ZKTB

ORIGINAL RESEARCH

Association Between Postpartum Depression and Synthetic Oxytocin Use for Postpartum Hemorrhage Prevention and Treatment

Postpartum Kanamanın Önlenmesi ve Tedavisinde Kullanılan Sentetik Oksitosinin Postpartum Depresyon ile İlişkisi

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ABSTRACT

Objective: *The aim of this study was to examine the relationship between postpartum synthetic oxytocin administration and the development of depressive and anxiety disorders after delivery.*

Material and Methods: *We hypothesized that women exposed to postpartum exogenous oxytocin would have a reduced risk of postpartum depressive and anxiety disorders compared with those without exposure. The cases were examined under two groups as "Oxytocin users" (n = 100) and "Control" (n = 100) groups . Oxytocin group was given introvenous oxytocin just after the delivery for postpartum hemorrhage prevention and treatment. Questionnaires of depression and maternal anxiety were performed at the sixth week after the delivery.*

Results: *The incidence of depression (4%) in the oxytocin group was significantly lower than the control group (14%) (p: 0.026, p <0.05). Patients who do not use oxytocin have a 3.9-fold greater risk of developing depression. We identified a relationship between using oxytocin for postpartum hemorragie and decreased postpartum depressive symptoms.*

Conclusion: *Our findings suggest using exogenous oxytocin may contribute to postpartum symptoms of depression and anxiety among women. Future research should watch the longitudinal role of exogenous oxytocin in maternal mood and anxiety, the safety of high-dose long-term use of oxytocin.*

Keywords: *postpartum depression, oxytocin, maternal behavio*

ÖZET

Amaç: *Doğum sonrası depresyon (PPD), en sık görülen doğum sonrası psikiyatrik bozukluktur. Oksitosin (OT), nöropsikiyatrik durumlar hakkında olası bir teşhis ve tedavi aracı olarak dikkat çekmiştir. Son zamanlarda, çalışmalar eksojen oksitosin uygulamalarının maternal beyin yanıtındaki rolünü incelemeye başlamıştır. Bu çalışmanın amacı postpartum sentetik oksitosin uygulaması ile doğum sonrası depresif ve anksiyete bozuklukları arasındaki ilişkiyi incelemektir.*

Gereç ve Yöntemler: *Postpartum ekzojen oksitosine maruz kalan kadınların, postpartum depresif ve anksiyete bozukluğu riskinin maruz kalmayanlara kıyasla daha düşük olacağı varsayılmıştır. Olgular "Oksitosin kullanılan" (n = 100) ve "Kontrol" (n = 100) grupları olmak üzere iki grup altında incelenmiştir. Oksitosin grubuna postpartum kanamanın önlenmesi ve tedavisi için doğumdan hemen sonra intravenöz oksitosin verildi. Doğum sonrası altıncı haftada depresyon ve maternal anksiyete anketleri yapıldı.*

Bulgular: *Oksitosin grubunda depresyon insidansı (% 4) kontrol grubundan (% 14) anlamlı derecede düşüktü (p: 0.026, p <0.05). Oksitosin kullanmayan hastalarda depresyon gelişme riski 3.9 kat daha fazla bulundu. Postpartum kanama için oksitosin kullanımı ile postpartum depresyon semptomlarının azalması arasında bir ilişki saptadık.*

Sonuç: *Bulgularımız ekzojen OT kullanılmasının kadınlarda doğum sonrası depresyon ve anksiyete semptomlarına katkıda bulunabileceğini göstermektedir. Daha fazla sayıda çalışma ile ekzojen oksitosinin maternal ruh hali ve kaygı üzerindeki uzun dönem sonuçları ve yüksek dozda uzun süreli OT kullanımının güvenilirliği araştırılmalıdır.*

Anahtar Kelimeler: *postpartum depresyon, oksitosin, maternal davranış*

INTRODUCTION

Maternal postpartum depression (PPD), is defined as the presence of a major depressive episode following childbirth, affecting ap- proximately 15% of women in industrial societies, (1) exerts long-term negative impact on children, includ- ing greater propensity to psychopathology, diminished emotio nal and behavioral regulation, lower social com- petencies and academic achievement, and disrupted stress response. (2) The International Classification of Dis- eases (ICD)-10 classifies depression “as associated with the puerperium” if the onset is within 6 weeks postpartum (3).

Common symptoms include depressed mood, loss of interest and energy, changes in sleep or eating patterns, diminished ability to think or concentrate, feelings of worthlessness, and recurrent suicidal ideations. While not currently a part of diagnostic criteria, anxiety is considered a prominent feature of PPD, present in approximately half of women diagnosed with PPD (4) In severe cases, PPD can be accompanied by psychotic features which may include delusions or command hallucinations to harm the infant (5).

The risk of PPD increases with a history of prenatal depression, prenatal anxiety, or PPD. (6). Despite negative impacts on both mother and child, the pathophysiology of postpartum depressive and anxiety disorders is poorly understood, with relatively few animal models (7) Due to its role in the modulation of social behavior, especially affiliative bonding, oxytocin has been identified as a potential mediator of postpartum depression and anxiety (8) Two clinical studies have found that low antepartum blood oxytocin levels are correlated with postpartum depression (9) and related work reports an association between prepartum depression and low oxytocin (10).

Oxytocin, a nine-amino-acid neuropeptide synthe- sized in the hypothalamus, provides the foundation for maternal–infant bonding and supports sociality, collaboration, and prosocial behavior in mammals (11).

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Studies have recently begun to examine the role of exogenous OT administrations in maternal brain responses. Intranasal administrations of OT were shown to increase the incentive salience of an unknown infant's laughter in a group of women, as evidenced by the enhanced connectiv- ity observed between the amygdala and emotion regulation regions (12).

Synthetic oxytocin has been used since the 1950's (13) and current indications for use include labor induction or augmentation and prevention or treatment of postpartum hemorrhage (14). Recent recommendations, including those from the World Health Organization, indicate the use synthetic oxytocin as the first line agent in the active management of the third stage of labor for hemorrhage prevention (15), and it is conceivable that most or all women giving birth will soon have some synthetic oxytocin exposure.

The objective of this study was to examine the relationship between postpartum synthetic oxytocin administration and the development of depressive and anxiety disorders after delivery. We hypothesized that women exposed to postpartum synthetic oxytocin would have a reduced risk of postpartum depressive and anxiety disorders compared with those without exposure.

MATERIAL AND METHOD

The study was carried out on a total of 200 female cases. This was an analysis of data from a clinical data repository of patients who delivered a single live born infant at Zeynep Kamil Eğitim ve Araştırma Hospital between April 2016-April 2018. In order to be eligible for this study, women had to be 18 years of age or over, and delivered a single infant Women were excluded from the sample if they delivered preterm (before 36 weeks of gestation) and their infants were admitted to neonatal intensive care. those who had been diagnosed with depression before birth were excluded.

An additional inclusion criterion was the ability to respond to questionnaires in turkish.

Oxytocin group was given introvenous oxytocin just after the delivery.indication of exposure to synthetic oxytocin was for postpartum hemorrhage prevention and treatment.Questionnaires were performed at the sixth week after the delivery. Demographic characteristics of the sample are shown in Table 1.

The cases were examined under two groups as "Oxytocin users" (n = 100) and "Control" (n = 100) groups. Depressive symptomatology was assessed using the Edinburgh Postnatal Depression Scale (EPDS).

The 10 items ask women to report on symptoms during the past 7 days. A score of 12 or higher has optimal sensitivity and specific- ity in relationship to a diagnosis of major depression.

Evalutation of parameters according to groups is shown in Table 2.

Table 1: Distributions of demographic characteristics.

		Min-Max	**Med±SS**	**Median**
Age		18-41	29,25±5,64	29
Gravida		1-6	2,85±1,12	3
Parity		0-5	1,49±0,95	1
Abortion		0-4	0,28±0,58	0
Number of siblings		1-16	4,97±2,32	4
Monthly Income (tl)		800-6000	2069,5 ± 907,89	2000
Beck score		0-16	6,63±3,95	6,5
Edinburg score		0-17	6,53±3,69	6
		n	**%**	
Curretage	Yes	11	5,5	
	No	189	94,5	
Ectopic pregnancy	Yes	9	4,5	
	no	191	95,5	
Family type	nuclear	155	77,5	
	Extended	45	22,5	
Working status	Yes	23	11,5	
	No	177	88,5	
Depresyon	Yes	18	9,0	
	No	182	91,0	

STATISTICAL ANALYSIS

When evaluating the findings obtained in this study, IBM SPSS Statistics 22 for statistical analysis (SPSS IBM, Turkey) programs were used. When the study data were evaluated, the normal distribution fitness of the parameters was assessed by the Shapiro Wilks test and the parameters were not normally distributed.

The Mann Whitney U test was used to compare the two statistical methods (mean, standard deviation, frequency) as well as the quantitative comparison of the parameters in the study. Chi-square test, Fisher's Exact Chi-square test and Continuity (Yates) correction were used for the comparison of qualitative data. The risk calculation for the meaningful parameter was done. Significance was assessed at $p < 0.05$ level.

Table 2: Evaluation of parameters according to groups.

		Oksitosin	Control	[1]p
		Ort±SS (median)	Ort±SS (median)	
Age		29,14±5,55 (29)	29,36±5,74 (30)	0,787
Gravidy		2,82±1,1 (3)	2,87±1,14 (3)	0,803
Parity		1,46±0,95 (1)	1,51±0,96 (1)	0,581
Abortion		0,26±0,6 (0)	0,29±0,57 (0)	0,602
Number of siblings		5,05±2,13 (5)	4,89±2,5 (4)	0,371
Monthly income (tl)		2032,5±848,9 (2000)	2106,5±966,16 (2000)	0,686
Beck score		6,02±3,72 (6)	7,24±4,1 (7)	0,053
Edinburg score		5,49±3,11 (5)	7,57±3,93 (8)	0,000*
		n (%)	n (%)	
Curretage	yes	7 (%7)	4 (%4)	[2]0,535
	no	93 (%93)	96 (%96)	
Ectopic pregnancy	Yes	5 (%)	4 (%4)	[3]1,000
	no	95 (%95)	96 (%96)	
Family type	Nuclear	76 (%76)	79 (%79)	[4]0,611
	Exten-ded	24 (%24)	21 (%21)	
Working status	yes	12 (%12)	11 (%11)	[2]1,000
	No	88 (%88)	89 (%89)	
Depression	Var	4 (%4)	14 (%14)	[2]0,026*
	Yok	96 (%96)	86 (%86)	
Beck score	Mini-mal	81 (%81)	70 (%70)	[2]0,100
	mild	19 (%19)	30 (%30)	

[1] Mann Whitney U Test [2] Continuity (yates) düzeltmesi
*[3] Fisher's Exact Test [4] Ki-kare test *p<0.05*

RESULTS

There was no statistically significant difference in age, gravida, parity, abortion, number of siblings and monthly income between oxytocin and control groups (p> 0.05).

Although the Beck score average of the oxytocin group was lower than the control group, this difference was close to meaningfulness but not statistically significant (p> 0.05).

The Edinburgh score average of the oxytocin group was statistically significantly lower than the control group (p: 0.000, p <0.05).

There was no statistically significant difference between the groups in terms of abortion, ectopic pregnancy, family type, working status and home knowledge (p> 0.05).

There was no statistically significant difference in age, gravida, parity, abortion, number of siblings and monthly income among depressed and unexplained cases (p> 0.05).

The mean Beck and Edinburg scores of depressed cases were found to be statistically significantly higher than the cases without depression (p: 0.000, p <0.05).

There was no statistically significant difference between the cases with and without depression in terms of abortion, ectopic pregnancy, family type, working status and home knowledge (p> 0.05).

Evaluation of parameters according to depression is shown in Table 3.

Table 3: Evaluation of parameters according to depression.

		Depression (n=18)	No depression (n=182)	[1]p
		med±SS (median)	med±SS (median)	
Age		30,78±4,82 (31)	29,1±5,7 (29)	0,219
Gravida		2,94±0,94 (3)	2,84±1,13 (3)	0,505
Parity		1,72±0,83 (2)	1,46±0,96 (1)	0,100
Abortion		0,11±0,32 (0)	0,29±0,6 (0)	0,213
Number of sibligns		4,28±1,84 (4)	5,04±2,35 (5)	0,158
Monthly income (tl)		2005,56±686,4 (2000)	2075,82±928,19 (2000)	0,976
Beck score		10,44±3,97 (10,5)	6,25±3,75 (6)	0,000*
Edinburg score		14,06±1,43 (14)	5,79±2,93 (6)	0,000*
		n (%)	n (%)	
Curretage	Yes	1 (%5,6)	10 (%5,5)	[3]1,000
	No	17 (%94,4)	172 (%94,5)	
Ectopic pregnancy	yes	1 (%5,6)	8 (%4,4)	[3]0,850
	no	17 (%94,4)	174 (%95,6)	
Family type	Nuclear	13 (%72,2)	142 (%78)	[3]0,561
	exten-ded	5 (%27,8)	40 (%22)	
Working status	Yes	4 (%22,2)	19 (%10,4)	[3]0,135
	no	14 (%77,8)	163 (%89,6)	

[1] Mann Whitney U Test [2] Continuity (yates) düzeltmesi
*[3] Fisher's Exact Test [4] Ki-kare test *p<0.05*

The incidence of depression (4%) in the oxytocin group was significantly lower than the control group (14%) (p: 0.026, p <0.05). Patients who do not use oxytocin have a 3.9-fold greater risk of developing depression (Odds Ratio: 3.907, 95% CI: 1.239-12.323).

Risk of developing postpartum depression according to groups is shown in Figure 1.

There was no statistically significant difference in depression levels between the groups (p> 0.05). Minor depression was observed in 81% of cases and slight depression was observed in 19% of cases using oxytocin. Minor depression was seen in 70% of cases and mild depression in 30% of cases.

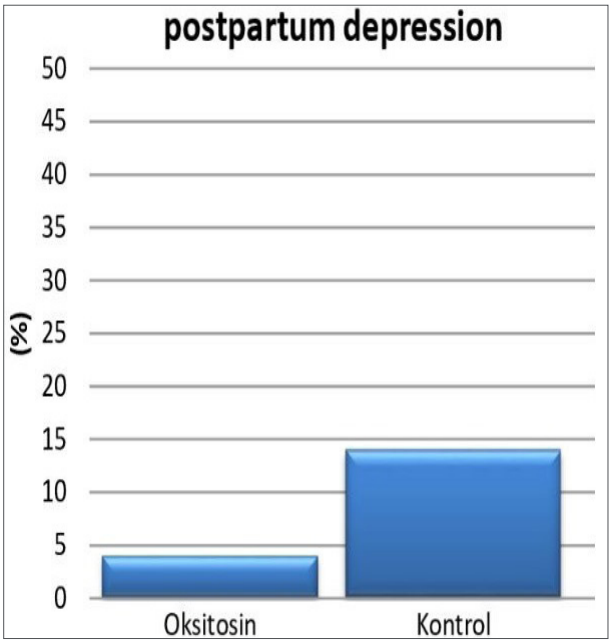

Figure 1: Risk of developing postpartum depression among the groups.

DISCUSSION

The literature on the role of exogenous oxytocin administration after the delivery results are conflicting. Several studies have examined the relationship between maternal plasma oxytocin and depressive symptomology (10, 16, 17) found that low oxytocin during pregnancy is associated with increased depressive symptoms and thus suggest that administering exogenous oxytocin, such as the synthetic oxytocin Pitocin, may alleviate or prevent negative postpartum mood. Another study found lower oxytocin levels during breastfeeding at 8 weeks postpartum in women with depressive symptoms compared to asymptomatic women (16). One recent study, found that the dose of synthetic oxytocin given during the labor and delivery (as determined retroactively from hospital charts) was positively correlated with both endogenous levels of oxytocin and depressive symptoms at 2 months postpartum (18), similar to the results from intravenous dosing.

PPD patients are different from each other inthe way of endogenous OT production,variability in OT receptor .so we can undertand the channges on the respons between the patients. Such results may not be apparent and may even be obscured in between-group designs, where effects are averaged across individuals and within-group indi- vidual differences are overlooked (19) Given the pattern of results reviewed, it is possible that exogenous OT may yield beneficial effects in PPD patients.

Our study was carried out on a total of 200 female cases. The cases were examined under two groups as "Oxytocin users" (n = 100) and "Control" (n = 100) groups. Oxytocin group was given introvenous oxytocin just after the delivery.indication of exposure to synthetic oxytocin was for postpartum hemorrhage prevention and treatment.

We found that the incidence of depression in the oxytocin group was significantly lower than the control group (p: 0.026, p <0.05). Patients who do not use oxytocin have a 3.9-fold greater risk of developing depression. We identified a relationship between using oxytocin for postpartum hemorragie and decreased postpartum depressive symptoms. Prior reports have identified lower prenatal oxytocin values as a risk factor for postpartum depressive symptoms (9).

In addition, the literature provides support that higher oxytocin values are related to positive postpartum maternal behaviors such as gaze, affect, touch, and vocalization during the first month postpartum (20).

In conclusion, our findings suggest using exogenous OT may contribute to postpartum symptoms of depression and anxiety among women.

Limitation of this study include; we couldn't measure the blood oxytocin level which is important to see the correlation between depression and oxytocin level.

We could watch the patients longer in terms of depression. As longitudinal data from the postpartum period may have provided a more complete understanding of the ways these factors are associated.

Future research should watch the longitudinal role of endogenous oxytocin in maternal mood and anxiety, the safety of high-dose long-term use of OT. It would be critical to understand that how should we use exogenous OT for treatment.They should research the women at high risk for depression and behavioral effects of exogenous peripartum oxytocin and may involve individual differences in the women with ppd.

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