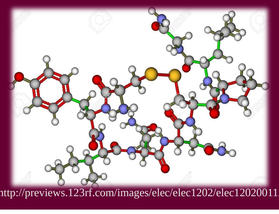

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High Plasma Oxytocin Levels Decrease Postpartum Depression Symptoms in Women Ages 25 - 45 Postnatal: A Literature Review

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INTRODUCTION[1]

Abstract

Background: Oxytocin is known for its capacity to alter social interactions and mother-infant bonding; as such, alterations in plasma level concentrations of this hormone are believed to be correlated with symptoms of postpartum depression (PPD). **Objective:** To assess the literature provided by such databases as Scopus, Pubmed, Medline, Ovid and Web of Science to investigate the association between oxytocin plasma levels and PPD in women in the postnatal period. **Methods:** The literature review was restricted to the following keywords: “oxytocin”, plasma oxytocin levels”, “postnatal depression”, “postpartum depression”, “oxytocin and postpartum depression”, and “oxytocin and maternal depression”. Articles selected were in English and experimental, consisting of prospective studies measuring plasma levels of oxytocin in participants, while also evaluating for severity of PPD symptoms using questionnaires such as the Edinburgh Postnatal Depression Scale (EPDS). **Results:** A total of 10 articles were reviewed. All 10 studies demonstrated a significant relationship between blood oxytocin concentrations and onset of PPD, as well as an association between fluctuations of this hormone and PPD symptom severity. **Conclusion:** The literature supports that plasma oxytocin levels significantly predict onset of depressive symptoms during the postpartum period. Further research is required to assess whether other factors—such as the hypothalamic–pituitary–adrenal (HPA) axis, or DNA methylation— in correlation with plasma oxytocin levels can produce similar outcomes in postnatal women.

Introduction

Postpartum depression is the most prevalent postnatal psychiatric disorder for women in the postpartum period, affecting between 10 to 15 % of all new mothers up to 6 months post delivery [1,2]. PPD is typically characterized by non-psychotic, depressive episodes that largely remain undetected due to the general public’s inability to accurately recognize symptoms, thus preventing affected women from seeking professional help [3]. For many, lack of diagnosis can be problematic as PPD symptomatology has been linked to marital and familial rifts, erosion of support networks provided by friends and family, episodes of depression in later life stages, and long-term negative social effects on children [3]. More specifically, in the postnatal period, PPD inhibits inherent emotional attachment between mother and offspring [4].

As a neuropeptide hormone, oxytocin is thought to play a vital role in mother-infant bonding by contributing to the development and maintenance of social affiliative behaviours in the mother [3]. Oxytocin is known for improving social behaviour by encouraging social engagement with others; it increases attention to, and accurate recognition of, salient social information [5]. Consequently, many believe fluctuations—specifically reductions—in plasma oxytocin concentrations might be a direct causal mechanism for PPD [2]. In light on this, the identification of a relationship between blood oxytocin levels and onset of PPD may be instrumental to the improvement of treatment modalities for those afflicted with this postnatal disorder. Thus, the purpose of this research is to investigate whether plasma levels of oxytocin are associated with postpartum depression in women in the postnatal period. A structured literature review including 14 scientific articles was undertaken in an attempt to answer this question.

Research Question

Are plasma levels of oxytocin associated with postpartum depression in women in the postnatal period?

METHODS[4]

Relevant studies were searched through the months of September to November 2016 with databases PubMed, Ovid, Lancet, University of Ottawa Library, Scopus and Gale CENGAGE Learning. MeSH terms used include: *oxytocin, plasma oxytocin levels, postpartum depression, perinatal, maternal depression, PPD, maternal women, obstetrics, maternal health, depression, postnatal depression, postpartum depression, patient, pregnancy, woman, obstet gynecol, mother, maternal behavior, low oxytocin, postpartum depression* and *postnatal psychiatric disorders.* Randomized Controlled Trials, Double-Blinded Randomized Controlled Trials, Cohort Studies, Systematic reviews, Meta-Analyses, Clinical Trials studies. Article that were fully accessible for free were reviewed for eligibility and relevance to the study topic. Studies were included in this literature review if they met the following criteria:

- All articles are peer-reviewed and in the English language
- Population studied in the article included women of all races between the ages of 25 to 45 years old including an equal number of women from all socio-economical background
- Studies included must explicitly state its aim to measure oxytocin levels in the population of interest
- Study had to have measured oxytocin levels before and after postpartum depression intervention
- Study had to have proper assessment of postpartum depression in mothers at the start of the study and at the end
- Outcome measured for study must be related to depressive symptomatology.

Studies were sought out individually by four students. After eliminating duplicate studies, totally gathering of articles yielded 25 studies. After carefully reviewing the studies and eliminating articles that did not support our inclusion criteria, total number of studies yielded 10.

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METHODS[3,4]

Table 1: Data Extraction Table

Author	Title	Design	Year	OT measurement	PPD measurement	Population	Result
(Bell et al., 2015)	Interaction between oxytocin receptor DNA methylation and genotype is associated with risk of postpartum depression in women without depression in pregnancy	case-control study	2015	Blood sampling	EPDS	14 541 pregnant women followed through to postnatal	There is a possibility that epigenetic variation can decrease the expression of the oxytocin receptor gene in a susceptible genotype thereby contributing to the onset of PPD.
(Clarici et al., 2015)	Intranasal administration of oxytocin in postnatal depression: implications for psychodynamic psychotherapy from a randomized double-blind pilot study	randomized double blinded study	2015	dose of intranasal oxytocin	(SWAP) scale; EPDS, ANPS, HRSD, EPDS	16 mothers from an obstetric ward, that meet > 4/13 of the inclusion criteria of Beck’s 2001 list for PPD	And increase in OT results in improvements of well-being allowing an opportunity to recognize and allow “interpersonal acceptance of the child … recogni[zing] … the child’s needs”
(Eapen et al., 2014)	Separation anxiety, attachment and inter-personal representations: Disentangling the role of oxytocin in the perinatal period	cross-sectional and longitudinal studies	2014	Blood samples	EPDS, STAI, ASA-27, MIBS MOPS questionnaires	127 women recruited during pregnancy from antenatal clinics	Demonstrated a link between lower oxytocin levels and depression anxiety suggesting reductions in plasma concentrations of this hormone could lead to PPD
(Jobst et al., 2016)	Oxytocin course over pregnancy and postpartum period and the association with postpartum depressive symptoms	Prospective study	2016	Blood samples	MADRS	100 pregnant women (35 week perinatal to 6 months postnatal	If MADRS scores ≥ 10, participants are labelled at risk of developing PPD were plasma oxytocin concentrations decreased from 38th week of gestation to the time of delivery (within 2 days postpartum) - Those not labelled as high risk demonstrated continuous increase in oxytocin plasma levels from pregnancy to the postpartum period. The administration of oxytocin to the mothers with a diagnosis of PPD did not increase maternal happiness.
(Mah, Van IJzendoorn, Smith, & Bakermans-Kranenburg, 2013)	Oxytocin in postnatally depressed mothers: its influence on mood and expressed emotion.	randomized, double-blind, placebo controlled	2013	Nasal spray intervention	EPNDS, Self - Assessment Manikin	25 postnatally depressed mothers with infants <1 year	
(Massey, Schuette, Pournajafi-Nazarloo, Wisner, & Carter, 2016)	Interaction of oxytocin level and past depression may predict postpartum depressive symptom severity	Prospective study	2016	Blood samples	MINI Version 5.0.0	66 healthy pregnant women	Women with higher plasma oxytocin concentrations in their third trimester had greater postpartum depression symptom severity especially in women with a history of MDD.
(Pratt et al., 2015)	Maternal Depression and Child Oxytocin Response Moderation By Maternal Oxytocin and Relational Behaviour	Cohort	2015	Blood samples		1983 women repeatedly assessed for depression (labour -6 years postnatal	There is an involvement of the OT system and can cause a vulnerability in children and the mother. Interventions can address the touch and contact between the mother and baby to induce dyadic effects. Medium or low OT was negatively impacted by maternal depression.
(Samuel et al., 2015)	Maternal Mental Health Moderates the Relationship Between Oxytocin and Interactive Behaviour	Case-control	2015	Blood sample	EPDS, GAD-7, GRS	110 women with high and low levels of depression and anxiety during pregnancy and postpartum	A significant interaction effect of mental health and OT on “non-depressive” interactive behavior was found, suggesting that maternal mental health moderated the relationship between OT levels and depressive interactive behaviors. Specifically, higher levels of OT were linked to less depressive behavior only in mothers with mood or anxiety disorder.
(Skrundz, Bolten, Nast, Hellhammer, & Meinlschmidt, 2011)	Plasma oxytocin concentration during pregnancy is associated with development of postpartum depression	Prospective study involving logistic regression analyses	2011	Blood samples	EPDS	100 women in third trimester followed through 2 week postpartum	Plasma oxytocin levels significantly predict symptom onset of depressive symptoms during the postpartum period. Low levels render women difficulties with obtaining maternal bonding behaviours.
(Zelkowitz et al., 2014)	Psychosocial stress moderates the relationships between oxytocin, perinatal depression, and maternal behavior	longitudinal study RCT	2014	Blood samples	self-report questionnaire assessing symptoms of depression	287 women followed from at 12 weeks of gestation to 9 weeks postpartum	Endogenous OT may act as a buffer against the effects of stress thereby protecting high risk women from developing depressive symptoms and promoting more sensitive maternal interactive behavior

Legend: PPD: Postpartum Depression; EPDS: Edinburgh Postnatal Depression Scale; STAI: State and Trait Anxiety Inventory; ASQ: Attachment Style Questionnaire; ASA-27: Anxiety Questionnaire; MIBS: Mother-to-Infant Bonding Scale; MOPS: Measure of Parental Style ; MINI: Mini International Neuropsychiatric Interview; MDD: Major Depression Disorders; MADRA: Montgomery-Asterg Depression Rating Scale; ASQ: Attachment Style Questionnaire; GAD-7: Generalized Anxiety Disorder Seven-time scale; GRS: Global Rating Scalesz ; SWAP: Shedler–Westen Assessment Procedure scale; ANPS: Affective Neuroscience Personality Scale ; HRSD: Hamilton Rating Scale for Depression

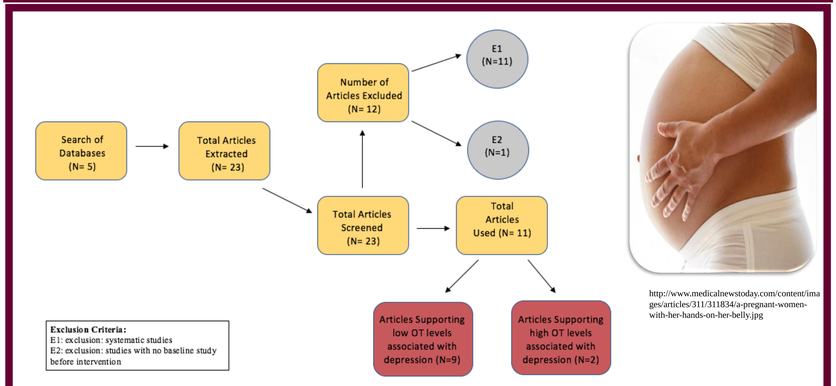

Figure 1. Flow Chart Diagram Describing the Data Selection and Reviewed Literature Process Conducted

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RESULTS[1, 2, 3]

A total 23 articles selected from multiple databases were analyzed. Due to exclusion criteria, there was an emphasis on articles which did not include literature and systematic reviews and studies which did not incorporate a baseline study before intervention. As a result, a total of ten studies were determined to be relevant to the study of PPD and oxytocin levels. Multiple intervention methods among these studies included: RCT’s, longitudinal studies, cohort studies, prospective studies, case-control studies and in person interviews.

Within the RCT studies, Zelkowitz et al. described a negative correlation between high plasma levels of oxytocin and a decrease in depressive symptoms. It was suggested that due to the high levels of oxytocin levels, women experienced fewer depressive symptoms and greater maternal sensitivity. Another RCT study performed by Mah et al. concluded otherwise; the study implied that women who were given the placebo experienced less depressive symptoms as opposed to the group who received oxytocin. The group administered oxytocin experienced greater depressive symptoms, however, this can be a biased conclusion as the measure of depression was defined by the feeling of sadness or happiness and not the psychological and physiological effects experienced by the hormone. Among the longitudinal studies, all experiments performed by Eapen et al., Zelkowitz et al. and Samuel et al. described the inversely proportional relationship between high depressive symptoms and low oxytocin levels. According to Eapen et al. and Gold et al., a high plasma level of oxytocin levels led to a decrease in depressive symptoms among mothers. Additionally, Samuel et al., further explained that although lower levels of oxytocin can lead to PPD, high levels of the hormone has the ability to reduce PPD in mothers experiencing mood and anxiety disorders. Prospective studies conducted by Jobst et al. reiterated a positive association between oxytocin plasma levels and maternal depressive behaviour, whereby the lower the oxytocin level was, the higher the depression and impaired emotional bonding between the mother and infant. Skrundz et al. further emphasized this finding with another prospective study describing the negative correlation while using a scale whereby any score ten and above was considered a PPD diagnosis and any score below ten was considered non depressive. A cohort study as well as case control study conducted by Pratt et al., and Bell et al., respectively reiterated the inversely proportional relationship between oxytocin and PPD, claiming higher oxytocin levels to act as a buffer to PPD. Bell et al. further explains this phenomena with the a study of DNA methylation whereby the greater the DNA methylation of oxytocin receptors (OXTR) were, the greater the risk of PPD. The last type of intervention study analyzed included an in person interview. The result of this study by Clarici et al. claimed PPD was a result of a higher levels of oxytocin, thus introducing a bias and a contradiction. As the study was subjective to the subjects, this could have possibly introduced an interview bias. In addition, it was described that the onset for PPD was higher when higher oxytocin levels were present in those who previously experienced major depressive disorder. Otherwise, the high oxytocin levels did not influence PPD positively. All in all, eight out of the ten articles (disregarding the two articles with bias) explained the negative correlation between oxytocin and PPD, whereby the higher the plasma levels of oxytocin led to a decrease in the onset of PPD.

CONCLUSION & DISCUSSION[1, 2, 3, 4]

Overall, our findings illustrate the existence of a relationship between plasma levels of oxytocin and the presence of PPD within mothers. Low levels of oxytocin are found to increase the onset of PPD; higher levels of the hormone, however, create a buffering effect against the evolution of PPD. When experiencing mood disorders, anxiety or major depressive disorders, subjects were found susceptible to developing PPD when oxytocin levels were lower. It is recognized in the field of obstetrics and gynecology that oxytocin is a hormone that assists with child labour and creating the mother-child bond postnatal. One can therefore infer that the existence of maternal depression after childbirth is related to poor bonding between the child and their mother. For this reason, the results obtained from this literature review were not surprising as the majority of the results obtained from the articles used demonstrated an inverse relationship between oxytocin levels and PPD.

This literature review contains many limitations that may have affected the outcome of this study. Our findings may have been subject to certain biases such as confirmation bias, as articles were selected to support a relation between low oxytocin levels and PPD. Furthermore, separation anxiety (Eapen et al., 2014) and prior history of depression (Massey et al., 2016) in study participants may have be confounding factors that cause the correlation thereby solidifying positive findings, while possibly falsifying the observed causal mechanism between these two variables. Selection bias with regards to the demographic of populations chosen in each study was not accounted for. For this reason, the results of the study may not universally apply to all women. In addition, the “postnatal state” of study populations was not clearly defined as part of our selection criteria. Consequently, some of the studies evaluated oxytocin concentrations while participants were still pregnant (Eapen et al., 2014), (Massey et al., 2016), (Jobst et al., 2016), (Skrundz et al., 2011). However, many of those studies gathered experimental data up to 6 months post-delivery (Jobst et al., 2016). The exclusion of research articles that were not written in the English language as well has the exclusion of articles that required a fee for access to the full text limits our research findings. To add, a limited time frame affected the number of articles chosen, leading to a smaller sample size and neglecting other articles that were accessible and contained stronger results which could have strengthened the outcome deduced by this review.

Recommendations for future research in regards to the association between oxytocin levels and PPD involves doing more research on this association, as information on this topic is limited. Furthermore, the method of intervention advised for future studies should focus primarily on using RCT studies and longitudinal studies. Further recommendations involve primarily focusing on women post-delivery, since a few of the studies retrieved for the literature review were done on women were currently pregnant. There should be a trial demonstrating the differences between oxytocin which are present naturally in the body compared to receiving an intranasal administration of oxytocin. This would be helpful to determine how reliable it is to receive oxytocin externally and how oxytocin behaves when present naturally in the body, which may demonstrate differing effects. Additionally, the determination of safe amounts of oxytocin administration to women should be determined to enhance clinical practice. Understanding the prevalence of postpartum depression in women of different races and demographics as well as determining early detection and prevention methods can assist physicians and health care professional to treating women in a more effective manor rather than waiting for observed evidence of PPD that can affect the health outcome of the child.

Information gathered by this literature review enables us to conclude that there exists an association with plasma oxytocin levels and onset of postpartum depression in women in the postnatal period. All 10 studies provide unanimous evidence supporting the inverse causal relationship between blood oxytocin concentrations and symptom severity of PPD; as the former lowers, the latter becomes greater. As a result, further research should be devoted to investigating the causal mechanism of hormonal variations in oxytocin as a potentially preventative measure for the onset of PPD. In this vein, future studies should expand on the effects of oxytocin in correlation with HPA axis, DNA methylation, and other variables that put women in both perinatal and postnatal periods at greater risk of developing PPD.