ORIGINAL RESEARCH

Pina Bozzo BSc¹
Thomas R Einarson PhD^{1,2}
Gideon Koren MD¹
Adrienne Einarson RN¹

¹ The Motherisk Program, The Hospital for Sick Children, Toronto, Canada

² The Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Canada

Nausea and vomiting of pregnancy (NVP) and depression: cause or effect?

Abstract

Background: Both nausea and vomiting and depression are common conditions affecting women during pregnancy. Several studies have linked depression with nausea and vomiting of pregnancy (NVP); however, researchers were unable to determine whether depression was caused by NVP or by a pre-existing condition.

Objective: To determine whether NVP is associated with depression in women with no history of depression prior to pregnancy.

Study design and methods: This was a prospective, observational, longitudinal study. Women with no diagnosis of depression who contacted The Motherisk Program prior to becoming pregnant or were at <6 weeks gestation were enrolled in the study. Each woman was interviewed at 8, 11, 18, 30 weeks gestation and at 6-18 weeks post-partum. At each interview, we administered the EPDS, Wellbeing and PUQE questionnaires and analyzed the data for correlation between depression and NVP.

Results: Data were analyzed obtained from 57 women. There were five EPDS scores ≥ 13 (one at baseline and two each at weeks 8 and 11) considered indicative of depression and 11 cases with PUQE scores ≥ 7 , indicative of moderate-high severity of NVP. We did not find an association between high PUQE scores and high EPDS scores and conversely, there was no relationship between high EPDS scores and high PUQE scores.

Conclusion: No association between depressive symptoms and NVP was observed; however, our sample size was very small and further studies could be done with a larger population of pregnant women.

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Correspondence to:
Adrienne Einarson
The Motherisk Program
Division of Clinical Pharmacology
The Hospital for Sick Children
555 University Avenue
Toronto, Ontario, M5G 1X8
E-mail: cinarson@sickkids.ca

Nausea and vomiting of pregnancy (NVP) is the most common medical condition of pregnancy, affecting an estimated 50-90% of all women [1,2]. Depression is also common during gestation, affecting approximately 10-15% of women [3]. There have been several studies examining the relationship between NVP and depression [4-8]; however, the authors were not able to establish if depression preceded or resulted from the symptoms of NVP. In a preliminary study by our group, depression and treatment with antidepressants prior to and during early pregnancy were not associated with the occurrence of NVP; however, the severity of neither NVP nor depression were examined at that time [9]. It has also been established that prenatal depression is a predictor for postpartum depression, which occurs in approximately 13% of women [10-13]; however, it has not been examined whether depression associated with NVP is a predictor for postpartum depression.

Thus, it remains uncertain whether there is a cause or effect between NVP and depression. All of the above studies had limitations and used different instruments to measure NVP as well as different tools to measure depressive symptoms. In addition, none of the women was enrolled prospectively, to rule out if there was underlying depression prior to pregnancy.

The objective of this current study was therefore to determine whether depression is associated with symptoms of NVP, using tools specifically designed and validated for use in pregnancy.

Methods

The Motherisk Program is a counseling service located at the Hospital for Sick Children in Toronto, where information on the safety and risks of exposures to prescription and over-the-counter (OTC) medications, natural health products, chemicals, radiation, and infectious diseases during pregnancy and breastfeeding is provided for women and healthcare professionals. An observational study was conducted involving women with no prior diagnosis of depression who contacted The Motherisk program. For each woman, an intake form was completed, which documented obstetric and medical histories, including medications taken and other exposures. For this study, the Motherisk counselor receiving the call identified women who did not have a history of depression or any other psychiatric conditions, was planning a pregnancy or was <6 weeks pregnant, which would be prior to the advent of NVP. Participants who had been exposed to a teratogen, or had serious medical conditions such as lupus, rheumatoid arthritis, epilepsy or MS and had sufficient English language skills, were excluded from the study. Women who agreed to participate in the study were connected with the study coordinator, who ex-

plained the details of the study and obtained verbal consent to participate.

Participants who were not yet pregnant were asked to telephone the coordinator when they were 8 weeks pregnant. In addition, they were given the option to be contacted at intervals of their choice (e.g., every 3 months), via email or telephone, to remind them to contact the coordinator once a pregnancy was confirmed. Each study participant was interviewed six times; at enrollment and subsequently at 8, 11, 18, and 30 weeks gestation, with the final interview at approximately 6-18 weeks post partum.

Together with documenting obstetrical and any other pertinent details, the Edinburgh Postnatal Depression Scale (EPDS) was administered during each interview. This tool was designed and validated to evaluate post-partum depressive symptoms and later validated for use in pregnant women [14]. Women who scored ≥ 13 prior to pregnancy were excluded from the study, and those who scored ≥ 13 at any time were asked for permission for us to contact their physicians, to make them aware of their patients' depressive symptoms, so they could institute treatment if necessary.

Details of NVP were also collected using the Pregnancy Unique Quantification of Emesis Scoring System (PUQE), which has been validated for measuring the severity of NVP [15]. Women were also asked to rate their overall wellbeing on a scale from 0 (the worst possible) to 10 (the best possible).

EPDS, PUQE and wellbeing scales were summarized at each time point using descriptive statistics, including mean, standard deviation, median, minimum and maximum scores. Scores were then dichotomized as above or below the cutoff point for moderate symptomatology and Fisher's Exact test was used to determine if any relationships existed between scores from the different scales.

This study received ethics approval from the Research board at the Hospital for Sick Children in Toronto, Canada.

Results

Consent to participate in the study was obtained from 80 women. Two women were excluded because they scored >12 on the EPDS prior to pregnancy and were referred to their physician. One woman was planning pregnancy when she was recruited; however, she did not contact us sufficiently early in her pregnancy and was excluded. Three women did not complete all the required interviews, and withdrew from the study following the first ($n=2$) and third interview ($n=1$). Two women had not become pregnant by the time of analysis and

TABLE. Summary of the scores obtained (N= 57 women).

Scale	Statistic	<6 weeks pregnant	8 weeks	11 weeks	18 weeks	30 weeks	Postpartum
EPDS*	Mean	3.3	4.0	3.5	2.5	2.9	3.2
	SD†	2.9	3.4	3.4	2.5	3.0	3.0
	Median	2	4	3	2	2	3
	Minimum	0	0	0	0	0	0
	Maximum	13	15	18	11	12	14
PUQE‡	Mean		5.1	4.9	3.6	3.4	
	SD†		1.9	2.1	1.4	1.0	
	Median		5	4	3	3	
	Minimum		3	3	3	3	
	Maximum		11	12	9	8	
Wellbeing§	Mean		7.4	7.6	8.6	8.1	
	SD†		1.6	1.6	1.2	1.1	
	Median		8	8	9	8	
	Minimum		3	3	3	4	
	Maximum		10	10	10	10	

*Edinburgh Postnatal Depression Scale (minimum =0, maximum = 30)

†Standard deviation

‡Pregnancy Unique Quantification of Emesis and Nausea Scale (minimum = 3, maximum = 15)

§General wellbeing as measured on an 11-point scale; 0=worst possible, 10=best possible

15 women miscarried. The remaining 57, who completed all six follow-ups, were included in the study (see Table).

When scores were classified as above or below the cutoff indicative of moderate–severe symptomatology (i.e., ≥ 7 on the PUQE and ≥ 13 on the EPDS), there was no correlation between scores at 8 weeks (Fisher's Exact $P=0.175$ for both).

As expected, PUQE scores were highest at weeks 8 and 11, although Wellbeing scores were constant over time. High scores on the EPDS and PUQE scales were examined and there were only five EPDS scores ≥ 13 , which would be considered indicative of depression (one at baseline and two each at weeks 8 and 11) and eleven high PUQE scores ≥ 7 , indicative of moderate-severe NVP. No association was seen between high PUQE scores and EPDS scores or, conversely, a relationship between high EPDS scores and high PUQE scores.

Discussion

To our knowledge, this is the first study to be conducted prospectively, beginning prior to pregnancy until and including the post partum period, attempting to find an association with NVP and depression, using questionnaires specifically designed and validated to measure both NVP and depression in pregnancy. Several published studies have linked NVP with depression. Kitamura and colleagues [4] administered a set of questionnaires in order to examine the severity of NVP and Zung's

Self Rating Depression Score to 1329 women who were attending a prenatal clinic. They observed that women in the depressed group had a significantly higher mean score of NVP than the comparison group [4]. Chou and coworkers⁵ examined the relationship between psychosocial factors and incidence of NVP in 113 women. They used the 20-item Center for Epidemiologic Studies Depression Scale (CES-D) to measure depressive symptoms and a checklist to examine the frequency of occurrence of NVP (occasional, frequent or absent) to establish NVP. They concluded that pregnant women without NVP had significantly lower CES-D scores than did women with frequent NVP, suggesting that depressive symptoms were positively correlated with NVP [5].

To measure psychiatric morbidity, Swallow and colleagues [6] evaluated 273 women using the General Health Questionnaire (GHQ), and to measure mood and illness perception, using visual analogue scales. These scores were compared with the scores of incidence and severity of NVP, which had been measured using the NVP instrument. They determined that high GHQ scores were associated with severe NVP [6]. Andersson and associates used the Primary Care Evaluation of Mental Disorders system for screening of depressive and anxiety disorders in 1495 women diagnosed with antenatal depression and anxiety. They concluded that women with a psychiatric diagnosis suffered from more NVP than did women with no psychiatric diagnosis [7]. Finally, Koken and

colleagues examined anxiety and depression in 230 pregnant women using the Hospital Anxiety and Depression Scale. These results were compared to the total Rhodes scale score, and they found that there was an association with anxiety and depression during early pregnancy and severity of NVP [8]. Thus, there appears to be a correlation between NVP and depression. The main limitation of the above studies is they did not examine this relationship prospectively; therefore, were not able to establish if depression preceded or resulted from symptoms of NVP.

In this study, an association between high PUQE scores and high EPDS scores was not evident, although high PUQE scores were associated with low Wellbeing scores. While several of the questions on the EPDS scales measure somatic symptoms, which were similar to some of the Wellbeing questions, an association was not observed between these two scores. In addition, the woman who scored highest on the EPDS scale (18) scored 4 on the PUQE scale, and the woman who scored the highest on the PUQE scale 12 scored 2 on the EPDS scale. There was one woman who scored 13 on 2 occasions, at 8 and 11 weeks, and at both time points, her PUQE scores were 7. Subsequently, she was treated for depression in the postpartum period. These findings suggest that she may have been suffering from an unidentified depression, which was not related to her symptoms of NVP.

The main limitation of our present study was that few of the women had severe nausea, with most cases reported as mild. A far larger sample size would be required to be able to follow enough women to include individuals suffering from more severe NVP, and therefore to allow a satisfactory comparison between high EPDS scores and high PUQE scores. Nevertheless, we have demonstrated a rigorous method for conducting such a study and other researchers could use this approach to conduct a similar study.

Conclusion

We were not able to separate the cause or effect of NVP and depression during pregnancy in this pilot study. However, with this study design, using these instruments of measurement and with a larger sample of women, it may be possible for further exploration of this important clinical question.

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