The Effect of Postpartum Depo-Provera® Injection on Breast Milk Production in Mothers of Preterm and Very Low Birth Weight Infants in the Neonatal Intensive Care Unit

Stefani Go

University of Florida College of Nursing
Abstract

By Stefani Go and Kelli Garner

Administration of the contraceptive Depo-Provera® prior to a mother’s discharge from the hospital is often routine care. If administered prior to the establishment of lactation, the progesterone in Depo-Provera® may hinder breast milk production. Because breast milk decreases complications in preterm infants, it is important to identify potential barriers to breast milk production. We aimed to determine the effect of Depo-Provera® injection prior to hospital discharge on breast milk production in mothers of preterm very low birth infants. This study analyzed 63 mothers of infants born < 32 weeks gestation with a birth weight < 1500 grams. Breast milk volume was determined by weighing each vial of breast milk the mother produced (1 gm = 1 mL). T-test results yielded no statistically significant differences in breast milk production at 7 days postpartum (368 versus 283 mL; p=0.14) or 14 days (345 versus 278 mL; p=0.24) between mothers who received Depo-Provera® injections and those who did not. However, mothers who did not receive Depo-Provera® experienced a greater increase in breast milk production between day 7 and 14 (18 versus -93 mL; p=.07). This suggests that postpartum Depo-Provera® administration may negatively affect the normal increase in breast milk production between 7 and 14 days postpartum.
I. Introduction

The administration of the drug Depo-Provera® (Medroxyprogesterone) in the early postpartum period has become more common in practice. The use of contraceptives after delivery is recommended to prevent early or unintended pregnancy. Depo-Provera® is an effective, long-acting injectable contraceptive that provides multiple benefits to mothers. The drug’s effect has a duration of twelve to fourteen weeks (Durham & Chapman, 2019), making it an easy-to-use contraceptive option for mothers who do not want to remember to take their birth control every day. In some hospitals, Depo-Provera® is offered to mothers before hospital discharge in order to prevent pregnancy prior to their six-week postpartum check-up (Kapp et. al, 2010).

Theoretically however, the administration of a progesterone-based contraceptive such as Depo-Provera® may adversely affect breastmilk production. The initiation of lactogenesis stage II (production of large amounts of breastmilk) is related to a decrease in progesterone levels after delivery of the placenta (Durham & Chapman, 2019). This decrease in progesterone occurs over the first three days of the postpartum period, during which the mother may also be preparing for discharge. Thus, administering a progesterone-based contraceptive such Depo-Provera® during this time may adversely affect the hormonal processes required for secretory activation. Additionally, Depo-Provera® may also adversely affect breast milk production by interfering with the binding of prolactin to the alveolar cells in the breast (“Contraception and Lactation,” 2007), another hormone required for lactogenesis. Preterm and very low birth weight infants experience increased risk for morbidity and mortality and breast milk consumption yields multiple benefits for this population, such as shortened hospital stays and minimizing complications such as necrotizing enterocolitis (Eidelman & Schanler, 2012).
There is currently a lack of previous research that studies the effect of postpartum Depo-Provera® administration in mothers of preterm and very low birth weight infants in the Neonatal Intensive Care Unit. However, previous research has examined the effects of progesterone-only contraceptives on breastfeeding outcomes in breastfeeding mothers of term healthy infants on breastfeeding outcomes. No significant differences in breastfeeding outcomes have been found between women who receive immediate postpartum hormonal contraception and those who delay the initiation of such contraceptives (Stanton & Blumenthal, 2019). One study addressed that although experts advise that Depo-Provera® administration should be delayed until after the first three days postpartum in order to avoid interfering with the establishment of lactation, no significant adverse impacts on breastfeeding occur when progestin-only contraceptives are initiated within the first three days postpartum (Halderman & Nelson, 2002). A systematic review of 47 studies that investigated the outcomes of mothers receiving progestin-only contraceptives found that there was no conclusive evidence that progestin-only contraceptives have a negative impact on breastfeeding (Kapp et al., 2010). However, one study included in this systematic review did find that mothers who received Depo-Provera® after three days postpartum were more likely to be exclusively breastfeeding at three months compared to those who received the drug prior to three days postpartum or did not receive the drug (Matias et al., 2012). In addition, a randomized controlled trial found that the insertion of a hormonal contraceptive implant between one and three days postpartum in mothers of healthy, full term infants resulted in no significant delay to reaching lactogenesis stage II and no negative impacts on breastfeeding outcomes over 6 months (Gurtcheff et al., 2011). However, none of the aforementioned studies were conducted on mothers of preterm, very low birth weight infants, a population that is more at risk for experiencing difficulties related to breast milk production.
In addition to the presence of the aforementioned research gap, there has also been a recommendation to advance research in studying the effects of long-acting reversible contraception on breastfeeding outcomes, especially in populations at high risk of impaired breastfeeding (Bennet & Mannel, 2018). This is because long-acting reversible contraceptive methods promote healthy birth spacing and help women who do not have the time, transportation, and finances to receive contraception at their 6-week postpartum checkup. In addition, the American College of Obstetricians and Gynecologists supports the administration of long-acting reversible contraceptives prior to hospital discharge to avoid unintended pregnancy (“Committee Opinion No. 670,” 2016).

If Depo-Provera® is shown to have negative adverse effects on breast milk production in mothers of preterm very low birth weight infants, then this evidence could initiate a practice change. If the drug is shown to cause significant differences in breast milk production when given in the early postpartum period, cessation of this clinical practice can benefit preterm, very low birth weight infants in the NICU, among whom breastmilk consumption is shown to reduce morbidity and mortality. However, if Depo-Provera® is not shown to have any significant adverse effects on breast milk production, then this information could be used by mothers and health care providers to safely consider Depo-Provera® as a postpartum contraceptive. Furthermore, if there are no statistically significant results, the findings can still contribute to expanding knowledge within the current research gap.

The purpose of this study was to determine the effect of Depo-Provera® injections on breast milk production in mothers of very low birth weight infants when given prior to discharge from the hospital. In addition, we examined possible cofounding variables in breast milk production, such as the demographics of the participants.
II. Project Narrative

Dr. Leslie Parker served as my group’s mentor for this project. This project arose from one of her larger studies examining lactation conducted at the University of Florida Shands Hospital and University of Florida College of Nursing. Multiple stakeholders were involved in this project, such as the mothers participating in the study, the infants in the NICU, the lactation consultants, nurses, and health care providers in the postpartum unit and NICU.

The design of this study was a secondary data analysis of a randomized controlled trial. We compared the volume of breast milk produced by 63 participants. 32 of these participants were mothers who received the drug Depo-Provera® prior to discharge, and 31 of these participants did not receive the drug. All participants were mothers of preterm very low birth weight infants at the NICU at UF Health Shands Hospital. Participants were included in the Depo-Provera® group if they received Depo-Provera® prior to hospital discharge and delivered a newborn that weighed less than 1500 g at less than 32 weeks’ gestation. Mothers who received Depo-Provera® after hospital discharge were excluded from the study. Mothers were included in the non-Depo-Provera® group if they never received the drug and delivered a newborn weighing less than 1500 g at less than 32 weeks’ gestation. Prior to the study, the participants signed an informed consent form.

Demographical data was gathered on the participants, such as age, race, ethnicity, whether this was the mother’s first pregnancy, gestational age, mode of delivery, the birth weight of the infant, the number of days lactated during the study, and whether the mother stopped lactating during the study. During the infants’ stay in the NICU, breast milk volumes were recorded daily by measuring the weight of all milk produced (1 gram = 1 mL). The demographics information and milk volumes were recorded in RedCap.
My partner and I first received the medical record numbers of all the participants involved in a larger, pre-existing randomized controlled study of 180 mothers. We then examined the medical records of the participants to determine whether they had received Depo-Provera® prior to discharge. This information was located within the medical administration record portion of the electronic health record. We found that 32 of the 180 mothers in the original cohort study received the drug prior to discharge. After establishing which participants received Depo-Provera® prior to discharge, our group organized participants into two groups: mothers who received Depo-Provera® and mothers who did not receive Depo-Provera®. We selected 32 participants who did not receive Depo-Provera® prior to discharge as a comparison group. One of the 32 participants was later removed from the study because although the mother’s infant was preterm, he/she was not very low birth weight (< 1500 g). Then, the volumes of breast milk produced on days 7 and 14 of the hospital stay were compared to determine differences in breast milk production between the groups.

Overall, the following information was collected: whether the patient received Depo-Provera® prior to discharge, ethnicity, race, age, whether this was the mother’s first pregnancy (primiparity), gestational age, mode of delivery (cesarean section or vaginal delivery), the mother’s body mass index, the birth weight of the infant; the milk volumes on days 7 and 14, the number of days lactated; and whether the patient experienced any health conditions such as diabetes, gestational diabetes, and pregnancy induced hypertension.

In order to analyze the data of all 63 participants, we used RedCap to view the volume of milk produced by the participants and collect demographical data. The demographics and milk volume data were compiled onto an Excel spreadsheet. This data was then used to compare milk volume production between the two groups: mothers who did receive Depo-Provera® prior to
discharge and mothers who did not receive the drug. We compared the mean milk volumes from postpartum day 7 to day 14 and the mean days lactated by the participants. Then, we calculated the standard deviations of these values. In order to assess for statistical significance, a T-test was done to compare the differences in milk volume and days lactated between the two groups. After this initial analysis, we then calculated the change in milk volume from day 7 to day 14 for each participant. The changes in milk volume from day 7 to day 14 were then averaged, and a T-test was performed to determine if the differences were statistically significant. Lastly, a T-test was done to look for significant differences in maternal age, gestational age, and birth weight between the two groups, as these are potential confounding variables that affect milk production.

One potential barrier that was anticipated during the beginning of the project was the need to take into account confounding variables. Multiple factors outside of Depo-Provera® administration, such as maternal age, gestational age, race, and birth weight can potentially affect breast milk production. In order to overcome this challenge, demographical data of the participants was also included in the data analysis. Three challenges regarding study design were recognized late into the project. First, there was a lack of randomization in the selection of participants. Second, there was a lack of generalizability due to it being a single center study. Third, there was no specific inclusion criteria regarding what day the participants received Depo-Provera®. When selecting participants who received Depo-Provera® prior to discharge, there was no specific inclusion criteria for how many days after delivery the participants received the drug. Thus, administration of Depo-Provera® among participants ranged from immediate to five days postpartum. At the end of the project, these limitations were discussed with the project mentor as possible ways to improve the study going forward.
III. Results and Discussion

We found that the administration of Depo-Provera® in the early postpartum period did not decrease the volume of breast milk produced. This is evident in our findings that there were no significant differences in breast milk volume on day 7 (p = 0.12) or day 14 (p = 0.29) between the two groups. On average, although not statistically significant, mothers who received Depo-Provera® produced more breast milk than the mothers who did not receive the drug (See Table 1). In addition, while not statistically significant, the average number of days mothers who received Depo-Provera® lactated was lesser than those who did not receive the drug.

One finding that trended towards significance was that, on average, the participants who received Depo-Provera® experienced a decrease in breast milk volume from day 7 to day 14 (-93 mL ± 214). In contrast, the participants who did not receive Depo-Provera® experienced an average increase in breast milk production from day 7 to day 14 (+15 ± 289), which is a normal and expected finding. The differences in the change in milk volume between the two groups was almost significant (p = 0.07).

<table>
<thead>
<tr>
<th>Table 1: Mean Milk Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received Depo-Provera (n = 32)</td>
</tr>
<tr>
<td>Day 7</td>
</tr>
<tr>
<td>Day 14</td>
</tr>
<tr>
<td>Change in Milk Volume from Day 7 - 14</td>
</tr>
<tr>
<td>Days Lactated</td>
</tr>
</tbody>
</table>
Figure 1: This graph demonstrates the observation that mothers who received Depo-Provera experienced a decrease in milk volume over time, whereas mothers who did not receive the drug experienced a normal increase.

Furthermore, there were no statistically significant differences between groups regarding maternal age, gestational age, and infant birth weight (See Table 2). However, we did find that a majority of the participants who received Depo-Provera® prior to hospital discharge were Black. Although the race of the study participants also included mothers who identified as White, Hispanic, American Indian or Alaskan Native, and other (See Figure 2), 69% of mothers who received Depo-Provera® were Black (See Table 3).

Figure 2: This graph depicts the distribution of race among participants. More Black mothers received Depo-Provera than any other race within the participants of this study.
Our results indicate that administering Depo-Provera® injections to mothers during the early postpartum period does not cause any significant differences in the volume of breast milk produced. Our group expected that mothers who received Depo-Provera® would produce less breast milk than mothers who did not. This hypothesis was founded on the concept that because a decrease in progesterone during the early postpartum period is involved in the initiation of lactogenesis, administering a progesterone-based contraceptive would impair breast milk production. However, similar to previous research in mothers of term infants, we found that there were no significant differences in breast milk production in mothers who received and did not receive the drug.

However, there were two unexpected findings. First, our group found that administration of the drug prior to hospital discharge may negatively affect the normal increase in breast milk between 7 and 14 days postpartum (See Table 1). This is evident in how participants who received the drug experienced a negative trend in milk volume during this period. Second, we observed that a significant majority of participants who received Depo-Provera® prior to hospital discharge were Black women. This finding prompts further investigation as to why a disproportionate number of Black women are receiving the drug.

### Table 2: Demographics

<table>
<thead>
<tr>
<th></th>
<th>Depo-Provera (n = 32)</th>
<th>No Depo-Provera (n = 31)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age (years)</td>
<td>25.4 ± 5</td>
<td>25.9 ± 6</td>
<td>0.50</td>
</tr>
<tr>
<td>Gestational Age (weeks)</td>
<td>27.1 ± 2</td>
<td>27.8 ± 2</td>
<td>0.17</td>
</tr>
<tr>
<td>Birth Weight (grams)</td>
<td>943.66 ± 300</td>
<td>1055.42 ± 289</td>
<td>0.08</td>
</tr>
</tbody>
</table>

### Table 3: Black Participants

<table>
<thead>
<tr>
<th></th>
<th>Depo-Provera (n = 32)</th>
<th>No Depo-Provera (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent</td>
<td>0.69</td>
<td>0.29</td>
</tr>
</tbody>
</table>
IV. Summary and Conclusions

The goal of this project was to determine the effect of Depo-Provera® in mothers of preterm and very low birth weight infants in the NICU. Utilizing a secondary data analysis, we found that early postpartum administration of Depo-Provera® did not cause statistically significant changes in breast milk production among mothers of preterm very low birth weight infants. This supports previous research findings, which state that the drug was not found to have any significant adverse effects on breastfeeding outcomes, such as breastfeeding status and continuation in mothers of breastfeeding term infants. In contrast to previous research, there was one finding that trended towards significance: On average, mothers who received Depo-Provera® experienced a decrease in the change in milk volume over time. This may be clinically significant to mothers of preterm and very low birth weight infants, in which breastmilk consumption reduces risk for morbidity and mortality.

Future research should examine how Depo-Provera® affects changes in breast milk volume, rather than milk volume alone, over a longer period of time. With further research, researchers can determine whether these changes in milk volume are significant enough to initiate a change in practice. In addition, future research should also utilize a larger sample size and use a randomized procedure, which would provide more conclusive evidence as to whether Depo-Provera® affects breast milk production. Additionally, future studies could investigate whether a disproportionate number of Black women are truly receiving Depo-Provera®. If this is true, then any potential adverse effects of administering of Depo-Provera® in mothers of preterm very low birth weight infants prior to hospital discharge are being experienced by more Black mothers than of other races. Lastly, researchers can also investigate the reasons as to why more Black mothers are receiving Depo-Provera®.
Through this study, I was able to gain experience with nursing research. In doing so, I learned more about strengths and challenges of a study design, how to analyze data for significance, and how to think critically about how research affects practice. Nursing practice is continuously growing and changing, and evidence-based practice is necessary to support or reject current practice. Furthermore, as a student interested in maternal and neonatal nursing, I also gained insight into the types of clinical issues that patients in these populations may experience.
References


