Seminars in Perinatology 38 (2014) 496–502

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The outpatient management and special considerations of nausea and vomiting in pregnancy

Shannon M. Clark, MD[a,*], *Eryn Dutta, DO*[a,b], *and Gary D.V. Hankins, MD*[a]

[a]*Department of Obstetrics & Gynecology, The University of Texas Medical Branch, 301 University Blvd., Galveston, TX 77555*

[b]*US Navy Medicine Professional Development Center, Bethesda, MD*

ARTICLE INFO

Keywords:
reflux
pregnancy
nausea
vomiting
outpatient management

ABSTRACT

With 50–90% of pregnant women experiencing nausea and vomiting of pregnancy (NVP), the burden of illness can become quite significant if symptoms are under-treated and/or under-diagnosed, thus allowing for progression of the disease. The majority of these women will necessitate at least one visit with a provider to specifically address NVP, and up to 10% or greater will require pharmacotherapy after failure of conservative measures to adequately control symptoms. As a result, initiation of prompt and effective treatment in the outpatient setting is ideal. Once NVP is diagnosed and treatment is started, it is crucial to track symptoms in order to assess for a decrease in or resolution of symptoms as well as an escalation in symptoms requiring additional therapy. Of note, co-existing gastro-esophageal reflux disease (GERD), *Helicobacter pylori* infection, and psychosocial factors may have a negative impact on the management of NVP. Ultimately, every woman has her own perception of disease severity and desire for treatment. It is critical that both the provider and patient be proactive in the diagnosis and management of NVP.

Introduction

Although NVP is a very common medical condition in pregnancy, symptoms are often minimized by both the patient and provider due to lack of discussion of severity of symptoms, under-diagnosis and/or under-treatment. NVP occurs in 50–90% of pregnancies, with approximately 50–55% of patients having both nausea and vomiting and 25% with nausea alone.[1] Symptoms typically start between 4 and 9 weeks of gestation, with maximal symptoms at 12–15 weeks, and resolution by 20 weeks gestational age.[1] Conservative, non-pharmacologic measures are often successful at treating symptoms. However, some women will require a trip (s) to the ER, provider's office or labor and delivery triage, and some will need hospitalization for treatment of more severe symptoms.

The views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States government.

Drs. Shannon M. Clark and Gary D.V. Hankins were investigators on the clinical trial, "Effectiveness of delayed-release doxylamine and pyridoxine for nausea and vomiting of pregnancy: a randomized placebo controlled trial." After conclusion of the study, they became paid consultants for Duchesnay, USA.

* *Corresponding author.*
E-mail address: shclark@utmb.edu (S.M. Clark).

http://dx.doi.org/10.1053/j.semperi.2014.08.014
0146-0005/

The symptoms of NVP can occur at any time of the day, last for varying periods of time, vary from day to day and can include any combination of the following: nausea, gagging, dry retching, dry heaving, vomiting, and odor and/or food aversion.[1–4] It is also common for women to report certain precipitating factors that trigger symptoms, i.e., movement, heartburn, and certain foods and/or odor triggers.[5] If symptoms are prolonged and/or severe, dehydration is likely. In this case, evaluation of the patient is advised to ascertain if hyperemesis gravidarum (HG), the more severe form of NVP, exists and if hospitalization is necessary in order to control symptoms and to provide adequate hydration. It is important to remember that every woman has her own perception of disease severity. As a result, providers should not dismiss complaints of symptoms of NVP because their clinical assessment may not equate with what is being reported.

When a patient presents with a complaint of nausea and vomiting, it cannot be assumed that symptoms are due to NVP. It is advised to take the pregnancy-related versus non-pregnancy-related approach when determining the etiology of symptoms, even if she is presenting with symptoms in the first trimester.[2] Patients who present with a complaint of nausea and vomiting for the first time before 9–10 weeks of gestation are more likely to indeed have NVP. However, a thorough history and physical exam and confirmation of pregnancy are still necessary to confirm the diagnosis. Questioning on the onset, timing, and severity of nausea and vomiting, and aggravating and alleviating factors may elucidate another etiology for symptoms. If symptoms present for the first time after 9–10 weeks of gestation, it is important to consider other causes of the nausea and vomiting.

Outpatient management

Conservative measures

The first opportunity to assess and treat the symptoms of NVP is in the outpatient setting. It is important for the provider and/or the patient to be proactive and initiate a dialog so that symptoms of NVP can be assessed. In addition, each woman has her own perception of disease severity and desire for treatment. As a result, it is crucial that the provider not dismiss complaints of nausea and vomiting, but instead thoroughly evaluate the patient to see if treatment—whether it consists of conservative or pharmacologic measures—is necessary. Oftentimes, symptoms go under-diagnosed or under-treated, which can allow for progression from NVP to HG. Early recognition is a key to successful management.

Before initiating pharmacologic treatment, dietary and lifestyle modifications should be discussed with the patient. First, any odor or food aversions should be avoided. Eating multiple small meals a day is recommended in order to keep some amount of food on the stomach at all times, in order to avoid hypoglycemic episodes and gastric over-distension.[6–8] Foods with higher protein and carbohydrate and lower fat content are helpful, especially during the most symptomatic period of NVP.[6–9] Initiation of the bananas, rice, applesauce, and toast diet (BRAT) is a good starting point, with the addition of foods containing higher protein content as the symptoms are more controlled. Along with avoidance of eating multiple small meals a day, drinking smaller volumes of liquids multiple times a day is also recommended.[10] Up to 2 liters of fluid, preferably containing electrolytes, should be consumed over time per day. In addition, prenatal vitamins containing iron or iron supplementation pills should be avoided until symptoms are under control and the patient has normal dietary intake. Finally, avoiding stress and getting adequate rest are helpful.

Pharmacotherapy

It is estimated that up to 10% of women will require pharmacotherapy to treat the symptoms of nausea and vomiting despite changes in lifestyle and nutrition.[11,12] Outpatient treatment can be attempted when there are no signs of dehydration, and the patient is able to tolerate some oral intake. The American Congress of Obstetricians and Gynecologists (ACOG) currently recommends that a combination of oral pyridoxine hydrochloride (vitamin B_6, 25 mg) and doxylamine succinate (antihistamine, 12.5 mg) be used as a first-line treatment of NVP after failure with pyridoxine monotherapy.[13] Pyridoxine is a water-soluble vitamin involved in the metabolism of amino acids, lipids, and carbohydrates.[14] Doxylamine is a histamine-1 (H_1) receptor antagonist that directly inhibits histamine action at the H_1-receptor, acts indirectly at the vestibular system, and exhibits some inhibition of muscarinic receptors to decrease stimulation of the vomiting center.[15,16] The combination of pyridoxine and doxylamine for the treatment of NVP has the most data on safety and efficacy, including data in the first trimester.[13,17–19] The over-the-counter oral pyridoxine and doxylamine combination has been studied in over 6000 patients and controls, with no evidence of teratogenicity, and in randomized trials it has been associated with a 70% reduction in nausea and vomiting.[13,20] Many case–control and cohort studies, including over 170,000 exposures, have also established the safety of doxylamine and pyridoxine.[14]

The combination of over-the-counter oral pyridoxine (25 mg) and doxylamine (25 mg) has been utilized by health care providers in the U.S. since 1983 after Bendectin®, a delayed-release combination of doxylamine and pyridoxine, was removed from the market as a result of unfounded allegations of teratogenicity. Doxylamine is available over the counter as Unisom Sleeptabs® (25 mg), or Nighttime Sleep Aid, and the patient is instructed to take half of a tablet with 25 mg of oral pyridoxine. The over-the-counter prescribing practice has proven difficult for multiple reasons. First, there are multiple Unisom® products, but only one contains doxylamine. Second, the patient must break the small tablet in half in order to get the 12.5 mg of doxylamine. Furthermore, it is not guaranteed that the patient will actually receive 12.5 mg of doxylamine since the active ingredient may not be evenly distributed within the 25 mg tablet. Thirdly, the patient is instructed to take doxylamine plus pyridoxine, 2 individual pills, 3–4 times a day, which may prove difficult if the patient is experiencing episodes of vomiting. Finally, this over-the-counter combination is immediate release, which may allow for periods of time where symptoms are not being adequately controlled.