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The effect of intrapartum labor induction with oxytocin on maternal depression scoring in early postpartum period: a retrospective cohort study

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ABSTRACT

Aims: Studies showing that synthetic oxytocin (SO) used for induction during labor increases the risk of postpartum maternal depression are increasing day by day in literature. Objective was to investigate the effect of SO administered for induction during labor on the tendency to maternal depression in early postpartum period.

Methods: The study encompassed nulliparous women, all of whom delivered at gestational weeks 37 to 41 between 2020 and 2022 and underwent standard postpartum assessments on the 10th day following delivery. Exclusion criteria comprised pregnant individuals with predisposing factors for depression before conception, during gestation, or in the postpartum period. Pregnants who were admitted to delivery room due to labor and gave birth without any induction method were classified as group C (n=137), and who were induced with SO were classified as group O (n=122). Edinburgh Postnatal Depression Scale (EPDS) scores on 0th day and 10th day postpartum of two groups were compared. Additionally, relationship between duration of induction and EPDS scores was analyzed.

Results: No statistically significant difference was detected between two groups in terms of age, gestational week, or educational status (p>0.05). No statistically significant difference was detected between the groups in EPDS scores on 0th or 10th day postpartum (p>0.05). There was no significant difference between induction time and EPDS scores on 0th or 10th day postpartum (p>0.05).

Conclusion: SO used for labor induction may not primary affect the tendency to postpartum depression in the early period. Further studies in populations without risk factors for depression are needed.

Keywords: Delivery, EPDS, labor induction, postpartum depression, synthetic oxytocin

INTRODUCTION

Oxytocin is a hormone necessary for various maternal abilities such as labor pains, breastfeeding, and the mother's bonding with the baby. As a neurotransmitter in the central nervous system, it affects various parts of the brain (hippocampus, amygdala and nucleus accumbens), such as the limbic system, which is related to emotions and social relationships. In the periphery, it helps with labor by causing the uterus to contract. It helps breastfeeding by stimulating the breast to release milk.[1] In the clinic, synthetic oxytocin is used to induce labor, augment labor pain and prevent postpartum hemorrhage.

In a study conducted, in the study group consisting of mothers with high psychosocial stress levels after birth, those with high endogenous oxytocin levels were less depressed.[2] Likewise, blood oxytocin levels of women with depressive features were found to be lower in the 2nd-month postpartum.[3] Researches indicate that physiological oxytocin levels have an impact on maternal mood during the postpartum period. Also, there are researches indicating that synthetic oxytocin used for labor induction increases the risk of postpartum depression.[4-6] Induction of labor with synthetic oxytocin is a common method applied by many physicians around the world. And can synthetic oxytocin have such a negative effect on maternal mood? In the studies mentioned and, in the literature, the Edinburgh Postnatal Depression Scale (EPDS) was used to understand mood assessment/tendency to depression. Although it varies from country to country, according to this 30-point scale, a score of 10 or higher suggests a mild to elevated risk of experiencing postpartum depression.[7,8]

Considering the studies showing that physiological and synthetic oxytocin may affect maternal mood, a question arises: Can synthetic oxytocin given for labor induction really be effective on maternal mood? Does the administered oxytocin

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protect from depressive tendencies in the early period, or does synthetic oxytocin taken from external sources cause a tendency to depression by increasing in maternal blood and decreasing rapidly after treatment?

Given this background, the aim was to analyze the influence of synthetic oxytocin administered for induction during labor on the tendency to maternal depression in the early postpartum period.

METHODS

Ethics

The study was planned and completed as a retrospective cohort study. The study was executed adhering to the ethical guidelines outlined in the Declaration of Helsinki. Approval was granted by the Ethics Committee of the Başakşehir Çam and Sakura City Hospital (Date: 26.10.2022, Decision No: KAEK/2022.10.340).

Design of the Study

Pregnant women who delivered at city hospital from September 2020 to September 2022 and received standard postpartum assessments on the 10th day after delivery childbirth were retrospectively screened via hospital records. It was evaluated whether there were risk factors that could predispose to depression before, during and after pregnancy. Women identified with such risk factors were excluded from the study. Whether participants received induction with synthetic oxytocin during the labor process were determined. EPDS scores were determined by the Edinburgh Postpartum Depression Scale, which was filled in right after birth. The records of puerperants who were routinely called for puerperium control on the 10th postpartum day and routine psychologist evaluation on the same day were examined. And on the 10th day EPDS scores were determined. Both the EPDS applied right after birth and the EPDS applied on the 10th postpartum day are routine practices of our hospital. Participants who did not attend psychologist appointments or had incomplete information regarding their EPDS scores were not included in the study (**Figure**).

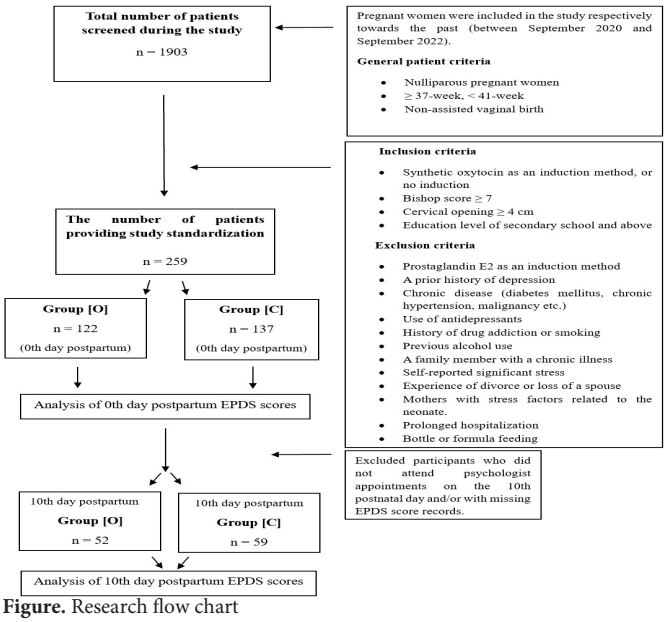

Figure. Research flow chart

2 groups were formed from the pregnant participants without depression risk factors.

Group oxytocin, (O): The group consisted of patients who were admitted to the delivery room due to labor and who were induced with synthetic oxytocin because of insufficient labor pain. As a routine practice in our hospital, an induction solution is prepared by adding 5 I.U. synthetic oxytocin (Synpitan forte, Deva, İstanbul, Turkiye) into 500 cc isotonic. Induction is started with a dose of 4 drops/hour and increased until an effective contraction (>200 montevideos/10 minutes) occurs. Afterwards, it is continued at a constant dose until labor is completed.

Group control, (C): Patients who were admitted to the delivery room due to labor and gave birth without any induction method because their labor pain was sufficient.

- EPDS scores on the 0th day postpartum of patients who received oxytocin induction and who did not receive any induction were compared.
- EPDS scores on the 10th day postpartum of two groups were compared.
- In the group receiving synthetic oxytocin induction, the relationship between the duration of induction and EPDS scores (day 0 or day 10 separately) was analyzed.

Inclusion and Exclusion Criteria

In order to mitigate the influence of various factors on EPDS scores, the study included nulliparous pregnant women aged between 20 and 38 years who were at or beyond 37 weeks of gestation. Pregnant women classified as post-term (41 weeks and beyond) were excluded from the study. The study included only patients who had a normal vaginal birth without assistance and who received only synthetic oxytocin as an induction method, or no induction method. Among the pregnant women who were induced with synthetic oxytocin, patients with a Bishop score at or above 7 and a cervical opening at or above 4 cm were included. Patients with an education level of secondary school and above who discharged with recovery 24 hours after birth were included.[9-16]

The study excluded patients who induced with Prostaglandin E2 or gave birth by cesarean section. Additionally, individuals with any of the following conditions were considered ineligible and excluded: a prior history of depression, presence of any chronic illness, use of antidepressants, history of drug addiction or smoking, previous alcohol use, a family member with a chronic illness potentially affecting domestic harmony, a first-degree relative who passed away within the last 5 years, self-reported significant stress, experience of divorce or loss of a spouse, and those who underwent a complicated delivery.[9-16] "Patients experiencing stress factors related to the neonate, such as admission to the neonatal intensive care unit, jaundice, or any condition necessitating additional follow-up, were also excluded from the study. Patients with prolonged hospitalization for any reason, mothers with feeding methods other than breastfeeding (eg, bottle or formula feeding) were excluded from the study".[16] In order to ensure patient standardization; the patient population was determined

with the depression risk criteria that have been applied in the literature.[9-16] Also, these criteria had been applied in our (Sivas et al.)[16] study where we investigated the importance of "number of breastfeeding sessions per day on postpartum depression".

Statistical Analysis

A power value of 0.80, a margin of error of 0.05 and an effect size of 0.6 was taken for determining the sample size. Calculations were performed in accordance with the protocol with gpower3.1 software (https://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower). It was determined that there should be at least 36 patients in each group for statistical significance. Due to the possibility of patient loss between day 0 and day 10 analyses, an attempt was made to increase the number of patients as much as possible. To evaluate the distribution of the data, the Shapiro-Wilk test was used. Mann-Whitney U test was used for comparisons between two independent groups. Pearson's chi-square test and Fisher's exact test were used for comparisons. The relationships between variables were analyzed with Spearman's correlation coefficient. A p-value of <0.05 was considered as statistically significant.

RESULTS

In the process of study, records of 1903 patients were initially reviewed. Following the application of inclusion and exclusion parameters, the study proceeded with 259 appropriate participants. Day 0 analyzes were conducted with 259 participants in total (group O 122 patients, group C 137 patients). After excluding the participants who did not attend psychologist appointments on the 10th postnatal day and/or with missing EPDS score records, the 10th day analyzes were conducted with 111 participants in total (group O 52 patients, group C 59 patients) (**Figure**).

Evaluation of Descriptive Statistics

No statistically significant difference was found between the two groups in terms of age, gestational week, or educational status on the 0th day postpartum (p>0.05) (**Table 1, 2**).

Table 1. Comparison of age, week of gestation and 0th-day EPDS scores between the groups

	Group	n	Median	Min	Max	p value
Age	Group C	137	24.00	20.00	38.00	0.583
	Group O	122	24.00	20.00	36.00	
Week of gestation	Group C	137	39.00	37.00	40.00	0.591
	Group O	122	39.00	37.00	40.00	
EPDS score (day 0)	Group C	137	5.00	0.00	21.00	0.748
	Group O	122	5.00	0.00	21.00	

p<0.05, Mann-Whitney U test, EPDS: Edinburgh Postnatal Depression Scale, Min: Minimum, Max: Maximum

No statistically significant difference was found between the two groups in terms of age, gestational week, or educational status on the 10th day postpartum (p>0.05) (**Table 3, 4**).

Table 2. Comparison of education status between the groups (based on postpartum 0th-day data)

			Group C	Group O	p value
Education status	Secondary school	n	67	52	0.192
		%	48.9%	42.6%	
	High school	n	38	34	
		%	27.7%	27.9%	
	Associate degree	n	9	9	
		%	6.6%	7.4%	
	University	n	23	25	
		%	16.8%	20.5%	
	Post graduate	n	0	2	
		%	0.0%	1.6%	

p<0.05, Fisher's exact test

Table 3. Comparison of age, gestation week, 10th-day EPDS scores between groups (postpartum 10th-day data)

	Group	n	Median	Min	Max	p value
Age	Group C	59	26.00	20.00	37.00	0.352
	Group O	52	24.00	20.00	32.00	
Week of gestation	Group C	59	39.00	37.00	40.00	0.703
	Group O	52	39.00	37.00	40.00	
EPDS score (day 10)	Group C	59	6.00	0.00	17.00	0.416
	Group O	52	7.00	0.00	20.00	

p<0.05, Mann-Whitney U test, EPDS: Edinburgh Postnatal Depression Scale, Min: Minimum, Max: Maximum

Table 4. Comparison of education status between the groups (based on postpartum 10th day data)

			Group C	Group O	p value
Education status	Secondary school	n	17	14	0.654
		%	28.8%	26.9%	
	High school	n	22	20	
		%	37.3%	38.5%	
	Associate degree	n	7	8	
		%	11.9%	15.4%	
	University	n	13	10	
		%	22%	19.2%	

p<0.05, Pearson's Chi-square test

Comparison of EPDS Scores Between Groups

There was no statistically significant difference between EPDS scores following labor (day 0) (p>0.05) (**Table 1**). When group O was evaluated within itself, no significant difference was found between induction time and the EPDS scores on the 0th day postpartum (p>0.05) (**Table 5**).

No statistically significant difference was found in the EPDS scores on the 10th day postpartum between the groups (p>0.05) (**Table 3**). When group O was evaluated within itself,

no significant difference was found between induction time and the EPDS scores on the 10th day postpartum (p>0.05) (Table 5).

Table 5. The relationship between induction time and 0th/10th day EPDS scores of group oxytocin

		Induction time (min)
EPDS score (day 0)	r	-0.072
	p	0.417
EPDS score (day 10)	r	-0.019
	p	0.898

p<0.05, Spearman's correlation analysis, EPDS: Edinburgh Postnatal Depression Scale, Min: Minute

DISCUSSION

When the results of the study were evaluated, the postpartum EPDS scores (day 0 or day 10) of pregnant women who received induction with synthetic oxytocin were not significantly different from those who did not receive induction. No significant relationship was found between the duration of synthetic oxytocin exposure during the labor and EPDS scores. There was no relationship between synthetic oxytocin and early postpartum depression.

Studies examining the relationship between physiological oxytocin in the postpartum period and postpartum depression are available in the literature. In a study examining maternal endogenous oxytocin levels during the puerperal period; in the study group consisting of mothers with high psychosocial stress levels, endogenous oxytocin levels were found to be higher in mothers who were found to be less depressed.[2] In the 8th week after delivery, blood oxytocin levels of puerperant with postpartum depression were found to be lower than those who were not depressed.[3] These studies suggest that endogenous oxytocin may have a protective effect against the tendency for depression. In another study conducted by measuring oxytocin levels in maternal saliva, oxytocin levels were not found to be lower in women with postpartum depressive or anxious behaviors.[17] While the current study reaches a different conclusion from the aforementioned studies, it suggests that there may be differences in oxytocin receptor and post-receptor molecular pathways in patients with the same oxytocin levels. In a systematic review based on related studies, it is emphasized that more studies should be conducted on this subject.[18] Furthermore, genetic analyses show that oxytocin receptor expression may vary depending on external factors.[19,20]

While there are studies on how endogenous oxytocin affects maternal mood, there are only a few studies in the literature on how synthetic oxytocin affects maternal mood. A study presenting results on the relationship of synthetic oxytocin with depression in the long term found that pregnant women who were administered synthetic oxytocin during the labor process had a higher risk of being diagnosed with maternal anxiety disorder/depression in the 1-year postpartum period. The study investigating the late-stage effects of synthetic oxytocin was completed based on patients who were diagnosed with depression after childbirth or prescribed psychotropic drug.[4] In another study, the EPDS scores in the first 48 hours postpartum were analyzed in patients who were exposed to synthetic oxytocin for a longer or less period during labor. Those who scored 12 and above in the EPDS score were proportionately higher in patients who received synthetic oxytocin for a longer period.[5] In the study indicating that mothers who received less synthetic oxytocin at birth had higher breastfeeding rates and less formula administration feeding, a positive correlation was reported between the amount of synthetic oxytocin administered and postpartum 2nd-month depressive symptoms.[6]

The above studies did not investigate whether patients included in the study had a history of depression and/or risk factors for depression in the prenatal period. A depressive background present before or during labor may have completely affected the study results. EPDS scores may have been detected higher in women who were prone to depressive tendencies due to depression risk factors. Women who were prone to depressive tendencies due to low endogenous oxytocin levels may have needed more synthetic oxytocin to accelerate the labor process. Therefore, EPDS scores may have been detected higher in those who received more synthetic oxytocin. Similarly, a pre-existing depressive disorder may have caused a high score in the EPDS scores administered at 48th- hour or 2th-month after birth.

Unlike the results of the mentioned studies, when we analyzed the results of the standardized patient population that we formed by excluding depression risk factors, we determined that synthetic oxytocin did not make a significant change in EPDS scores both on postnatal day 0 and day 10. The fact that there was no significant difference in postnatal day 0 results indicates that synthetic oxytocin did not have a major positive or negative effect on patient EPDS scores at the time of use. In addition, the low EPDS scores observed in both groups on day 0 indicate the homogeneity and success of standardized groups created by excluding pregnant women with depression risk factors. Similarly, when the patients in the synthetic oxytocin group consisting of standardized patients were evaluated within the group, there was no significant difference between the duration of synthetic oxytocin exposure and EPDS scores.

One notable strength of the current study lies in its utilization of a standardized population. The assessment of depression risk factors both before and after childbirth was conducted, thereby mitigating the potential effects and variables mentioned earlier. Furthermore, the study analyzed the EPDS scores of women postpartum, adding to its comprehensiveness. Through the establishment of a standardized patient group, the study exclusively investigated the impact of synthetic oxytocin on EPDS scores. This characteristic makes our study the first in the literature to explore the effects of synthetic oxytocin on maternal mood independently of depression. Our study contributes to the literature as it obtained different results from the existing studies.

Limitations

The first limitation is the low number of participants fitting the standardized profile. Although this study included a 2-year patient archive, the number of participants to be included in the study was severely reduced when patients with

depression risk factors were excluded. Other limitation is that this study does not have the criteria to exclude the effect of receptor and downstream pathways when investigating the effect of synthetic oxytocin infusion. Likewise, epigenetic factors affecting receptor expression were not investigated. Simultaneous measurement of blood oxytocin levels while examining EPDS scores will increase the sensitivity of the study. Additionally, the labor duration of the groups should be taken into account.

CONCLUSION

Synthetic oxytocin used for labor induction may not primary affect the tendency to postpartum depression in the early period. Further studies with large populations consisting of participants with depression risk factors excluded, examining the effects of synthetic oxytocin on postpartum depression in early/late period are needed.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated with the approval of Başakşehir Çam and Sakura City Hospital Ethics Committee (Date: 26.10.2022, Decision No: KAEK/2022.10.340).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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