MOTHERISK *UPDATE*

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Nausea and vomiting of pregnancy

Evidence-based treatment algorithm

ABSTRACT

QUESTION One of my patients suffers from a moderate-to-severe form of morning sickness. She responded only partially to doxylamine and pyridoxine (Diclectin), and I wish to try adding another medication. What should my priority be?

ANSWER An algorithm used by Motherisk to manage thousands of patients takes a hierarchical approach to this condition. This approach is evidence based with regard to fetal safety as well as efficacy.

RÉSUMÉ

QUESTION Une de mes patientes souffre d'une forme modérée à grave de nausée matinale. Elle a réagi seulement en partie à la doxylamine et à la pyridoxine (Diclectin) et j'aimerais essayer d'ajouter un autre médicament. Quelle devrait être ma priorité?

RÉPONSE Un algorithme utilisé par Motherisk dans la prise en charge de milliers de patientes se fonde sur une approche hiérarchique à l'endroit de ce problème. Cette approche est fondée sur des données probantes en ce qui concerne à la fois la sécurité fœtale et l'efficacité.

Nausea and vomiting of pregnancy (NVP) affects an estimated 80% of all pregnant women, making it the most common medical condition during pregnancy.[1] In most cases, symptoms are worse in the morning; severity usually peaks by 8 to 12 weeks' gestation.[2] Some women are affected throughout the day, and the condition sometimes continues beyond the first trimester and even until the birth.[2]

Hyperemesis gravidarum is the most severe form of morning sickness, affecting 0.05% to 1% of pregnant women. Hyperemesis gravidarum is characterized by dehydration and electrolyte imbalance, and might require hospitalization. Nausea and vomiting of pregnancy has serious detrimental effects on the lives of women, even those with a milder presentation.[3] Termination of otherwise wanted pregnancies among women suffering from severe and prolonged NVP has been reported.[4]

Inappropriate treatment common

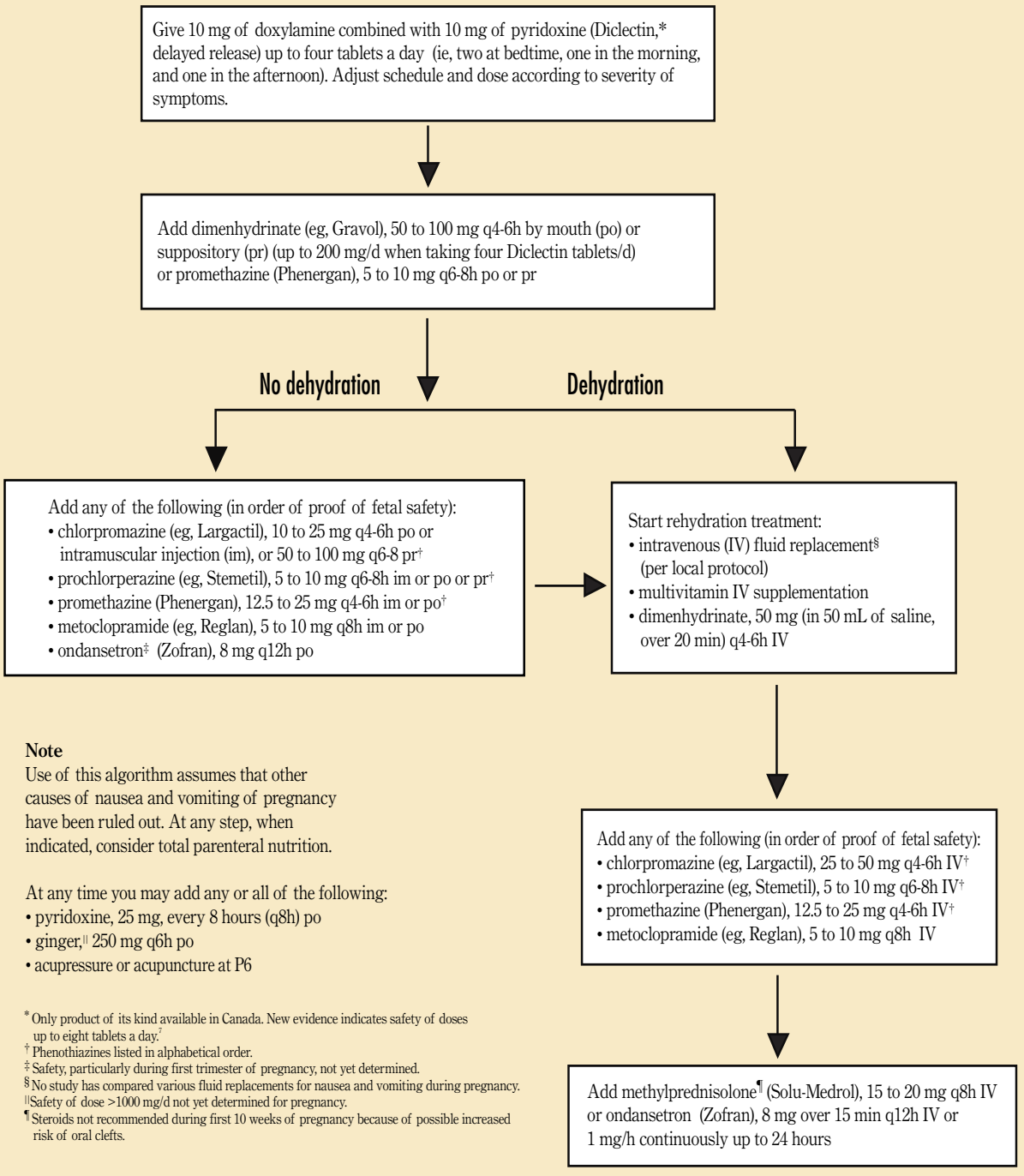
Ample evidence indicates that most women with NVP do not receive appropriate pharmacologic or nonpharmacologic treatment for the condition.[5] In 1996, the Motherisk Program in Toronto, Ont, initiated the NVP Healthline (1-800-436-8477) to counsel and support women and health professionals in managing NVP. Members of Motherisk systematically review available data on treatment in an attempt to obtain the best available evidence on efficacy and safety. Callers and clinic patients are advised on both pharmacologic and nonpharmacologic management.

This paper provides clinicians with a simple evidence-based algorithm on the efficacy and safety of treatments for NVP.

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 to the Motherisk Program by fax at (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 on the Motherisk website (**www.motherisk.org**) also.

Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. **Dr Levichek**, **Dr Atanackovic**, **Dr Oepkes**, **Ms Maltepe**, **Ms Einarson**, *and* **Dr Magee** *are members and* **Dr Koren** *is Director of the Motherisk Program.* **Dr Koren** *is a Senior Scientist at the Canadian Institute for Health Research and holds the Duchesnay and Canadian Foundation for Women's Health Chair for Better Pharmacotherapy During Pregnancy and Lactation.*

Figure 1. Treatment algorithm for nausea and vomiting of pregnancy: *If no improvement, proceed to next step*



Note

Use of this algorithm assumes that other causes of nausea and vomiting of pregnancy have been ruled out. At any step, when indicated, consider total parenteral nutrition.

At any time you may add any or all of the following:
- pyridoxine, 25 mg, every 8 hours (q8h) po
- ginger,‖ 250 mg q6h po
- acupressure or acupuncture at P6

* Only product of its kind available in Canada. New evidence indicates safety of doses up to eight tablets a day.[7]
† Phenothiazines listed in alphabetical order.
‡ Safety, particularly during first trimester of pregnancy, not yet determined.
§ No study has compared various fluid replacements for nausea and vomiting during pregnancy.
‖ Safety of dose >1000 mg/d not yet determined for pregnancy.
¶ Steroids not recommended during first 10 weeks of pregnancy because of possible increased risk of oral clefts.

continued on page 277

MotherRisk

continued from page 268

Rationale

In planning and evaluating management of NVP, fetal safety is clearly the primary concern, followed by efficacy. This order of priorities dictates that, in general, older medications, for which there are more data on fetal safety, are preferred over newer, perhaps more effective, drugs for which there are as yet fewer data on safety.

Methods

The algorithm is based on a recent systematic review of the literature on safety and efficacy of management of NVP conducted by members of the Motherisk Team.[6] The course of NVP ranges in severity, length, and response to treatment. We addressed treatment of NVP in a decision tree (**Figure 1**[7]). It begins with pharmacologic management of relatively mild cases and progresses to treatment of patients who cannot tolerate oral treatment or are dehydrated, or both. At any stage of the algorithm, physicians can add or, when there is improvement, withdraw treatment. The systematic review[6] included meta-analyses whenever the data permitted.

The quality of the evidence on fetal safety and maternal efficacy varies. There is large and convincing evidence on the safety and efficacy of doxylamine and pyridoxine (Diclectin). Evidence on the safety of other H_1 blockers is as strong, but evidence of efficacy is less strong. Many studies on the efficacy of phenothiazines offer convincing evidence, but the number of studies on safety is much smaller (birth defects are generally rare). Evidence on the safety and efficacy of ondansetron and metoclopramide is preliminary.

The hierarchy presented in the algorithm is based on the strength of evidence for fetal safety, and only treatments shown to be efficacious were included. It has been used by the Motherisk Program for treating a large number of patients.

Acknowledgment

This study was supported by a grant from Duchesnay Inc in Laval, Que.

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