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Comparison the Effect of Fennel on Maternal Serum Prolactin Level and Neonatal Weight Gain with Effect of Domperidon and Placebo

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ABSTRACT

Aims Breastfeeding is an economic and valuable method to protect infant health during the life and provides unique biological and emotional effect for mothers and infants. The aim of this study was to compare the effect of fennel on maternal serum prolactin level and neonatal weight gain to effect of domperidon and placebo on these variables.

Materials & Methods In this single blind randomized clinical trial (RCT), 150 volunteer mothers who had delivery and their newborns in Imam Sajad Hospital of Yasuj University of Medical Science, Yasuj, Iran in 2018, were selected by convenience sampling method and randomly assigned into three equal groups: placebo, domperidone, and fennel groups. Participants used placebo, domperidone tablets and fennel seeds powder for 14 days. Serum prolactin levels of mothers were measured with ELISA method before and after interventions. The weight of newborns were measured using digital scales on birth day, 14th and 28th days of study. Data were analyzed by SPSS 21 software using Chi square test, paired t-test, and one-way ANOVA.

Findings The mean serum prolactin level of the mothers before and after intervention in all three groups were not significantly different ($p>0.05$). The mean weight of neonates on the birth day, 14th day and 28th day in three groups did not show any significant difference ($p>0.05$).

Conclusion Fennel and domperidone have no effect on the serum prolactin level of lactating mothers and weight gain of newborns.

Keywords Fennel; Prolactin; Domperidone; Breastfeeding; Lactation

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Introduction

Breastfeeding as a natural, beautiful and admirable practice is considered to be the best food and the normal standard nutrition for infants [1-3] that plays an important role in promoting the health of mothers and their infants [1].

Milk production can be affected by maternal nutritional, hormonal and psychosocial factors. After delivery, the production and secretion of milk in the breasts will be started by the decrease of estrogen and progesterone hormones and the increase of prolactin [2]. The main hormone involved in milk biosynthesis is prolactin [2] which is a polypeptide hormone that is produced in anterior hypophysis. Breast suckling by newborn causes increase of prolactin production and on the other hand, hypothalamus secretes dopamine and after transferring to anterior hypophysis blocks prolactin secretion [1, 2].

Breast milk is an ideal diet for infants and plays a very important role in the physical development and development of neurological, cardiovascular, gastrointestinal and immunity system [4].

The most common cause of breastfeeding failure in the early days of the newborn's birth is insufficient milk production [5]. Insufficient breast milk and the concern of significant number of mothers in the first days after birth leads to use of formula and in many cases breastfeeding failure [4].

History of using breast milk enhancers (galactagogues) come back to thousands year ago when Hippocrates advised seeds and roots of fennel to mothers with insufficient milk production [6]. Several drugs and herbals have been studied as galactagogues including domperidone, Metoclopramide, Fenugreek, and fennel, which have no significant side effects except allergic reaction in a few number of cases [5, 7]. We didn't find a comparison between the effect of domperidone and fennel on neonatal weights and blood serum prolactin levels in breast fed mothers, which are factors and indicators of milk production in mothers.

The aim of this study was to compare the effect of fennel on maternal serum prolactin level and neonatal weight gain as indicators of amount of maternal lactation to effect of domperidon and placebo on these variables.

Materials and Methods

This single blind randomized clinical trial (RCT) was conducted on mothers who had delivery and their newborns in Imam Sajad Hospital of Yasuj University of Medical Science, Yasuj, Iran in 2018.

Inclusion criteria included lapse of 1 to 2 day after delivery, no contraindication for breastfeeding, healthy newborns, absence of cardiovascular disease in mothers, written and informative consent. Excluded criteria were formula feeding, significant complication in mother or newborn, illness in mother or newborn, no desire in mother to continue the study and no desire in mother to continue breastfeeding. The sample size was calculated using the interventional studies sample size assignment formula based on a similar study [6], and according to power (β)=80%, α=0.05, level of confidence=95%, p_1=44%, and p_2=16% was determined 42 people in each group. Therefore 150 volunteer mothers and their newborns were selected by convenience sampling method.

After explaining the different steps of the study for participant mothers, they signed informed consent and then were randomly assigned into three groups by block randomization: placebo group who received capsules containing inert base, domperidone group who received domperidone tablets 10mg three times in a day and fennel group who received capsules containing fennel seeds powder of Dena Mountain fennel, 1g three times in a day. Volunteers used placebo, domperidone tablets and fennel capsules for 14 days.

Blood samples of mothers were taken before starting the study and on 14th day after using the above drugs. Blood serum prolactin levels were measured with ELISA method by using pro-bind kit (Saman Tajhiz Noor; Iran). The weight of mothers, newborns were measured on birth day, 14th and 28th days of study by using ZYKDS-05 Zyklusmed digital scales (Zyklusmed; Germany), with precision of 5 grams, and all of them were written in special data forms.

From 150 participants in the study some of them (44 cases) were excluded due to incorrect or insufficient use of the drugs, no refer for measuring the weight of the newborns, no refer for measuring the serum prolactin, use of formula, and hospital admission of the mother or infant. Finally, 106 participants, (placebo group 33 cases, domperidone group 37 cases and fennel group 36 cases) completed the study steps.

Data normal distribution was checked by Kolmogorov Smirnov test and normal distribution of data was verified with 95% confidence level. Collected data were analyzed by SPSS 21 software using Chi square test, paired t-test, and one-way ANOVA.

Findings

There was no significant difference among studied groups in terms of demographic variables (Table 1).

The mean serum prolactin levels of the mothers before intervention (p=0.970) and after intervention (p=0.788) among the fennel group, placebo group and domperidone group showed no significant difference. The serum prolactin levels before and after intervention in all three groups were not significantly different (p>0.05; Table 2).

The mean of neonate's weight in birth day (p=0.468), 14th day (p=0.616), and 28th day (p=0.811) had no significant difference in three groups of study (Table 3).

Table 1) Comparison of absolute and relative frequency distribution of demographic variables among studied groups (the numbers in parentheses are percentages)

Variables	Placebo group	Domperidone group	Fennel group	Total	p. value*
Gender					
Male	22 (66.7)	20 (54.1)	19 (52.8)	61 (57.5)	0.441
Female	11 (33.3)	17 (45.9)	17 (47.2)	45 (42.4)	
Maternal gravid					
1	13 (39.4)	16 (43.2)	14 (38.9)	43 (40.6)	0.462
2	13 (39.4)	9 (24.3)	10 (27.8)	32 (30.2)	
3	4 (12.1)	4 (10.8)	8 (22.2)	16 (15.1)	
≥4	3 (9.1)	8 (21.6)	4 (11.1)	15 (14.1)	
Maternal age (years old)					
≤20	1 (3.0)	2 (5.4)	2 (5.6)	5 (4.7)	0.687
21-30	21 (63.6)	19 (51.3)	22 (61.1)	62 (58.5)	
31-39	10 (30.3)	16 (43.2)	12 (33.3)	38 (35.8)	
≥40	1 (3.0)	0	0	1 (0.9)	
Total	33	37	36	106	-

*Chi square test

Table 2) Comparison of the mean of maternal serum prolactin (mg/dl) of birth day (PRL-1) and 14th day (PRL-2) in three groups of study

Groups	PRL-1	PRL-2	p. value*
Placebo	57.28±16.79	66.55±18.05	0.091
Domperidone	55.36±17.59	62.60±11.60	0.198
Fennel	57.36±18.11	64.19±15.09	0.646
p. value**	0.970	0.788	-

*Paired t-test; **One-way ANOVA

Table 3) Comparison of the mean of neonate's weight (g) in birth day, 14th day, and 28th day in three group of study

Neonate's weight	Placebo group	Domperidone group	Fennel group	p. value*
Birth day	3145.75±486.72	3000.94±611.58	3009.44±423.77	0.468
14th day	3566.51±474.57	3464.45±430.39	3477.63±463.79	0.616
28th day	4145.75±582.10	4068.82±414.78	4125.44±537.52	0.811

*One-way ANOVA

Discussion

Breast milk is an ideal diet for infants and plays a very important role in optimal growth and development [4] and the most common cause of breastfeeding failure in the early days of the newborn's birth is insufficient milk production [5]. Insufficient breast milk in significant numbers of mothers in the first days after birth leads to use of galactagogues [4], therefore we design this study to find safe, effective and economic solution for this common problem.

Analysis of demographics data of participants did not show significant difference among three groups that shows random allocation.

Our study showed that fennel, domperidone and placebo had no significant difference on serum prolactin level in lactating mothers in comparison of each group to the other groups, and the intervention in each group had no significant effect on the level of prolactin in the lactating mothers in comparison to before to intervention.

Also there was no significant difference in weight of newborns among three groups on 14th and 28th day and the analysis of weight gain of newborns in all three groups, in each intervention, showed an increase in weight from birth day to 14th and 28th day (which was appropriate to normal weight gain, and it had no relation to the type of intervention). We did not see or hear any side effect in mothers and their neonates in our study.

Previous researches on effect of domperidone on increasing milk production and as a result on maternal serum prolactin level and newborn weight gain had showed significant increase [8-11].

But results about fennel were different (some of them showed increase and the others showed no significant effect) [2, 12, 13].

Siahi *et al*. showed aqueous extract of fennel seeds had no significant effect on serum prolactin level of female rats [14] that was similar to our study.

Sekhavat *et al*. in another study on 48 mothers who suffering from insufficient milk production in Yazd, showed that domperidone increases serum prolactin level and volume of milk production [8] that was against our study. This different result may be due to selecting of mother with insufficient milk production.

Shariati *et al*. in a RCT study on 158 mothers with deficient milk production in Mashhad showed shirafza drop containing fennel seed extract has no significant effect on volume of milk production and newborn weight gain [15] that was similar to our study.

Osadchy *et al*. in a systematic review study showed that domperidone can increase milk production [13].

da Silva *et al*. in a RCT study on 16 mothers with premature neonates in 2001 showed that

dompridone increases maternal milk production [6]. In this study neonates were preterm, but in our study all of them were full term.

Honarvar *et al*. in a RCT study on 46 mothers in Ahvaz showed that fennel seed powder can increase serum prolactin level [5] that our study did not show it. Different result may be due to type of fennel that we used which was obtained from Dena Mountains in different climate and altitude or may be due to different foods and vegetables in their diets that can interfere our study.

The ineffectiveness of our interventions on breast milk production with measuring serum prolactin level and newborn weight gain may be due to specific genetics of this region's population or the particular dietary habits of the people of this region, including the use of variety of vegetables or vegetable seeds in their diet that can affect serum prolactin level and/or volume of milk production. Therefore, for more precise comparison researcher must use the similar effective extract of herbal drugs and prepare similar participants and conditions. As a result, judgment about effect of galactagogues on serum prolactin level and volume of milk production needs more research and study.

There was some limitations in our study: one of them was non-attendance of the participants, in spite of the appointment sheet and the date and time of the visit, and despite the phone call the day before the visit, and another limitation was non-compliance with study conditions, such as non-breastfeeding by some mothers or other medications.

Conclusion

Fennel and domperidone have no effect on the serum prolactin level of lactating mothers and weight gain of newborns.

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Ethical Permission: This study approved by the Ethics Committee of Yasuj University of Medical Science (code: IR.YUMS.REC.1397.002). Written informed consents of volunteer participants were obtained and the privacy policy has been completely regarded.

Conflict of Interests: The authors declare that they have no conflict of interest.

Authors' Contribution: Keshtkari A. (First author), Introduction author/ Original researcher/ Discussion author (35%); Ghatee MA. (Second author), Methodologist/ Statistical analyst (20%); Bagheri N. (Third author), Assistant (10%); Mehboudi A. (Fourth author), Introduction author/ Original researcher/ Discussion author (35%)

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