MOTHERISK UPDATE

Managing women with nausea and vomiting of pregnancy

Canadian Consensus

abstract

QUESTION I have a 30-year-old pregnant patient who is asthmatic and is taking prednisone. Whenever she decreases her prednisone dose, her nausea increases tremendously even though she is taking two tablets of doxylamine and pyridoxine combination (Diclectin®) daily. She is already at 26 weeks' gestation, and I really do not want her to continue the prednisone beyond what is needed for her asthma, but two attempts to taper prednisone off failed because of unbearable nausea.

ANSWER Several controlled trials show the efficacy of prednisone for nausea and vomiting of pregnancy (NVP), but your case is fascinating in proving the point by challenge-rechallenge. You should try to decrease the prednisone while increasing doxylamine and pyridoxine to its recommended dose of two tablets before sleep, one in the morning, and one in the afternoon.

résumé

QUESTION J'ai une patiente asthmatique enceinte, âgée de 30 ans, qui prend de la prednisone. Aussitôt qu'elle réduit sa dose de prednisone, ses nausées augmentent considérablement, malgré qu'elle prenne deux comprimés par jour de doxylamine et de pyridoxine (Dilectin®). Elle en est déjà à 26 semaines de gestation et je ne veux vraiment pas qu'elle continue la prednisone au-delà de ce qui est nécessaire contre l'asthme. Par contre, deux tentatives de diminuer progressivement la prednisone ont échoué en raison des nausées insupportables.

RÉPONSE Plusieurs essais contrôlés font valoir l'efficacité de la prednisone contre les nausées et les vomissements associés à la grossesse, mais votre cas est fascinant en ce sens qu'il prouve ce point par test de provocation réitéré. Vous devriez essayer de réduire la prednisone tout en augmentant la doxylamine et la pyridoxine jusqu'à leur dose recommandée de deux comprimés avant le coucher, un le matin et un l'après-midi.

The Canadian medical establishment can pride itself on several initiatives aimed at improving management of women suffering from NVP. Many of these initiatives have helped bring to an end the typical trivialization of this medical condition.

In 1997, The Society for Obstetricians and Gynaecologists of Canada produced an effective pamphlet on management of NVP. The same year, the Motherisk Program initiated the NVP Helpline to counsel and support women and health professionals in managing this condition. The Motherisk Program is currently conducting several studies on NVP.

In 1998, the Canadian Consensus on NVP was developed by a national group of family physicians, obstetricians, internists, clinical pharmacologists, nurses, and dietitians. This paper will highlight seven key points in management of NVP as they appear in the Consensus. These points are supported by findings from recent research by the Motherisk Program.

Patient-centred approach

Different women have different needs. A certain number of vomiting incidents daily, for example, could be well tolerated by one woman but disastrous to another. Nausea itself can be very debilitating.

Among 256 women calling the NVP Helpline about their main concerns regarding NVP,[1] 140 (53.8%) identified nausea as most bothersome, while only 19 (7.3%) mentioned vomiting, and 97 (37.3%) were concerned about both (**Table 1**).

Motherisk research has discovered high rates of psychosocial suffering among women with NVP, including depression, rage, and a sense of isolation. Time lost from work or serious adverse effects on family life can be devastating. Women should not be told "it is all in their heads."

Do you have questions about the safety of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them by fax to (416) 813-7562; they will be addressed in future Motherisk Updates. Published Motherisk Updates are available on the College of Family Physicians of Canada website (www.cfpc.ca). Some articles are published in *The Motherisk Newsletter* and Motherisk website (www.motherisk.org) also.

Motherisk questions are prepared at the Hospital for Sick Children in Toronto. **Drs Dempster, Einarson, Koren, Ellis, Leduc, MacKinnon, Magee, Ross, Schofield,** *and* **van Dadelszen,** *and* **Ms Einarson,** *and* **Ms Tipping** *participated in developing the Canadian Consensus on managing women with NVP.* *This research was supported by an educational grant from Duchesnay in Laval, Que.*

Table 1. Psychosocial concerns of women with NVP

CONCERN (SAMPLE)	WOMEN REPORTING CONCERNS N (%)
Most bothersome symptom (256)	
• Nausea	140 (53.8)
• Vomiting	19 (7.3)
• Both	97 (37.3)
Feeling depressed about NVP (257)	
• Always or most of the time	94 (36.2)
• Some of the time	67 (25.8)
• Rarely or never	95 (36.5)
Considered elective termination due to NVP (257)	31 (11.9)
Time lost from paid employment (162)	127 (78.4)
Sick leave taken (120)	82 (68.3)
Adverse effect on relationship (257)	126 (48.5)
Adverse effect on partner's day-to-day life (259)	143 (55)

Many health professionals still do that, despite there being no proof. Nothing is more frustrating to a woman than telling her that NVP is due to her "rejection of the pregnancy."

The full consensus document on management of women with NVP is available upon request to the NVP Helpline at 1-800-436-8477. The document contains the Consensus' algorithm for a patient-centred approach.

Reassurance

Be careful not to dismiss your patient's complaints by saying, "It will go away by 12 weeks." Not uncommonly, severe cases of NVP continue beyond the first trimester and, sometimes, throughout gestation. A Motherisk study described terminations of otherwise wanted pregnancies among women suffering NVP for longer than the first trimester.[2]

Think of associated conditions

Remember that multiple pregnancies, molar pregnancies, and hydramnios increase the likelihood and severity of NVP. Other conditions with similar effects are listed in **Table 2**.

Think of differential diagnoses

Among the 500 000 women in the first trimester of pregnancy in Canada every year, some could have other conditions that manifest as nausea and vomiting. Some of these conditions are listed in **Table 3**.

Table 2. Conditions associated with NVP: *This list is based on the Canadian Consensus.*

PREGNANCY-RELATED CONDITIONS
Hydatidiform mole
Multiple gestation
Hydramnios
OTHER CONDITIONS
Drug toxicity
Diabetes
Central nervous system lesions
Ketoacidosis
Hyperthyroidism
Vestibular disorders

Clinical assessment

Turgor, urine output, electrolyte imbalances, and acetonuria are all important predictors of the severity of NVP. A new study of 555 women counseled by the Motherisk Program for NVP[3] found the following correlation best describes the association between maximal number of vomiting incidents and mean maximal weight loss:

Mean maximal weight loss = 0.5 x (number of vomiting incidents) + 1 ($r^2 = 0.99$).

These values varied greatly: even a woman vomiting 10 times a day might not lose weight if she managed to keep up her fluid and calorie intake. The correlation, however, can give physicians a general sense of where their patients are compared with others and can be a guide for judging severity of weight loss.

For example, if mean weight loss for one vomit daily is 1.5 kg and your patient has lost 6 kg, she might not be receiving optimal treatment, and she could be at higher risk of low caloric intake and dehydration. This new measure is not meant to replace clinical methods of assessing dehydration, such as investigations for turgor, electrolyte levels, and acetonuria, but women with NVP could lose a lot of weight not from dehydration but from suboptimal calorie intake.

Safe drugs for NVP

It is amazing how many women are still not offered pharmacotherapy for NVP when dietary interventions fail. Of 222 women followed prospectively by Motherisk, about half were not offered pharmacologic treatment even though they needed it.

Antiemetic drugs proven safe for fetuses are H_1-blockers, haloperidol,

Table 3. Differential diagnosis of NVP

GASTROINTESTINAL DISEASES
Peptic disorders
Appendicitis
Viral gastroenteritis
Irritable bowel disorder
Bowel obstruction
Pancreatitis
LIVER DISEASES
Hepatitis
GENITOURINARY TRACT DISEASES
Urinary tract infection
Ovarian torsion
Fibroid degeneration
Uremia

and vitamin B_6. The only drug approved in Canada for NVP, however, is a doxylamine and pyridoxine combination. Unfortunately, other scientifically proven safe drugs (most notably H_1-blockers) are labeled by their manufacturers as unsafe, putting physicians at risk of litigation if they prescribe them.

Prescribe effective doses

Subtherapeutic doses of prescribed drugs are not helpful. Two tablets of doxylamine and pyridoxine in the evening help morning symptoms of NVP for most women because the drug is delayed-release, but this regimen might not address symptoms at noon or in the evening. An additional morning tablet will help most patients around noon and during the afternoon and, when needed, a tablet at noon will help in the evening.

The case presented in the question above documents the need to use effective antiemetic doses rather than minimal doses. An effective antiemetic drug (prednisone) given for asthma was tapered off, while the drug of choice for NVP was used at half of its recommended dose despite uncontrolled symptoms.

If you wish your patients to participate in protocols for better management of NVP, please call 1-800-436-8477.

References

1. Mazzotta P, Magee LA, Maltepe C, Koren G. The perception of teratogenic risk by women with NVP. *Reprod Toxicol* 1999;13(4):313-9.
2. Mazzotta P, Magee L, Koren G. Therapeutic abortions due to severe morning sickness: unacceptable combination. *Can Fam Physician* 1997;43:1055-7.
3. Emelianova S, Mazzotta P, Einarson A, Koren G. Prevalence and severity of nausea and vomiting of pregnancy and the effect of vitamin supplementation. *Clin Invest Med* 1999;22(3):106-10.

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All research used by Motherisk is developed by a team of experts and is subject to rigorous peer review. At least three other scientists, besides the authors, evaluate and critique the quality of the research and agree that the science is correctly interpreted. The conflict surrounding Dr Gideon Koren in no way compromises the quality of the peer-reviewed research of the Motherisk program. Public statements unsupported by evidence that could undermine the scientific integrity of that research unduly compromise the ability of pregnant women to get the crucial information they need.