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# Relationship between vitamin use, smoking, and nausea and vomiting of pregnancy

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**Background.** Nausea and vomiting in pregnancy (NVP) is a common complaint but risk factors for NVP are not well characterized.

**Methods.** Occurrence of NVP was studied by questionnaires given to pregnant women at their first visit to the antenatal care unit and were returned around gestational week 28.

**Results.** Analysis of 3675 completed questionnaires was made. Nausea and vomiting in pregnancy was reported by 79% of the women, approximately half of which had been vomiting. Various therapies (drugs, acupuncture, acupressure) were tried by 18% of the women with NVP, of which the majority used drugs, most notably antihistamines (specifically meclizine). Hospitalization occurred in 1% of all women. Nausea and vomiting in pregnancy caused 28% of all sick-leaves during the first 28 weeks of pregnancy. Low maternal age and parity 1+ independently increased the risk for NVP. Smoking before pregnancy and using vitamins in early pregnancy were associated with a decreased risk for NVP. Women working outside the home had a lower rate of NVP than housewives and women out of work.

**Conclusions.** Nausea and vomiting in pregnancy is a common complaint with a significant impact on leave of absence from work. The study identifies a number of factors that are related to the occurrence of NVP and that may give hints on the etiology of the condition.

**Key words:** drugs; epidemiology; nausea and vomiting in pregnancy; smoking; vitamins

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The majority of pregnant women experience nausea and vomiting of pregnancy (NVP). The etiology of the condition is debated (1) but products from the early chorionic villi are probably of importance for the condition. Prostaglandin E<sub>2</sub> production correlates with the appearance of NVP (2); other factors like human chorionic gonadotrophin have also been discussed (3). Detailed descriptive studies on the occurrence and strength of NVP are available [e.g. (4)]. A protective effect of smoking has been seen in an analysis based on a detailed study of 363 women (5).

The purpose of the study was to investigate the prevalence of and certain risk factors for NVP, the treatments used, the association between the work situation of the woman and NVP, and the impact of NVP on sick leave from work.

## Materials and methods

A prospective study of NVP in the southern province of Sweden (Skåne) was undertaken. Data collection started in June 1999 and was supposed to continue for 1 year but a few late incoming questionnaires were accepted and the last case had been recorded in December 2000. Women who attended the antenatal care centers in Skåne were given a short questionnaire and were asked to complete and return it at their visit around gestational week 28 when routine glucose tolerance tests are performed. The content of the questionnaire is shown in Table I.

Questionnaires were obtained from 4041 women but some lacked identity numbers. This file was linked with the Medical Birth Registry, a

Table I. Content of questionnaire used

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Personal identification number in order to permit matching.  
 Date of first attendance to the antenatal care center.  
 Did you use vitamin tablets the weeks before this pregnancy?  
 Did you use vitamin tablets the first two months after getting pregnant?  
 Did you smoke the month before you got pregnant? No, < 10 cigarettes/day, 10 cigarettes per day or more.  
 Have you had nausea/vomited during pregnancy? Yes, No  
 If yes:  
   Had nausea but not vomited? If yes, how many weeks?  
   Had nausea and vomited a few times? If yes, how many weeks?  
   Daily vomiting? If yes, how many weeks?  
 Have you been away from work because of nausea and vomiting? If so, how many days?  
 How many days have you in total been away from work because of disease before week 28?  
 Have you been hospitalized because of nausea and vomiting?  
 Have you used any drugs for nausea and vomiting? If yes, which type?  
 Have you had acupuncture for the problems?  
 Have you used acupressure for the problems?

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computerized register of practically all women who give birth in Sweden, and to a local register of delivery outcome (PRS, Perinatal Revision Syd). In this way, the following variables were obtained: singleton or twin delivery, birth weight, gestational duration, infant sex, and maternal smoking in early pregnancy (at the first visit to the antenatal care center).

Linkage was possible for 3675 women (91%). The majority of the women were delivered in one of the hospitals in Skåne, but approximately 4% were delivered outside the region. It was difficult to estimate how such a large percentage of the women who had attended the antenatal care centers during the study period had actually completed the questionnaire. The number of deliveries in Skåne during the year 2000 was 12 178, which indicates that approximately 30% of the women participated and returned questionnaires that could be linked to the Medical Birth Registry.

The recorded variables are described herein and an analysis of risk factors for NVP is presented. A Mantel-Haenszel analysis was performed with NVP as outcome and analyzing maternal age, parity, smoking habits, working situation, vitamin use, and smoking before pregnancy as risk factors. Each factor will be studied after adjustment for the other factors. Risks were expressed as odds ratios (OR). Ninety-five percentage confidence intervals (95%CI) using Miettinen's method.

The study was approved by the local Ethics Committee.

## Results

### *Presence of NVP*

Among the 3675 women, 2906 reported NVP (79%) and 769 stated that they had no NVP.

Among the former, 57 did not specify their problems, 1443 had only nausea, 938 reported occasional vomiting, and 468 daily vomiting. The average total length of reported problems (irrespective of type) was 9.2 weeks: 2.8 weeks when the woman did not specify her complaints, 8.2 weeks with only nausea, 9.5 weeks with occasional vomiting, and 12.3 weeks when daily vomiting was reported.

### *Risk factors for NVP*

Women reporting NVP were compared with those not reporting NVP for some variables (Table II). Each comparison was made with adjustment for the other variables. There was a clear-cut maternal age effect with a decline in the rate of NVP with age. A test for trend gave  $z = 3.8$ ,  $p < 0.001$ , but there was a significant scattering around the regression line (chi-square = 15.1 at 5 d.f.,  $p = 0.01$ ). The major increase in risk occurred in women aged younger than 25 years.

Women expecting their first baby (parity 0) had a decreased risk for NVP: parity 3+ showed a lower OR than parities 1–2, but this may well be random.

Women who worked outside home had a lower risk for NVP than housewives/women on maternity leave or who were out of work. The 'other' group is a composite, consisting of students and women who, for one reason or other, had leave of absence from work.

Vitamin use that had started before pregnancy and continued into pregnancy had a clear-cut protective effect. A similar effect was seen in women who had begun taking vitamins during pregnancy, while women who had used vitamins only before pregnancy but not during pregnancy had an increased risk for NVP, as based on rather few cases.

Table II. Numbers and odds ratios (OR) with 95% confidence intervals according to some characteristics of the participating women. The OR for each variable is stratified for the other variables. For maternal age and parity, each group is compared with all other groups

| Variable                               | Number of women |             | OR   | 95%CI     |
|--|-----------------|-------------|------|-----------|
|  | with NVP        | without NVP |      |           |
| Maternal age                           |                 |             |      |           |
| –19                                    | 34              | 7           | 1.64 | 0.68–3.94 |
| 20–24                                  | 345             | 82          | 1.34 | 1.03–1.75 |
| 25–29                                  | 1021            | 257         | 1.12 | 0.94–1.33 |
| 30–34                                  | 1023            | 252         | 0.92 | 0.78–1.09 |
| 35–39                                  | 420             | 130         | 0.76 | 0.61–0.95 |
| 40–                                    | 63              | 21          | 0.77 | 0.44–1.33 |
| Parity                                 |                 |             |      |           |
| 0                                      | 1243            | 396         | 0.65 | 0.55–0.77 |
| 1                                      | 1109            | 234         | 1.36 | 1.14–1.62 |
| 2                                      | 404             | 89          | 1.35 | 1.05–1.73 |
| 3+                                     | 150             | 50          | 0.89 | 0.63–1.28 |
| Smoking before pregnancy               |                 |             |      |           |
| No                                     | 2217            | 540         | 1.00 | reference |
| < 10 cig./day                          | 313             | 96          | 0.78 | 0.60–1.00 |
| 10+ cig./day                           | 361             | 123         | 0.70 | 0.55–0.88 |
| any smoking                            | 674             | 219         | 0.72 | 0.60–0.87 |
| Unknown                                | 15              | 5           | –    | –         |
| Working situation                      |                 |             |      |           |
| Working outside home                   | 2755            | 755         | 1.00 | reference |
| Housewife or out of work               | 123             | 10          | 2.86 | 1.49–5.46 |
| Other/unknown                          | 28              | 4           | 2.02 | 0.79–5.14 |
| Vitamins before and in early pregnancy |                 |             |      |           |
| No                                     | 1985            | 540         | 1.0  | reference |
| Before and in early pregnancy          | 563             | 147         | 0.79 | 0.65–0.96 |
| Only before pregnancy                  | 101             | 9           | 2.33 | 1.23–4.42 |
| Only in early pregnancy                | 225             | 61          | 0.72 | 0.53–0.97 |
| Unknown                                | 32              | 12          | –    | –         |

NVP = nausea and vomiting in pregnancy.

Smoking before pregnancy also had a protective effect: the odds ratio for smokers with NVP was approximately 0.7.

As can be seen from Table II, approximately 25% of all women reported smoking before pregnancy. When the women were asked at the first antenatal care visit, this percentage had been halved. Table III compares smoking before pregnancy with during early pregnancy. There was no significant difference in the percentage of women who stopped or reduced smoking according to the presence or absence of NVP. Only few women started to smoke or increased their smoking during pregnancy.

#### *Sick leave because of NVP*

Among women who worked, 494 (14%) reported that they had stayed away from work because of NVP. The length of leave was only stated by 437 women: the average length of leave was 13 days but the median was 5 days, and two-thirds (289) had less than 10 days of leave. The total number of days of sick leave because of NVP was

5583 days. This can be compared with the total number of sick days among all women: 20071. Nausea and vomiting in pregnancy thus caused some 28% of all sick leave during pregnancy before week 28.

#### *Therapies used*

Among 2906 women who complained of NVP, only 516 had tried some kind of therapy (18%). The majority, 478 (16%), had used drugs and 104 (4%) had used acupuncture or acupressure, thus 66 had used both drugs and other therapies. Among the 104 women using acupuncture or acupressure, 64 had used acupuncture, 54 acupressure, and 14 both.

Among women using drugs, the majority (88%) had used an antihistamine, sometimes combined with other drugs. Meclozine was the most commonly used antihistamine, and in 22% of cases the women combined meclozine with other drugs. The second-most common drug used was promethazine.

Thirty-nine women had been hospitalized because of NVP (1.3%).

#### *Low birth weight among singletons*

Low birth weight was studied among singleton infants with adjustment for infant sex, maternal age, parity, smoking habits in early pregnancy, and vitamin usage. The odds ratio when the mother reported NVP compared with when she did not report NVP was 0.55 (95%CI 0.33–0.92). The OR was the same for women who reported the use of drugs and women who did not.

#### **Discussion**

In our study, 79% of the women reported signs of NVP. In a detailed prospective study of NVP problems among 160 women, a frequency of 74% was reported (4). The two percentages do not differ ( $p=0.10$ ). In our study, half of the women with NVP problems reported vomiting; in the other study 51% reported vomiting (4). The two studies gave thus very similar results. In spite of the fact that only approximately 30% of all pregnant women participated in the study, these figures suggest that no major selection of participants occurred according to the presence or absence or severity of NVP. The low participation rate will not affect risk estimates noticeably.

In our study, one per cent of the women were hospitalized because of NVP: this rate agrees with the highest rate for hospitalization for hyperemesis among different hospitals in a

Table III. Smoking habits before pregnancy (as reported in the questionnaire) and in early pregnancy (as reported at the first antenatal care visit) according to the presence and absence of NVP

| Smoking before pregnancy | Smoking in early pregnancy<br>NVP |      |      |      | No NVP       |     |      |      |            |
|--------------------------|-----------------------------------|------|------|------|--------------|-----|------|------|------------|
|                          | NS                                | No   | < 10 | 10 + | NS           | No  | < 10 | 10 + |            |
| NS                       | 0                                 | 11   | 3    | 1    | 0            | 5   | 0    | 0    |            |
| No                       | 65                                | 2150 | 1    | 1    | 24           | 513 | 3    | 0    |            |
| < 10 cig./d              | 3                                 | 217  | 89   | 4    | 9            | 59  | 25   | 3    |            |
| 10 + cig./d              | 12                                | 112  | 153  | 84   | 7            | 30  | 53   | 38   |            |
| Stopped smoking          | 329/659 = 50%                     |      |      |      | 89/208 = 43% |     |      |      | $p = 0.07$ |
| Reduced smoking          | 153/237 = 65%                     |      |      |      | 53/91 = 58%  |     |      |      | $p = 0.29$ |

NS = not stated; NVP = nausea and vomiting in pregnancy.

'Reduced smoking' represents women who smoked 10 cigarettes or more per day before pregnancy and continued smoking < 10 cigarettes per day during early pregnancy.

Swedish study that made use of the Hospital Discharge Registry (6).

However, in our study the average duration of NVP problems was stated as 9.2 weeks (64 days) while in the other study it was quoted as only 35 days (4). This difference may be the result of the different ways of data collection: in our study we asked for the number of weeks and in the other study the estimate was based on a daily recording of symptoms, which certainly will give a better estimate.

We found the usual pattern of NVP occurrence according to maternal age and parity: a decreasing rate with age (adjusted for parity), and a lower rate in primiparous women than in multiparous women (adjusted for age). This pattern agrees with that described among Swedish women who used antihistamines for NVP (7) and for women who had been hospitalized because of hyperemesis (6).

Maternal smoking before pregnancy was a significant protective factor against NVP even after consideration of maternal age, parity, vitamin use, and working situation. This association has been mentioned previously in the literature (5). However, another study found no overall association between smoking and NVP, but among women who smoked, a relationship was seen between the amount smoked and NVP (4). Also, in the study of antihistamine use during pregnancy (7), maternal smoking in early pregnancy was associated with a reduced use of antihistamines for NVP (but not for antihistamines used for allergic complaints). This could be explained if women with NVP stopped smoking more often than other pregnant women. Our comparison of smoking information before and during early pregnancy showed such a tendency, but the difference in the rate of stopping or reducing smoking according to NVP status was not statistically significant.

If NVP is an expression of a well-functioning placenta, the negative association with smoking may be because of a negative effect of maternal smoking on early placenta development.

On the other hand, vitamin supplementation during (but not before) early pregnancy seems to protect against NVP, which could hardly be explained by the same mechanism. However, it is possible that women who experienced early NVP and perhaps had difficulties of eating properly started using vitamin preparations. An association between vitamin supplementation and prevention of NVP has previously been described (8,9). One study found a similar effect if the woman had used vitamins before the beginning of NVP symptoms, which would indicate that a direct protective effect occurred (10).

An interesting finding is a lower rate of NVP among women who worked outside home compared with housewives/women on maternity leave and women who were out of work. It is unlikely that NVP would prevent a woman to seek or get a job, as the event occurs for only a few weeks. Even if the major interest in NVP is nowadays directed against its biological background, this observation indicates that also psychological factors may be of significance, as has been repeatedly suggested in the literature.

Sixteen per cent of women reporting NVP said they had used drugs to relieve the complaint, mainly antihistamines and notably meclizine. The specific effect of antihistamines against NVP on delivery outcome has been studied in a larger study (7): beneficial effects were seen on pregnancy duration, birth weight, infant survival, and cardio-vascular malformations. It is likely that these effects are coupled to the NVP condition. In the present study, a reduction of the rate of low birth weight was seen (adjusted OR = 0.55). The same OR was found in the presence or absence of drug use against NVP. In a

study of antihistamines used against NVP, a corresponding OR of 0.82 was found (7). No effect of NVP on birth weight was found in another study (4), however, it was too small to permit any conclusions.

To conclude, the present study indicates that except for well-known predictors of NVP like maternal age and parity, both maternal smoking before pregnancy and vitamin use in early pregnancy result in a reduced frequency of NVP. The mechanisms behind these effects can only be speculated on.

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