as a contraceptive in the immediate post partum period was found to be a safe and effective alternate method with no deleterious effect on mother's milk and infant's growth.

Keywords: Injectable DMPA, Infant health, Immediate puerperium, Lactation

INTRODUCTION

In developing countries, 17% women of reproductive age have unmet needs for family planning [1,2] and 20.6% of pregnancies are reported to occur during previous lactation [3]. The incidence of unintended pregnancy during the first year postpartum was found to be 12.8 per 100 women years and 86% had resulted from non use of contraception [3]. Delaying contraception until first visit to hospital or sixth week postpartum increase the risk of unintended pregnancy. Progesterone only contraceptives in form of injectable depot medroxy progesterone acetate (DMPA) is a highly effective method for contraception especially in postpartum period.

Progesterone contraception after birth is frequently recommended but the timing of initiation of depot medroxy progesterone acetate (DMPA) after delivery is controversial. Product labelling recommends initiating depot medroxy progesterone acetate (DMPA) four to six weeks postpartum regardless of breastfeeding status [4]. WHO recommends depot medroxy progesterone acetate (DMPA) in breastfeeding women should be initiated at 6 weeks [5]. ACOG recognizes the need for clinical judgement and weighing the need for contraception against theoretical risks and endorses the earlier initiation of DMPA postpartum in certain clinical situations, such as high risk of being lost to follow-up postpartum [6]. Theoretical concerns of infant safety and premature inhibition of lactation remain with early postpartum administration of depot medroxy progesterone acetate (DMPA). It is thought that newborn's system is immature to metabolize steroid hormones and therefore early initiation could affect the new born adversely [5]. However studies

indicate that infants are neither able to metabolize nor absorb progestin effectively until three months of age and the amount of hormone transferred is 0.05% of the maternal dose [7]. Another issue of interference with milk quality and production is also addressed and it has been shown that Progesterone only contraception may not impair lactation [8-10].

Thus there exist a gap between existent evidence regarding early initiation of postpartum medroxy progesterone use and its impact on infant health and breast feeding. In present study we aimed to evaluate impact of short term use of inj DMPA in early postpartum period on infant health and breast feeding performance.

MATERIALS AND METHODS

A prospective case control study was conducted in department of Obstetrics and Gynaecology in a tertiary care teaching hospital. A total of 250 women who wanted some form of reversible contraception immediately after delivery were recruited in the study. All the women who were included were apparently healthy, 20-35-year-old women and had delivered a baby of gestational age ≥ 36 weeks and birth weight ≥ 2.5 kg. The recruited subjects had no medical or surgical illness including local abscess/ inverted nipple or breast pathology. Baby was with mother since birth and women were ready to follow-up. Grand multiparous women or those who had preterm or IUGR babies, or were under nourished or severely anaemic, women whose baby had congenital disease or disease that could affect oral feeding or if the baby was in nursery were excluded from the study.

Lactation Frequency		Study Group	% age	Controls Group	% age	z-score
Primipara	Satisfied	36	100	38	95	0.54**
	Dissatisfied	0	0	2	5	0.54**
Multipara	No change [§]	42	65.6	45	75	0.36**
	Increased	16	34.4	11	18.4	0.67**
	Decreased	0	0	4	6.6	1.25**

[Table/Fig-1]: Effect of depot medroxy progesterone acetate (DMPA) on Lactation

[§]compared to previous pregnancy ** not significant

Breast feeding Frequency (per day)	6 weeks No. of patients			3 months No. of patients			6 months No. of patients		
	Study	Control	z-score	Study	Control	z-score	Study	Control	z-score
< 4	0	0	***	3	6	1.02**	24	36	1.85**
4 to 8 + 1 NF	19	23	0.69**	35	41	0.87**	63	57	0.86**
9 to 12+ 2NF	68	59	1.32**	54	48	0.85**	11	7	0.99**
>12 feeds	13	18	0.97**	8	5	0.86**	2	0	1.43**

[Table/Fig-2]: Effect of depot medroxy progesterone acetate (DMPA) on frequency of breast feeding

NF : Night feed** not significant ***could not be determined

Duration of DMPA	Av. Wt. (kg) ± SD		z-score	Av. Wt.gain (kg) ± S.D		z-score
	Study Group	Control Group		Study Group	Control Group	
0 weeks	2.95±0.29	3.00±0.26	0.61**	-	-	-
6 weeks	3.86±0.33	3.93±0.31	0.81**	0.89±0.11	0.93 ± 0.10	0.71**
3 months	4.82±0.36	4.78 ± 0.34	0.83**	1.77 ± 0.17	1.78 ± 0.16	1.07**
6 months	6.48±0.36	6.46 ± 0.37	1.33**	3.53±0.30	3.46 ± 0.33	1.19**

[Table/Fig-3]: Effect of depot medroxy progesterone acetate (DMPA) on average (Av) weight (wt) and weight gain in infants

** not significant

Duration of DMPA	Av. ht. (cm) ± S.D		z-score	Av.ht.gain (cm) ± S.D		z-score
	Study Group	Control Group		Study Group	Control Group	
0 weeks	47.46 ± 0.90	47.55±0.82	0.57**	-	-	-
6 weeks	51.82±0.69	51.88±0.62	0.64**	4.36 ±0.56	4.33 ± 0.54	0.38**
3 months	59.9±0.64	59.95±0.59	0.57**	12.44 ± 0.73	12.40 ±0.71	0.39**
6 months	64.76 ±0.77	64.83±0.72	0.65**	17.30±0.91	17.28 ± 0.83	0.16**

[Table/Fig-4]: Effect of depot medroxy progesterone acetate (DMPA) on average (Av) height (ht) and height gain in infants

** not significant

Breast feeding was started ½ -1 hour after delivery and 2-3 hourly thereafter. As a result most of the women had adequate lactation even on 2nd postpartum day. All women were breast feeding at time of discharge and intended to continue breast feeding at home. A preliminary contact was made on the day of delivery. Mothers were explained about all the available methods of contraception. A detailed explanation regarding study procedure was given. Eligibility was then determined and after obtaining informed consent women were enrolled.

A total of 150 women, who opted for hormonal contraception in form of depot medroxy progesterone acetate (DMPA) were recruited as study group. Hundred postpartum women, not using hormonal contraception were taken as controls. A thorough general physical examination including breast examination of the mother was done. Status of infant's health, weight (by analog scale with standard error

	Day on which mother received DMPA	z-score			
		2-4 (n=50)	5-7 (n=36)	8-10(n=14)	
Mean wt. (kg) ± SD	3 months	4.89 ± 0.32	4.67 ± 0.39	4.96 ± 0.28	0.54**
	6 months	6.53 ± 0.3	6.41 ± 0.31	6.48 ± 0.41	0.36**
Mean wt.gain (kg) ± SD	3 months	1.86 ± 0.19	1.84 ± 0.12	1.99 ± 0.14	0.67**
	6 months	3.50 ± 0.27	3.58 ± 0.36	3.51 ± 0.32	1.25**

[Table/Fig-5]: Effect on Infant's weight (Wt.) according to the day of start of depot medroxy progesterone acetate (DMPA)

** not significant

	Day on which mother received DMPA	z-score			
		2-4 (n=50)	5-7 (n=36)	8-10 (n=50)	
Mean Ht. (cm) ± SD	3 months	59.20 ± 0.58	60.77 ± 0.66	66.16 ± 0.63	0.71**
	6 months	64.93± 0.72	64.65 ± 0.71	64.43 ± 0.79	1.07**
Mean Ht. gain (cm) ± SD	3 months	11.92 ± 0.76	13.22 ± 0.68	12.30 ± 0.71	0.86**
	6 months	17.65 ± 0.83	17.10 ± 0.93	16.57 ± 0.92	0.37**

[Table/Fig-6]: Effect on Infant's height (Ht.) according to the day of start of depot medroxy progesterone acetate (DMPA)

** not significant

Illness spells	Study Group		Control Group		z-score
	No of women	%	No of women	%	
URI	7	7	6	6	0.28**
Diarrhoea	6	6	4	4	0.65**
Fever	3	3	4	4	0.38**
Rash	1	1	2	2	0.57**

[Table/Fig-7]: Effect of depot medroxy progesterone acetate (DMPA) on illness spells in infants

URI : Upper respiratory track infection, ** not significant

of 0.1 kg) was recorded. Exclusive breast feeding was emphasized. This comprised frequent suckling on demand and night feeding. All women who chose to use (DMPA) received inj. DMPA 150 mg intra muscularly before discharge from hospital (Day 2 to Day 10 of their delivery) and at three months and then they were followed to complete a full 6 months follow-up. Injection depot medroxy progesterone acetate (DMPA) was given only after confirming establishment of lactation.

Duration and frequency of lactation were noted. Mothers were followed up at 6 weeks, 3 months and 6 months along with their child. The parameters noted were effect on duration and frequency of lactation, supplementation of breast feed in first 6 months, time of introduction of formula milk or other supplements. A note was made of gain in weight and height, any illness spells in the infant. However, out of total 150 women who were included in study group only 100 women completed full six months follow-up and therefore 50 subjects who did not complete 6 months follow-up were excluded from study group for the purpose of analysis. The statistical analysis was carried out by using SPSS version software [7]. The statistical technique used was z score (significance shown by z score > 1.96) and repeated measure analysis (two way ANOVA technique).

RESULTS

Hundred percent of primigravidas in the study group and 95% in the control group were satisfied with their lactation amount. [Table/Fig-1] In multigravidas 65.6% in the study group and 75% in the control group felt no change in lactation amount, as compared to their previous experience. Few subjects even reported some increase in lactation but it was comparable with controls [Table/Fig-1]. When frequency of breast feeding was compared in study and control group it was observed that no significant difference in frequency of lactation existed at 6 weeks, 3 months and 6 months follow-up [Table/Fig-2].

Average weight of the infant at the start of study was 2.95 ± 0.29 kg in study group and it was comparable with controls (3.00 ± 0.26 kg) [Table/Fig-3]. The infants of the mothers in the study group gradually gained weight in subsequent follow-up with a mean weight of 3.86 ± 0.33 , 4.82 ± 0.36 and 6.48 ± 0.36 kg at 6 weeks, 3 months and 6 months. These values were also comparable to infants in control group. The average weight gain was also found to be consistently comparable in both the groups at all the follow-ups [Table/Fig-3].

Average height of the infant at the start of the study was 47.46 ± 0.90 cm in study group and it was comparable with controls (45.23 ± 0.82 cm). The infants of the mother in the study group gradually gained height in subsequent follow-up with a mean height of 51.82 ± 0.69 , 59.90 ± 0.64 and 64.76 ± 0.77 cm at 6 weeks, 3 months and 6 months. These values were comparable to infants in control group. The average height gain was also consistently comparable in both the groups at all the follow-ups [Table/Fig-4].

To determine any growth retardation associated with early administration of depot medroxy progesterone acetate (between Day 2 – Day 4 postpartum) effects of depot medroxy progesterone acetate (DMPA) on infant weight were analysed according to the day on which DMPA was administered to the mother. The average weight of the infant was comparable in all the three categories at three months as well as six months follow-up. The weight gained by infants whose mother received injection between Day 2 to Day 4 did not differ significantly from infants whose mothers received injection later [Table/Fig-5]. The average height of infants was also comparable in all the three categories at three months as well as six months follow-up. Also the height gained by infants whose mother received injection between Day 2 to Day 4 did not differ significantly from infants whose mothers received injections later [Table/Fig-6]. There was no significant difference in illness spells among infants in study and control groups [Table/Fig-7].

DISCUSSION

In present study no adverse effects were found in the amount and duration of lactation in early depot medroxy progesterone acetate users. In fact, some of the multiparous women reported an improved lactation with depot medroxy progesterone acetate usage. Similarly no detrimental effect of depot medroxy progesterone acetate on duration of lactation, frequency of lactation and timing of introduction of formula milk was observed in previous studies [8,11,12].

In a trial 969 women were randomized to receive various hormonal contraceptive methods. The authors concluded that women who received DMPA immediately postpartum had a statistically significant longer median breast feeding duration (6.7 vs 4.8 median months) relative to the control group, and the women received DMPA one month postpartum also breast feed their infants significantly longer than control group (9.3 vs 5.3 months) [13].

A study was conducted on 30 mothers receiving depot medroxy progesterone acetate 150 mg on 2nd to 4th postpartum day and compared them with 25 controls. The milk volume obtained by manual breast pump was found to be statistically higher in depot medroxy progesterone acetate group than in controls. Quantity of milk among DMPA using mothers were not significantly different than control group [14]. The increase in milk production could be attributed due to depot medroxy progesterone acetate induced release of prolactin and also indirectly by enhancing the release of prolactin in response to suckling stimulus [15]. Another study showed that women who initiated depot medroxy progesterone acetate (DMPA) after 72 hours postpartum had higher odds of exclusive breast feeding at three months [16].

Major concern of giving depot medroxy progesterone acetate (DMPA) in lactating mothers is that the depot medroxy progesterone acetate (DMPA) and its metabolites are secreted in breast milk which would be then transferred to infants. In present study, consistent gain in weight and height was observed at subsequent follow-ups

in both the groups. Amount of depot medroxy progesterone acetate (DMPA) metabolites in breast milk is estimated to be 0.08 to $0.2 \mu\text{g/ml}$ [17]. Virutamasen et al., [7] also reported that no metabolite could be measured in urine of infants of mothers receiving depot medroxy progesterone acetate (DMPA). Since the amount is very small no ill effect was found in mature infants. However, there is a possibility that a preterm may not be capable of metabolizing the (DMPA) metabolites; hence it should not be given to preterm infants before its safety is established in them.

A long term study on effect of depot medroxy progesterone acetate (DMPA) on growth and development of infant if administered to mother during lactation and found no meaningful differences in physical and mental growth and development between the children in the depot provera group and those in the control group [14]. In another study authors compared 210 newborns whose mothers received depot medroxy progesterone acetate in postpartum with controls for weight gain and number of infectious illnesses. During an average 1.5 years follow-up, no significant difference was found except a slight increase in infection, when depot medroxy progesterone acetate was started two days postpartum [18]. However, in our study there was no increase in illness spells.

No adverse effects on infant growth and development are reported in the exposed infants [19,20]. One follow-up study of 1215 children whose mothers received depot medroxy progesterone during nursing reported a delayed appearance of pubic hair (reported by mothers) in pubescent girls, but not boys [21]. No other effects on growth were observed after correction for socioeconomic status. In a study 51 breast feeding women received progestogen only method and another 89 received non hormonal contraception. It was found that there is no effect of progestogen only method on components of breast milk. The anthropometric variables of the infants were similar in both groups with the exception of head circumference at 10-14 weeks of age, which was higher in infants of the hormonal group. In this study the growth of infant fed by breast milk was not affected by hormonal contraceptives as assessed by the rate of changes in weight, height and head circumference [22].

CONCLUSION

Injectable depot medroxy progesterone acetate (DMPA) use as a contraceptive in the immediate postpartum period was found to be a safe and effective alternate method with no deleterious effect on mother's milk and infant's growth. It is also easy to administer not requiring compulsory follow-up of the woman after delivery. It is important however that depot medroxy progesterone acetate (DMPA) be injected only after breast feeding has been properly initiated.

REFERENCES

- [1] Ross JA, Winfrey WL. Contraceptive use, intention to use and unmet use during the extended postpartum period. *International family planning perspectives*. 2001;27(1):20-7.
- [2] Dim C, Ugnu E, Illoghalu E. Duration and determinants of interdelivery interval among women in Enugu, south eastern Nigeria. *Journal of Obstetrics and Gynaecology*. 2013;33:175-79.
- [3] Huang YM, Merkatz R, Kang JZ, et al. Postpartum unintended pregnancy and contraception practice among rural-to-urban migrant women in Shanghai. *Contraception*. 2012;86(6):731-8.
- [4] Pfizer. Depot-Provera contraceptive injection medroxy-progesterone acetate injectable suspension, USP. Physician information. Pfizer, New York, 2006.
- [5] Brownell EA, Fernandez DI, Howard CR, et al. A Systematic Review of early postpartum medroxyprogesterone receipt and early breastfeeding cessation: evaluating the methodological rigor of the evidence. *Breast feed Med*. 2012; 7(1):10-8.
- [6] ACOG practice bulletin. No.73: Use of hormonal contraception in women with co existing medical conditions. *Obstet Gynecol*. 2006;107:1453-72.
- [7] Virutamasen P, Leepipatpaiboon S, Kriengsinyot R, et al. Pharmacodynamic effects of depot-medroxyprogesterone acetate (DMPA) administered to lactating women on their male infants. *Contraception*. 1996;54:153-7.
- [8] Hannon PR, Duggan AK, Serwint JR, Vogelhut JW, Witter F, DeAngelis C. The influence of medroxy progesterone on duration of breast feeding in mothers in an urban community. *Arch Paediatr. Adolesc Med*. 1997;151(5):490-6.

- [9] Rodriguez MI, Kaunitz AM. An evidence-based approach to postpartum use of depot medroxyprogesterone acetate in breastfeeding women. *Contraception*. 2009;80(1): 4-6.
- [10] Guiloff E, Ibarra-Polo A, Zanartu J, et al. Effect of contraception on lactation. *Am J Obstet Gynecol*. 1974;118:42-5.
- [11] Karim M, Ammar S, el Mahqoub S, el Ganzoury B, Fikri F, Abdou I. Injected progestogen and lactation. *BMJ*. 1971;1(5742):200-3
- [12] Halderman LD, Nelson AL. Impact of early postpartum administration of progestin-only hormonal contraceptives compared with nonhormonal contraceptives on short-term breast-feeding patterns. *Am J Obstet Gynecol*. 2002;186:1250-8.
- [13] Guiloff E, Ibarra-Polo A, Zanartu J, et al. Effect of contraception on lactation. *Am J Obstet Gynecol*. 1974;118:42-5.
- [14] Koetsawang S, Nukularn P, Fotherby K, et al. Transfer of contraceptive steroids in milk of women using long-acting gestagens. *Contraception*. 1982; 25(4):321-31.
- [15] Choudhary RR, Chompootaweep S, Dusitsin N, Friesen H, Tankeyoon M. The release of prolactin by medroxyprogesterone acetate in human subjects. *Br J Pharmacol*. 1977; 59(3): 433-4.
- [16] Matias SL, Nommsen-Rivers LA, Dewey KG. Determinants of exclusive breastfeeding in a cohort of primiparous periurban peruvian mothers. *Journal of Human Lactation*. 2012;28(1): 45-54.
- [17] Borell G, Andolack L. Reports of the international medical advisory panel on DMPA. Communication from international planned parenthood federation London Oct 1980.
- [18] Dahlberg K. Some effects of depot medroxy progesterone acetate. Observations in the nursing infant and in the long term user. *Int J gynecol Obstet*. 1982;20(1): 43-48.
- [19] Anon. Progestogen-only contraceptives during lactation. I. Infant growth. World Health Organization Task force for Epidemiological Research on Reproductive Health; Special Programme of Research, Development and Research Training in Human Reproduction. *Contraception*. 1994;50:35-53.
- [20] Diaz S, Zepeda A, Maturana X, et al. Fertility regulation in nursing women IX. Contraceptive performance, duration of lactation, infant growth, and bleeding patterns during use of progesterone vaginal rings, progestin-only pills, Norplant implants, and Copper T 380-A intrauterine devices. *Contraception*. 1997;56:223-32.
- [21] Pardthaisong T, Yenichit C, Gray R. The long-term growth and development of children exposed to Depo-Provera during pregnancy or lactation. *Contraception*. 1992;45:313-24.
- [22] Baheiraei A, Ardsetani N, Ghazizadeh S. effects of progestogen-only contraceptives on breast feeding and infant growth. *International Journal of Gynecology and Obstetrics*. 74(2001); 203-05.

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