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A NOVEL PHARMACOLOGICAL APPROACH FOR NAUSEA AND VOMITING OF PREGNANCY

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ABSTRACT

Up to 80% of pregnant women are affected by Nausea and vomiting of pregnancy (NVP). Symptoms can vary from mild nausea alone to nausea with vomiting that is inexorable. This is usually self-limiting condition, but the symptoms can be upsetting and obstruct with social activities, work, and sleep. Symptoms can frequently be managed by diet and lifestyle modifications, but these interventions may not be successful for every person. The FDA approved in 2013 doxylamine succinate 10 mg with pyridoxine hydrochloride 10 mg as the first drug to exclusively treat NVP in over 30 years. This review is on the etiology & controlling of NVP and highlighting the indications & dosage of doxylamine succinate / pyridoxine hydrochloride and nursing interventions associated with its use to treat NVP.

Keywords: Morning sickness, Nausea, Vomiting, Pregnancy, NVP.

INTRODUCTION

Nausea and vomiting of pregnancy (NVP) is a common problem that can affect up to 80 percent of all pregnant women. Symptoms range from mild nausea alone to nausea with vomiting that is unrelenting [1]. The most severe form, hyperemesis gravidarum, affects a smaller proportion of women and can lead to serious complications including dehydration, weight loss and electrolyte imbalance that can necessitate hospitalization [2]. Women with NVP report higher levels of discomfort, lower quality of life and lost time from work [3, 4].

Etiology of NVP

The precise etiology of NVP is unknown, although rising levels of human chorionic gonadotropin and other endocrine factors, such as unpredictable levels of estrogen, progesterone and TSH, have been implicated in the development of NVP [5,6] Other possible causative factors include slowed peristalsis of the GIT from

mechanical and hormonal factors and changes in carbohydrate metabolism [7].

Controlling NVP

Women with NVP are well-informed about the characteristic course of symptoms and strategies to ease these symptoms, and are encouraged to keep away from potential triggers such as foods, odors and situations that may amplify the likelihood of nausea and/or vomiting. Women's and health care providers' worried about possible teratogenic effects of drugs during pregnancy, especially during the first trimester, has led to many health care providers being vigilant about prescribing pharmacologic treatments for NVP [2,8]. Hence, drugs that are safe and effective are regularly underutilized, and women who may perhaps benefit from treatment are not able to entirely explore this preference.



A novel approach

The U.S. Food and Drug Administration (FDA) approved doxylamine succinate 10 mg with pyridoxine hydrochloride 10 mg (brand name Diclegis®) in April 2013, for the treatment of NVP. For NVP in more than 30 years this is the first drug approved exclusively [9]. The drug is a new translation of Bendectin®, which was initially manufactured by Merrill Dow but was willingly removed from the market by the company in the early 1980s because of concerns over birth defects and expenditures associated with malpractice proceedings. Subsequent evidence based reviews and meta-analyses did not reveal the increased risk of birth defects [11,12] and the FDA concluded that presently no reproductive risks to the developing fetus associated with the use of doxylamine succinate/pyridoxine hydrochloride in pregnancy [10].

Medication Overview

Doxylamine succinate 10 mg with pyridoxine hydrochloride 10 mg is a combination drug consisting of an antihistamine and a Vit.B6 analog¹³. This delayed-release oral drug is indicated for NVP that has not responded to other treatment modes, such as dietary modification and lifestyle management.

Mechanism of Action

The specific mechanism of action of the combination of doxylamine succinate/ pyridoxine hydrochloride works to alleviate NVP is not entirely known. The center for vomiting in medulla of the brain collects signals from the cerebrum, the inner ear and the sensory organs through numerous neurotransmitters, with histamine. When the pathway of the neurotransmitters is sporadic, the vomiting reflex is minimized or eliminated. Doxylamine, an antihistamine, may disrupt the histamine pathway and reduce vomiting [2]. Vitamin B6 alone and/or combined with other medications (such as doxylamine) has shown to be effective in reducing nausea according to some clinical trials, though the therapeutic mechanism is imprecise [8]. Although the mechanism is unclear, the combination of doxylamine with pyridoxine has been shown to be effective over placebo in clinical trials [14].

Dosage and Administration

The dose amount with schedule is determined by response to the drugs. The initial starting dose is 2 tablets at bedtime. If symptoms are relieved, the next day this dosing schedule can be maintained. If symptoms persist, the dose can be improved to 1 tablet in the morning and 2 tablets at bedtime. If still sufficient relief is not obtained, the dose can be improved a final time to 1 tablet in the morning, 1 at noon and 2 at bedtime. the maximum dose that can be taken each day is 4 tablets [13].

Adverse Reactions

The most commonly reported side effects of doxylamine succinate 10 mg with pyridoxine hydrochloride 10 mg are connected to the sedating effects of antihistamines, and include sleepiness, drowsiness and somnolence. Use of other CNS depressants such as alcohol, narcotics, antianxiety drugs and sleep aids will potentiate these effects and increase the risk for accidents and falls. Women who are taking doxylamine succinate with pyridoxine hydrochloride should not use these drugs. Monoamine oxidase inhibitors extended the CNS effects of doxylamine succinate/ pyridoxine hydrochloride and never be combined. Additionally, the doxylamine component has anticholinergic properties and should be used with caution in women who have a history of asthma and urinary retention [13].

Special Populations

Doxylamine succinate with pyridoxine hydrochloride is proposed for use by pregnant women, as its main indication is to alleviate nausea and vomiting specially caused by pregnancy. It is considered a category A drug in pregnancy, indicating that no well controlled studies have confirmed a risk to the fetus in the first and subsequent trimesters. This drug is not suggested for women who are breastfeeding. Both doxylamine and pyridoxine are excreted in breast milk and to the infants exposed to doxylamine via breastfeeding, irritability and sedation have been documented. Safety and efficacy have not been established in women under the age of 18 [13].

Suggestions for Nurses

Though NVP is often mild and self-limiting, can be very worrying to women and can interfere with sleep, work, relationships and social activities [7]. It may even increase anxiety on pregnancy and is allied with depressive symptoms [3]. Nurses who concern for pregnant women should monitor for NVP, with severity and associated symptoms. NVP differs from hyper-emesis gravidarum, the severe form of NVP, and careful assessment will help identify women who may need more aggressive treatment. intractable cases of NVP, chiefly when linked with weight loss and clinical symptoms of dehydration, might require hospitalization, parenteral nutrition and or tube feeding [6]. For women who are clinically stable with mild to moderate NVP, nurses recommend dietary and behavioral changes that might help improve or lessen NVP. Though many of these interventions have not been supported through randomized clinical trials, they are not related with maternal or fetal harm and may provide various level of relief. Individual results will vary, and women may need to try different combinations of dietary and behavioral interventions earlier to experiencing symptom improvement. Moreover, NVP may continue into the second trimester. Anticipatory



guidance should be provided about the expected duration of symptoms to decrease anxiety related to prolonged symptoms. Women who are considering taking doxylamine succinate/pyridoxine hydrochloride must be informed of the dosing structure and side effects. This is a delayed-release medication and should not be crushed or chewed. Food may empty stomach. Because the major potential side effects are drowsiness and somnolence, women should be cautioned to avoid activities that necessitate attention and concentration, such as driving, until they know how they will react to the drug. Extreme drowsiness can lead to falls and, therefore, women should be conscious of their surroundings and use caution on stairs, slippery and/or uneven surfaces, areas rugs and in decreased lighting until they know how they will react to the drugs. In addition to provide education about how to take the drugs and about its potential side effects, nurses who care for pregnant women could need to dispel myths about safety and provide hope to women who may be concerned about medication use during pregnancy. Several women may have received information from family and friends that is incorrect. Nurses have the

responsibility to support evidence-based practice and provide current and clinically accurate information based on the best available evidence. Even so, women may still be reluctant to take medication during pregnancy.

CONCLUSION

A common condition, NVP is most often associated with the first trimester of pregnancy. Up to 80 percent of pregnant women may report various form of NVP that can range from mild, intermittent nausea to inexorable vomiting. The majority of cases of NVP are self-limiting and can be managed with lifestyle and dietary changes. But for women who are still experiencing symptoms despite these behavioral changes, the FDA has approved doxylamine succinate 10 mg with pyridoxine hydrochloride 10 mg as the first drug combination to treat NVP in 30 years. This sustained-release medication is a combination of an antihistamine with a vitamin B6 analog and can titrated up or down based on the symptoms. This signifies an added option for women who are experiencing NVP and reporting inadequate relief with other non-pharmacologic treatments.

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