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ORIGINAL ARTICLE

Comparison of domeperidone versus metoclopramide to increase the milk production in lactating mothers.

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ABSTRACT… Objective: To compare domeperidone and metoclopramide to increase the milk production in lactating mothers. **Study Design:** Randomized Controlled Trial. **Setting:** Department of Gynecology and Obstetrics, Sheikh Zayed Hospital, Rahim Yar Khan. **Period:** February 2021 to August 2021. **Material & Methods:** A total of 190 lactating mothers within 1 month of delivery and milk production less than 160 ml/kg/day were included. Women in Group-A were given metoclopramide in a dose of 10 mg three times a day in oral form and those in Group-B were given tablet domeperidone in the same dose and protocol. These women were then followed up and assessed at day-10 regarding the milk production over the previous 24 hours. Treatment compliance was also noted. **Results:** In a total of 190 women, the mean age was 29.86±5.49 years ranging between 20-40 years. Majority of the women, 114 (65.3%) were aged between 31-40 years. The mean weight was 71.78±8.75 kg while the mean parity was 2.32±1.06. Pre-treatment mean milk production was 159.43±89.67 ml in metoclopramide group versus 157.98±78.59 ml in domperidone group (p=0.9058). After 10 days of treatment, mean milk production was noted to be 183.61±31.44 ml in metoclopramide versus 245.63±68.84 ml in domperidone and the difference was noted to be significant favoring domperidone group (p<0.0001). Treatment compliance was statistically similar in both treatment groups (58.2% vs. 64.4%, p=0.4617). **Conclusion:** Domperidone is better in increasing the milk production in lactating mothers as compared to metoclopramide.

Key words: Compliance, Domperidone, Lactating Mothers, Metoclopramide, Milk Production.

INTRODUCTION

Breast milk is the perfect food for infants that promotes neurodevelopment and plays in important role in preventing infections.[1] Expression of the breast milk is suggested to the mothers who have their in neonatal care units. However, at times, it becomes difficult for mothers to have adequate production of breast milk to fulfill the need of newborn babies for a longer period of time before they can be fed directly from the breast.[2] In the neonatal intensive care unit (NICU), mothers undergo a variety of events and emotions like exhaustion, anxiety and unresolved grief.[3]

A general decrease in the practice of breastfeeding has been noted in many countries. The exclusive breastfeeding rates of around 75% have been reported in the UK showing a drop of 14.8% at 6 months.[2] It was reported that 74.4% of the US newborns were exclusively breastfeeding, but over a period of six months this rate dropped to 34.7%. The Academy of Breastfeeding Medicine (ABM) claimed that insufficient supply was one of the most frequent causes cited by mothers to discontinue breastfeeding with the reported prevalence ranging between 19.8-74.0%.[4] The reasons behind the decreases could be that women have been passing through many challenges to maintain human milk production up to an adequate level.[5]

Specific non-pharmacological mediations like providing close skin-to-skin contact to the baby, making earliest milk expression after delivery, maintaining the frequency of pumping up to

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12 times over a period of 24 hours, counseling for lactating mothers and easing techniques may produce favorable results.[6,7] However, in some mothers lactation gets compromised so pharmacological methods are recommended to enhance their milk supply. Pharmacological effects of majority of the galactogogue drugs are produced through their interaction with dopamine receptors, which enhance the levels of prolactin, and consequently milk supply is augmented.[8,9]

The safety and effectiveness of metoclopramide is well established but it is known to cross the blood-brain barrier and some of the mothers may experience tremor, bradykinesia (slow movements) and other dystonic reactions.[10] In contrary, domperidone has minimal chances of crossing the blood-brain barrier and getting transferred into breast milk, hence remains risk free and less toxic for mother and infant.[4] In a study done by Ingram JC et al, they compared domeperidone with metoclopramide and it was seen that mean milk production was 173.6±126.2 ml vs 132.5±115.4 with mean difference of 42.9 ml and after the treatment this was 284.7±158 vs. 211±154.3 with mean difference of 74.1 ml.[11]

Not much data comparing metoclopramide versus domperidone is available regarding their effectiveness in increasing breast-milk so the present study was planned. The findings of this might help in finding a better drug for the routine practice to decrease the burden of the issue in the lactating mothers. The objective of this study was to compare domeperidone and metoclopramide for increase in the milk production in lactating mothers.

MATERIAL & METHODS

We carried out this randomized controlled trial at the department of gynecology and obstetrics, Sheikh Zayed Hospital, Rahim Yar Khan from February 2021 to August 2021. The sample size was calculated as 190 (95 in each group) considering 95% confidence level, 90 % power and post treatment milk production as 284.7±158 vs. 211±154.3 ml in domeperidone and metoclopramide respectively.[11] Non-probability, consecutive sampling technique was adopted. Approval from Institutional Ethical Committee was acquired (Ref. No. 671/IRB/SZMC/SZH). Informed and written consents were obtained from the subjects.

Inclusion criteria were lactating mothers aged between 20-40 years with less than 1 month of delivery time and having less than 160 ml/kg daily milk production. On the basis of previous history and medical record, those cases were excluded who had documented hypersensitivity against any of the medication studied in this research. Established cases of end-stage renal disease or liver failure were also excluded.

Age (years), weight (kg), daily milk production (calculated by collection of milk via a pump in a container and was calculated for 24 hours), parity, previous history of breastfeeding, educational status (educated/uneducated), residential status (rural/urban) and monthly income were noted among all women. Women were divided into two equal groups by sealed opaque envelope method labeled as metoclopramide group or domperidone group. Women in metoclopramide group were given metoclopramide orally in a dose of 10 mg thrice a day. In domperidone group, women were given tablet domeperidone in the same dose and protocol as in Group-A. All women were then followed up and assessed at day-10 regarding the milk production over the 24 hours. Women were also asked about compliance of the studied drugs. All the study data was collected on a specially designed format.

The data was analyzed using "Statistical Package for Social Sciences (SPSS)", version 26.0. Quantitative variables were represented as mean and standard deviation (SD) while qualitative variables were highlighted as frequency and percentages. Baseline and post-treatment mil production, and other quantitative variables were compared using independent sample t-test. Effect modifiers were controlled through stratification and post-stratification chi-square was applied. P value below 0.05 was taken as significant.

RESULTS

In a total of 190 women, the mean age was

29.86±5.49 years ranging between 20-40 years. Majority of the women, 114 (65.3%) were aged between 31-40 years. The mean weight was 71.78±8.75 kg while the mean parity was 2.32±1.06. Pre-treatment mean milk production was 159.43±89.67 ml in metoclopramide group versus 157.98±78.59 ml in domperidone group (p=0.9058). Table-I is showing comparison of baseline characteristics among women of both study groups.

After 10 days of treatment, mean milk production was noted to be 183.61±31.44 ml in metoclopramide versus 245.63±68.84 ml in domperidone and the difference was noted to be significant favoring domperidone group (p<0.0001) as shown in Figure-1.

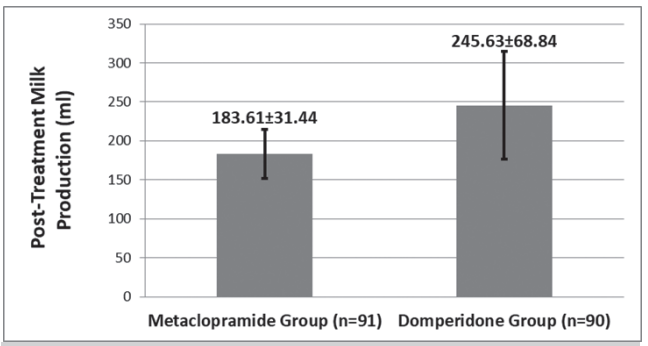

Figure-1. Comparison of mean post-treatment breast milk production

Treatment compliance was statistically similar in both treatment groups (58.2% vs. 64.4%, p=0.4617) as shown in Table-II.

Stratification of Post-treatment milk production according to all study variables is shown in Table-III. Statistically significant differences were found for all study variables favoring metoclopramide treatment (p<0.0001).

DISCUSSION

Multiple non-pharmacological interventions have been presented as effective mediations in the promotion of breastfeeding.[12] However, mothers may pursue therapy with galactogogues in response to insufficient milk supply since non-pharmacologic measures did not always work.[13,14] Galactogogues are certain pharmaceutical substances which are believed to facilitate the initiation, maintenance or augmentation of the milk supply of lactating mother. Previous studies suggested that needs for pharmaceutical galactogogues is increasing.[15,16]

Current literature demonstrates that domperidone and metoclopramide are the most extensively used galactagogues.[8,17]

Characteristics		Total (n=190)	Metoclopramide Group (n=95)	Domperidone Group (n=95)	P-Value
Age (years)	20-30	76 (40.0%)	36 (37.9%)	40 (42.1%)	0.2140
	31-40	104 (60.0%)	59 (62.1%)	45 (57.9%)	
	Mean±SD	30.74±5.43	31.02±5.39	29.86±5.49	0.1434
Weight (kg)	≤70	84 (44.2%)	46 (48.4%)	38 (40.0%)	0.6179
	>70	96 (55.8%)	49 (51.6%)	47 (60.0%)	
	Mean±SD	71.78±8.75	71.22±9.70	72.25±8.92	0.4470
Parity	1-2	103 (54.2%)	57 (60.0%)	46 (48.4%)	0.1092
	3-5	87 (45.8%)	38 (40.0%)	49 (51.6%)	
	Mean±SD	2.30±1.06	2.26±1.11	2.32±1.06	0.7036
Residence	Rural	100 (52.6%)	52 (54.7%)	48 (50.5%)	0.5611
	Urban	90 (47.4%)	43 (45.3%)	47 (49.5%)	
Education	Uneducated	63 (33.2%)	34 (35.8%)	29 (30.5%)	0.4410
	Educated	127 (66.8%)	61 (64.2%)	66 (69.5%)	
Monthly Income (Pakistani Rupees)	<20000	59 (31.1%)	30 (31.6%)	29 (30.5%)	0.9514
	20000-40000	73 (38.4%)	37 (39.0%)	36 (37.9%)	
	>40000	58 (30.5%)	28 (29.4%)	30 (31.6%)	
Past history of breastfeeding		88 (46.3%)	46 (48.4%)	42 (44.2%)	0.6551
Pre-treatment milk production (ml)		158.38±84.20	159.43±89.67	157.98±78.59	0.9058

Table-I. Comparison of baseline characteristics

Treatment Compliance	Metoclopramide Group (91)	Domperidone Group (n=90)	P-Value
Yes	53 (58.2%)	58 (64.4%)	0.4617
No	42 (41.8%)	37 (35.6%)	

Table-II. Distribution of treatment compliance

Characteristics		Metoclopramide Group (n=95)	Domperidone Group (n=95)	P-Value
Age (years)	20-30	189.92±28.32	276.78±68.98	<0.0001
	31-40	181.23±32.41	222.98±59.75	<0.0001
Weight (kg)	≤70	185.59±35.99	256.92±77.33	<0.0001
	>70	181.76±26.73	238.11±62.12	<0.0001
Parity	1-2	180.12±31.77	254.78±72.99	<0.0001
	3-5	188.84±30.61	237.04±64.25	<0.0001
Residence	Rural	178.63±32.80	235.83±65.91	<0.0001
	Urban	189.63±28.95	255.64±71.01	<0.0001
Education	Uneducated	185.41±38.57	231.55±66.89	<0.0001
	Educated	182.61±26.98	251.82±69.27	<0.0001
Monthly Income (Pakistani Rupees)	<20000	195.57±37.19	226.45±79.21	<0.0001
	20000-40000	176.49±30.99	253.61±70.89	<0.0001
	>40000	180.21±20.85	254.60±52.02	<0.0001
Past history of breastfeeding		179.96±32.11	250.19±69.88	<0.0001
Treatment Compliance		186.40±35.92	239.21±75.02	<0.0001

Table-III. Stratification of post-treatment milk production (ml) according to study variables

Both inhibit dopamine effect at receptor sight and can promote milk production.[18] However, the ABM does not recommend any specific galactogogues for clinical practice due to insufficient supportive evidence, and domperidone and metoclopramide are not approved as galactogogues in the US due to cardiac-toxicity and neuro-toxicity concerns.[19] Therefore, available evidence regarding efficacy and safety of both metoclopramide and domperidone is controversial.

In our study, it was seen that pre-treatment mean milk production was 179.43±89.67 ml in metoclopramide group versus 167.98±78.59 ml in domperidone group (p=0.9058) and after 10-days treatment, it was 183.61±31.44 ml versus 245.63±68.84 ml in metoclopramide and domperidone groups respectively (p<0.0001). For the comparison of domperidone and metoclopramide regarding their effectiveness iin milk production, we found two randomized control trials in which 85 mothers were involved.[11,20] The use of domperidone resulted in a slightly higher volume of expressed milk compared with a placebo, but no significant difference was observed (p=0.20). A randomized crossover trial illustrated that both 30mg and 60mg doses of domperidone resulted in significant increases in milk production among mothers of preterm infants, but women who received 60mg doses had higher value in increased milk volume than 30mg (367% and 215% respectively).[21] Another RCT involving 15 women of preterm infants revealed that a dose of domperidone as 60mg was associated with a clinical increase in milk production when compared with 30mg.[22] But the trial also reported that women who received 60mg of domperidone reported more frequent side effects comparing with 30mg domperidone.[22] A case-control study noted that domperidone was associated with sudden cardiac death when given in high doses so it is better to avoid higher doses of domperidone.[23] Regarding metoclopramide, a placebo-controlled, cross-over trial including women with term infants demonstrated that dose of 30mg or 45mg significantly increased human milk volume, whereas 15mg of metoclopramide showed no significant effects.[24] Dose-effects of domperidone and metoclopramide should be taken into consideration when used in relatively higher doses as has been shown in the previous studies.[23,24]

This study had some limitations. Being a single center study, more multi-centric trials involving large sets of lactating mothers should be conducted to verify the findings of this study. Follow up period was relatively short and we were unable to evaluate treatment related adverse effects.

CONCLUSION

Domperidone is better to increase the milk production in lactating mothers as compared to metoclopramide. Domperidone can be used as primary drug for increasing milk production in lactating mothers.

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2	Hina Shahid	Data collection, Final approval.	
3	Riffat Afzal	Literature review, Methodology.	
4	Mamoona Zahoor	Literature review, Methodology.	
5	Afshan Nadeem	Drafting, References.	