SOGC CLINICAL PRACTICE GUIDELINE

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The Management of Nausea and Vomiting of Pregnancy

This Clinical Practice Guideline has been prepared and reviewed by the Clinical Practice Obstetrics, Maternal-Fetal Medicine, Medico-Legal, Family Physician Advisory and Guideline Management and Oversight Committees and approved by the Board of the Society of Obstetricians and Gynaecologists of Canada.

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Key Words: Nausea, vomiting, pregnancy, treatment, hyperemesis gravidarum, pharmacology, teratogenicity

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Abstract

Objectives: To review the evidence-based management of nausea and vomiting of pregnancy and hyperemesis gravidarum.

Evidence: MEDLINE and Cochrane database searches were performed using the medical subject headings of treatment, nausea, vomiting, pregnancy, and hyperemesis gravidarum. The quality of evidence reported in these guidelines has been described using the Evaluation of Evidence criteria outlined in the Report of the Canadian Task Force on Preventative Health Care.

Benefits: Nausea and vomiting of pregnancy has a profound effect on women's health and quality of life during pregnancy as well as a financial impact on the health care system, and its early recognition and management is recommended.

Cost: Costs, including hospitalizations, additional office visits, and time lost from work, may be reduced if nausea and vomiting in pregnancy is treated early.

Recommendations

1. Women experiencing nausea and vomiting of pregnancy may discontinue iron-containing prenatal vitamins during the first trimester and substitute them with folic acid or adult or children's vitamins low in iron. (II-2A)
2. Women should be counselled to eat whatever pregnancy-safe food appeals to them and lifestyle changes should be liberally encouraged. (III-C)
3. Ginger may be beneficial in ameliorating the symptoms of nausea and vomiting of pregnancy. (I-A)
4. Acupressure may help some women in the management of nausea and vomiting of pregnancy. (I-B)

Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventative Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in the category	D. There is fair evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E. There is good evidence to recommend against the clinical preventive action
	I. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in The Canadian Task Force on Preventive Health Care.

5. Mindfulness-based cognitive therapy as an adjunct to pyridoxine therapy may be beneficial. (I-B)
6. Pyridoxine monotherapy or doxylamine/pyridoxine combination therapy is recommended as first line in treating nausea and vomiting of pregnancy due to their efficacy and safety. (I-A)
7. Women with high risk for nausea and vomiting of pregnancy may benefit from preemptive doxylamine/pyridoxine treatment at the onset of pregnancy. (I-A)
8. H_1 receptor antagonists should be considered in the management of acute or chronic episodes of nausea and vomiting of pregnancy. (I-A)
9. Metoclopramide can be safely used as an adjuvant therapy for the management of nausea and vomiting of pregnancy. (II-2B)
10. Phenothiazines are safe and effective as an adjunctive therapy for severe nausea and vomiting of pregnancy. (I-A)
11. Despite potential safety concerns of ondansetron use in pregnancy, ondansetron can be used as an adjunctive therapy for the management of severe nausea and vomiting of pregnancy when other antiemetic combinations have failed. (II-1C)
12. Corticosteroids should be avoided during the first trimester because of possible increased risk of oral clefting and should be restricted to refractory cases. (I-B)
13. When nausea and vomiting of pregnancy is refractory to initial pharmacotherapy, investigation of other potential causes should be undertaken. (III-A)

ABBREVIATIONS

H.P.	*Helicobacter pylorus*
HG	hyperemesis gravidarum
MBCT	mindfulness-based cognitive therapy
NVP	nausea and vomiting of pregnancy
PV	prenatal vitamin
RCT	randomized controlled trial

INTRODUCTION

NVP is common, affecting 50% to 80% of women.[1] The impact of NVP on those affected falls along a spectrum ranging from a mild temporary disruption to significant debilitating distress. The physical and emotional impact of NVP often results in feelings of anxiety and worry about the effect of the symptoms on the fetus. NVP has a negative impact on health-related quality of life, including family relationships[2,3] and women's working abilities. Forty-seven percent of working women with NVP feel job efficiency is reduced,[4] 35% lose work time (mean loss of 62 working hours per woman),[4] and 25% lose time from housework (mean loss of 32 hours per woman).[1,4–6] NVP can be comparable in severity with the nausea experienced by those undergoing cancer chemotherapy[7] and is cited as a reason for elective termination of pregnancy.[8]

HG lies on the extreme end of the NVP spectrum. It affects approximately 0.3% to 2% of pregnancies, is the leading cause of hospitalization in the first half of pregnancy, and can lead to significant morbidity.[9,10] The *International Statistical Classification of Disease and Related Health Problems, Tenth Revision*, defines HG as persistent and excessive vomiting starting before the end of the 22nd week of gestation and subdivides the diagnosis as mild or severe.[11] Severe HG may include metabolic disturbances such as carbohydrate depletion, dehydration, and electrolyte imbalance.[11] Large ketonuria and a significant weight loss of at least 5% from pre-pregnancy weight are often included as criteria for diagnosis, but there is no universal agreement on these. HG occurs more frequently in multiple pregnancies, hydatidiform mole, and with a female fetus. It carries a higher risk of low birth weight, preterm birth, small for gestational age, and lower Apgar scores. HG is associated with maternal inheritance, previous affected pregnancies, lower maternal body mass index, and psychiatric and mood disorders.[9] Early recognition and management of NVP can have a profound effect on women's health and quality of life during pregnancy and reduce the financial impact on the health care system.

The pathogenesis of NVP is poorly understood, and the etiology is likely to be multifactorial. Other causes of nausea and vomiting must be ruled out, including gastrointestinal, genitourinary, central nervous system, and toxic/metabolic problems. Idiopathic NVP must be distinguished from NVP of known associations, such as hydatidiform mole or multiple gestation. The use of a validated, easy to use tool that measures severity of NVP, such as the pregnancy-unique quantification of emesis and nausea scoring system (PUQE or PUQE-24), can assist with monitoring progression and treatment.[12,13]

Pharmacological antiemetic therapy is still used with great caution by some patients and health care providers to treat NVP and is erroneously considered to be contraindicated in pregnancy.[6] This caution occurred in the aftermath of the profound teratogenic effects encountered with thalidomide. Despite the absence of any proof of deleterious effect from the product combination of pyridoxine/doxylamine with or without dicyclomine, the product was withdrawn from the market. Care providers play a major role in counselling and reassuring patients on safe and effective treatments available for NVP.[6]

This document aims to provide an evidence-based guideline for the treatment of NVP based on current evidence and the maternal and fetal safety of the medications and therapies available. The authors of this guideline acknowledge the limitations of the evidence available regarding the treatment of NVP.[14] Early discussion of all treatment options is preferable, after appropriate history-taking and physical examinations have been conducted. Recognizing and treating NVP in a timely fashion may prevent the progression of NVP to HG. Early treatment may also reduce maternal complications, the risk of parenteral therapy, and HG-related costs, including hospitalizations, additional office visits, and time lost from work. This should eventually result in improved maternal health and quality of life and better family relationships.

DIETARY AND LIFESTYLE CHANGES

Advice for women experiencing NVP has traditionally revolved around dietary changes. However, there is limited evidence supporting the effectiveness of dietary changes on relieving NVP symptoms. Recommendations have included separating solids and liquids; eating small, frequent meals consisting of bland foods; avoiding fatty foods such as potato chips; and avoiding drinking cold, tart, or sweet beverages. Protein may offer more tolerability over fats and carbohydrates.[15] One study reported that women with NVP had high intakes of carbohydrate and added sugar, primarily from sugar-containing soft drinks. It was not clear whether this was a precursor to the NVP or a strategy to manage it.[16] Other advice has been to avoid sensory stimuli, particularly strong odours. Women tend to alter their dietary habits to eat small, frequent meals to tolerate NVP, making an RCT of these habits very difficult to perform. There is no evidence that short-term dietary deficiencies during the early weeks of pregnancy will have long-term consequences on pregnancy outcome. Women should be counselled to eat whatever pregnancy-safe food appeals to them.

Vitamin supplements, including B-complex, taken preconception and in early pregnancy may be associated with reduced nausea in pregnancy.[17,18] However, some women experience NVP attributed to the iron content of PV supplements.[19] Iron requirements do not increase during the first trimester.[20] Unless the woman has iron deficiency, routine iron supplementation may not be indicated in the first trimester when most women experience NVP. Women calling a national phone support service for NVP were advised to discontinue their iron-containing PV in the first trimester and substitute that with either folic acid or adult or children's chewable vitamins. In follow-up the participants reported a significant reduction in NVP symptoms within days of discontinuing their PV.[21] It is reasonable to recommend avoiding iron-containing PV in the first trimester of pregnancy while maintaining folic acid supplementation because supplemental iron is not required at that time. Caution is also warranted with supra-pharmacological doses of individual vitamins, given the paucity of data regarding their safety for the fetus. It is important to maintain folic acid supplementation.[22]

Fatigue can exacerbate NVP, and sleep requirements increase in early pregnancy.[23] It is appropriate for health care providers to adopt a liberal attitude toward recommendations for increased rest and leaves-of-absence from work. Such a policy should ultimately shorten the number of days lost from work.

Enlisting the support and understanding of close friends and family and supportive counselling may be of benefit to the woman experiencing NVP.

Recommendations

1. Women experiencing nausea and vomiting of pregnancy may discontinue iron-containing prenatal vitamins during the first trimester and substitute them with folic acid or adult or children's vitamins low in iron. (II-2A)
2. Women should be counselled to eat whatever pregnancy-safe food appeals to them. and lifestyle changes should be liberally encouraged. (III-C)

NON-PHARMACOLOGICAL THERAPIES

Ginger

Ginger (*Zingiber officinale*) is a flowering plant. The root is used as a spice commonly added to foods and beverages and is also available in tea or tablets. Because ginger is non-regulated, tablet extracts and most preparations available are of uncertain purity and composition. Pharmaceutical grade ginger is available and provides access to more reliable composition. It is considered safe and effective with a significant reduction in NVP.[24] Although more robust data on safety could be provided by larger studies, ginger is a common food additive used around the world with no evidence of harm.[24,25] There is evidence that ginger has dopamine and serotonin antagonist activity resulting in improved gastric motility with no significant side effects. The recommended dosage is 250 mg by mouth 4 times per day.

Recommendation

3. Ginger may be beneficial in ameliorating the symptoms of nausea and vomiting of pregnancy. (I-A)

Acupuncture and Acupressure

Stimulation of the P6 (Nei Guan) point (Figure 1) has been used for thousands of years by acupuncturists to treat nausea and vomiting from a variety of causes. This acupoint is located 3 fingers' breadth proximal to the wrist, between the tendons of palmaris longus and flexor carpi radialis muscles. There is good evidence to support the use of acupuncture for nausea and vomiting.[26] However, there is insufficient data for this intervention in pregnant women.[10] Acupressure applied to P6 has been demonstrated to reduce nausea and episodes of vomiting for women with NVP, although there are limitations to these findings.[14,27–29] Acupressure is affordable, is easy to self-administer, appears safe, and may be beneficial in reducing NVP for some women.[14]

Recommendation

4. Acupressure may have some value in the management of nausea and vomiting of pregnancy. (I-B)

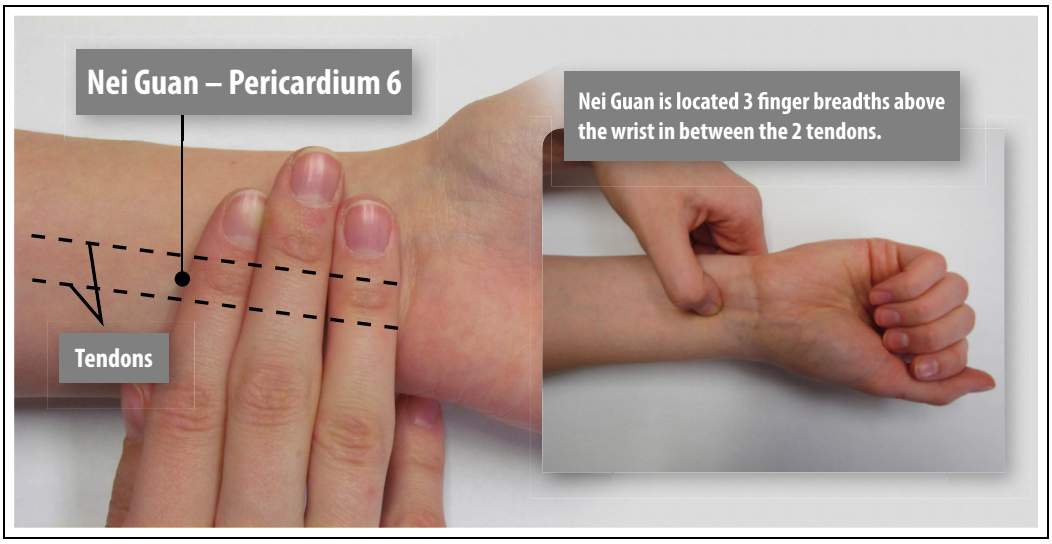
Psychotherapy

An RCT compared the impact of pyridoxine 40 mg per day to pyridoxine plus 3 weeks of psychotherapy in the form of mindfulness based cognitive therapy.[30] Women who received MBCT experienced a significant reduction in NVP symptoms, anxiety, and depression scores and were more likely to report improved symptoms overall post-treatment and in follow-up 7 weeks later. The study was small (n = 86) and did not blind participants or offer placebo psychotherapy. The authors acknowledged that the extra time offered to the women experiencing moderate NVP in the course of the 7 sessions may have accounted for their results. However, psychotherapy in the form of MBCT may be helpful to women with moderate NVP as an adjunct to medical therapy. More research is indicated.

Recommendation

5. Mindfulness-based cognitive therapy as an adjunct to pyridoxine therapy may be beneficial. (I-B)

Figure 1. Stimulation of the P6 (Nei Guan) point



PHARMACOLOGICAL THERAPIES

When conservative measures have not been effective, pharmacological intervention is warranted. Treatment should start as soon as possible after the diagnosis of NVP.

Included in this guideline is an evidence-based algorithm for NVP that was developed from studies on the safety and efficacy of available medications (Figure 2).[31] Therapies are discussed in the same order as they appear in the algorithm.

Vitamins

Pyridoxine

Pyridoxine (vitamin B_6) is a water-soluble vitamin that has been associated with the treatment of NVP since 1942. Several studies report it to be non-teratogenic at doses of up to 200 mg a day.[32–34] The effectiveness of pyridoxine in reducing NVP symptoms has been reported in several RCTs.[35–37] A Cochrane systematic review supports possible benefit from vitamin B_6 monotherapy; however, the data are limited.[14] More evidence is required to determine whether vitamin B_6 therapy results in greater efficacy at higher doses.[38]

Recommendation

6. Pyridoxine monotherapy or doxylamine/pyridoxine combination therapy is recommended as first line in treating nausea and vomiting of pregnancy due to their efficacy and safety. (I-A).

Antihistamines

Doxylamine/pyridoxine

Doxylamine is an H_1 receptor antagonist that has been shown to be safe and effective in the treatment of NVP.[39–42]

Doxylamine 10 mg is fixed in combination with pyridoxine 10 mg in a delayed-release formulation (Diclectin in Canada and Diclegis in the United States). The standard recommended starting dose is 4 tablets a day. However, a review of the safety of doxylamine/pyridoxine taken in doses as high as 5 to 12 tablets a day has been reported.[32]

Preemptive treatment in multipara with a high risk of recurrence of severe NVP has been evaluated.[43] Doxylamine/pyridoxine treatment reduced the duration and severity of NVP in women at increased risk of NVP who took the medication at the onset of pregnancy. Women should be informed that the doxylamine/pyridoxine treatment is not for acute relief. It should be taken on a regular basis to prevent the occurrence or reduce the severity of nausea and vomiting. When the nausea has remitted, the doxylamine/pyridoxine treatment should be tapered rather than stopped at once.

Recommendation

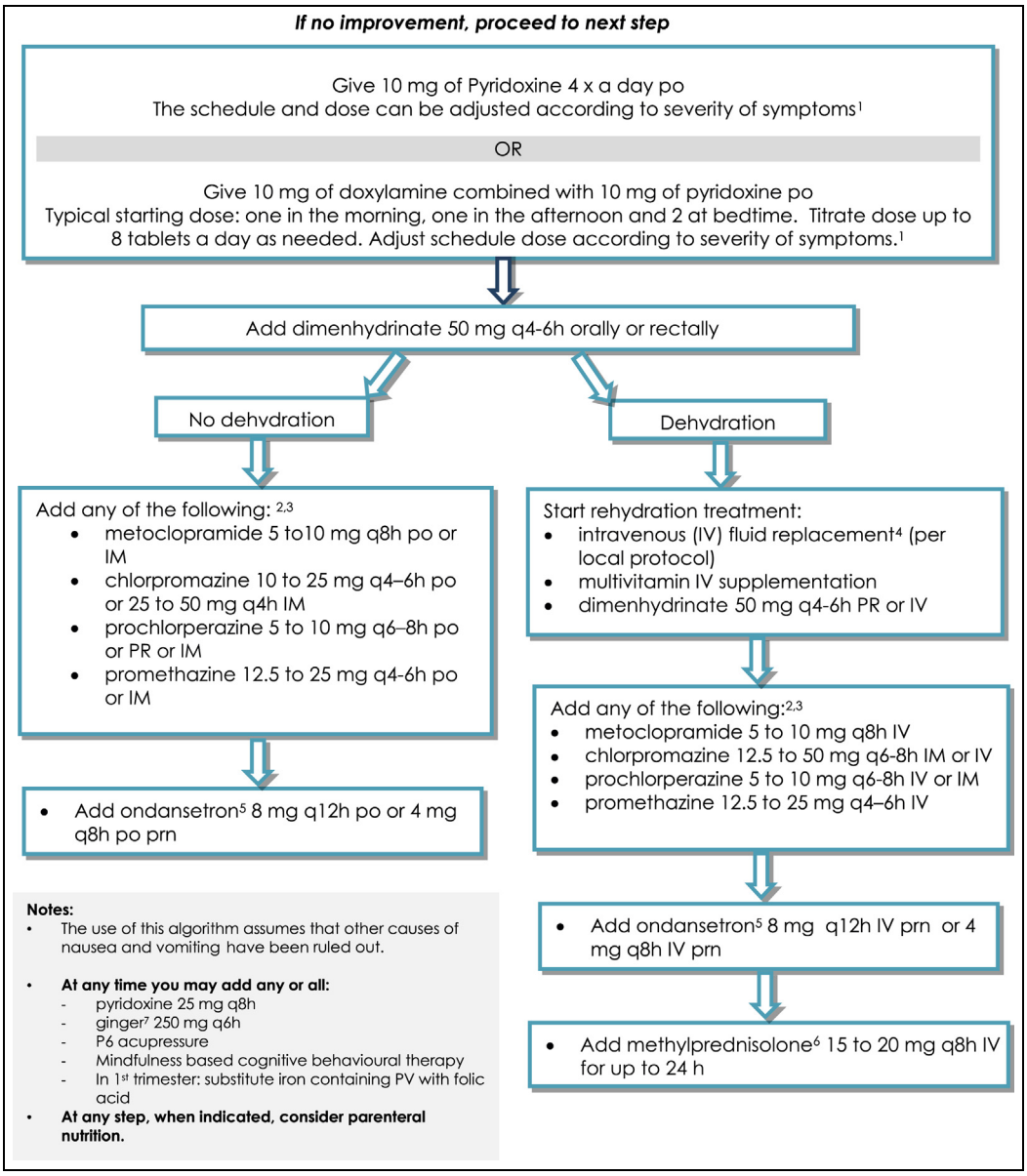
7. Women with high risk for nausea and vomiting of pregnancy may benefit from preemptive doxylamine/pyridoxine treatment at the onset of pregnancy. (I-A)

Other antihistamines

Other H_1 receptor antagonists (e.g., dimenhydrinate, diphenhydramine) are considered safe in pregnancy. This conclusion is supported by a wide body of evidence and meta-analysis[16] of first trimester exposure to various antihistamines.[44]

Pooled data from 7 controlled trials investigating the effectiveness of various antihistamines for NVP indicate that these drugs are effective.[45] Availability in parenteral and suppository formulations makes these agents a good

Figure 2. Treatment algorithm for NVP.[31]



[1]One study assessing the safety of higher-than-standard doses of pyridoxine in pregnancy reported no adverse events with a mean dose of 130 mg/d.[34] [2]No medication has been demonstrated to be superior at this time; metoclopramide is preferred based on additional maternal/fetal data. [3]All medications can be used PRN or regularly scheduled depending on symptom control. [4]No study has compared different fluid replacements for NVP. [5]Safety, particularly in the first trimester of pregnancy, is controversial. This medication has been associated with an increased risk of oral clefts and cardiac anomalies in some of the literature. In addition, maternal adverse effects such as bowel obstruction and corrected QT interval (QTc) prolongation need to be considered. [6]Steroids may increase risk for oral clefts in the first 10 weeks of gestation. [7]Safety of doses higher than 1000 mg/d is not yet determined in pregnancy. IM, Intramuscular; PO, by mouth; PR, per rectum; PRN, as needed

choice for treatment of acute or breakthrough episodes of NVP. Caution should be taken to avoid excessive dosing of H_1 receptor antagonists by combining different antihistamines in therapy; if adverse effects occur, consider revising drug dosing.

Recommendation

8. H_1 receptor antagonists should be considered in the management of acute or chronic episodes of nausea and vomiting of pregnancy. (I-A)

Dopamine Receptor Antagonists

Metoclopramide

Metoclopramide is an upper gastrointestinal motility stimulant that blocks dopamine receptors and in higher doses can block serotonin receptors in the central nervous system. Because NVP is associated with gastric dysrhythmia, the use of metoclopramide is common in clinical practice in many countries. Numerous studies have reviewed this medication's suitability in pregnancy, and information to date is reassuring.[46–49] More than

40 000 women using metoclopramide in the first trimester have been studied and no associations with increased risk of anomalies, spontaneous abortion, low birth weight, preterm delivery, or perinatal death have been reported.[47,48]

Compared with the serotonin 5-HT_3 receptor antagonist ondansetron, metoclopramide had similar antiemetic/antinauseant effects and the length of stay in the hospital was the same.[50] As expected, metoclopramide caused more drowsiness and dry mouth.[50] In a clinical trial of 83 pregnant women randomly assigned to ondansetron or metoclopramide, ondansetron treatment resulted in significantly lower vomiting ($P = 0.042$) but not nausea scores compared with metoclopramide.[51] In addition, an observational study using home subcutaneous therapy for HG suggested that metoclopramide is effective, safe, and economical.[52] Women should be advised of the extrapyramidal side effects that can occur.

Recommendation

9. Metoclopramide can be safely used as an adjuvant therapy for the management of nausea and vomiting of pregnancy. (II-2B)

Phenothiazines

Like antihistamines, phenothiazines (i.e., chlorpromazine, perphenazine, prochlorperazine, promethazine, trifluoperazine) have also been proven safe for use in pregnancy. Prospective and retrospective cohort, case-control, and record-linkage studies of patients with exposure to various and multiple phenothiazines have failed to demonstrate an increased risk for major malformations.[45] Significant therapeutic effect was demonstrated by 3 RCTs of various phenothiazines versus placebo for the treatment of severe NVP.[45,53] Women should be advised of the extrapyramidal side effects that can occur.

Recommendation

10. Phenothiazines are safe and effective as an adjuvant therapy for severe nausea and vomiting of pregnancy. (I-A)

Serotonin 5-HT_3 Antagonists

Limited data are available on 5-HT_3 antagonist safety and efficacy.

Ondansetron

The safety and efficacy data for ondansetron in pregnancy are controversial; an increased risk of birth defects, in particular cleft palate and cardiac anomalies, has recently been reported with use in the first trimester.[54–59] The clinical relevance of these increased risks is unknown; thus, this medication should be considered as a last-line treatment when other medication combinations have failed.

Several trials have investigated the effectiveness of ondansetron for NVP. Intravenous ondansetron did not demonstrate a therapeutic benefit for the treatment of HG compared with intravenous promethazine.[60] Ondansetron resulted in decreased vomiting compared with doxylamine/pyridoxine[61]; however, the doxylamine/pyridoxine product used in the study was not the delayed-release product typically used in clinical practice and the dose was not optimized. Another study reported no significant difference in nausea and significantly fewer vomiting episodes with ondansetron compared with metoclopramide; however, the clinical significance of this difference and the limitations of this study make this finding questionable.[51] When compared with metoclopramide, ondansetron had similar antiemetic/antinauseant effects and hospital length of stay and metoclopramide was associated with drowsiness and dry mouth.[50]

In one study that compared the use of ondansetron with other antiemetic agents (metoclopramide, promethazine, prochlorperazine) for treatment of NVP in the emergency department, there was no difference in time from drug administration to disposition or administration of additional antiemetics among the agents.[62]

There have been 4 published case reports of bowel obstruction with the use of ondansetron in pregnancy.[63,64] Although the adverse effect is rare, maintaining adequate hydration and prompt treatment of constipation are recommended. Drug interactions with ondansetron are common (e.g., antibiotics, antidepressants); the benefits and risks of using medication combinations when drug interactions exist should be assessed on an individual basis (e.g., corrected QT interval prolongation, serotonin syndrome). Ondansetron is also significantly more expensive per dose than are other more affordable, safe, and effective outpatient therapies for NVP.

Recommendation

11. Despite potential safety concerns of ondansetron use in pregnancy, ondansetron can be used as an adjunctive therapy for the management of severe nausea and vomiting of pregnancy when other antiemetic combinations have failed. (II-1C)

Corticosteroids

The data on effectiveness of steroid use in the treatment of NVP are weak. Although a few controlled studies showed

some effectiveness,[65] pooled results of studies comparing corticotropin with placebo and methylprednisolone with promethazine in HG women failed to show a reduction in the number of subsequent readmissions to the hospital compared with control patients.[45] In addition, corticotropin was not found to be superior to placebo based on "severity" or "relief" scores.[45,65] When compared with promethazine, prednisolone has a slower onset of action but is reported to be superior in long-term management primarily due to its lower side effect profile.

Systemic use of steroids has been implicated in cases of cleft lip with or without cleft palate,[66] although a large retrospective study of inhaled steroids in Denmark showed no association.[67] Until more data are available, corticosteroids should be kept as the last line of therapy under 10 weeks' gestation and only when maternal benefits outweigh fetal risk.

Recommendation

12. Corticosteroids should be avoided during the first trimester because of possible increased risk of oral clefting and should be restricted to refractory cases. (I-B)

ADJUVANT THERAPIES

Gastroesophageal Reflux Therapies

Gastroesophageal reflux is common during pregnancy[68] and may increase the severity of NVP.[69] The following adjuvant therapies are used primarily to reduce esophageal acid reflux associated with NVP[68] but may also reduce severity of NVP.[69]

Antacids containing magnesium, calcium, or aluminum are used in pregnancy as first-line treatment for reflux. There is no evidence of teratogenic effect when used in recommended doses.[68,70,71] Antacids containing bicarbonate should be avoided in pregnancy because they may cause metabolic alkalosis and fluid overload in both mother and fetus.[68]

H_2 receptor antagonists, including cimetidine, ranitidine, and famotidine, are the most commonly used drugs to manage reflux when antacids are not effective. Use of these medications has not been associated with an increased risk for major malformations following first trimester exposure.[45,68,70,72] Cimetidine and ranitidine have been used in pregnancy for 3 decades with excellent safety records.[68]

Proton-pump inhibitors, including omeprazole, lansoprazole, rabeprazole, esomeprazole, and pantoprazole, have a high safety profile when used in pregnancy.[68,70–73]

Rehydration

When dehydration is demonstrated at any time in the course of evaluation and treatment of NVP, intravenous rehydration may be warranted. Careful attention should be paid to electrolyte imbalances, and appropriate crystalloid therapy should be instituted. An intravenous multiple vitamin supplement may be provided at the same time. Home parenteral therapy for NVP may be an appropriate option where available.

OTHER CAUSES OF NVP

When NVP is refractory to initial pharmacotherapy, it may be appropriate to investigate other potential causes or exacerbating factors associated with NVP. Electrolytes, TSH, renal function, liver function, drug levels, ultrasound, and H.P. testing may be considered.

Recommendation

13. When nausea and vomiting of pregnancy is refractory to initial pharmacotherapy, investigation of other potential causes should be undertaken. (III-A)

MOOD DISORDERS

It is common for mood disorders to accompany NVP. Some of these disorders may require treatment with therapeutic agents, such as antidepressants. The benefits and risks of antidepressant therapy in pregnancy need to be discussed with the woman prior to commencement.

Mirtazapine has been reported to have some efficacy for improving NVP symptoms and increasing oral intake in about a dozen case reports of women with treatment-resistant NVP and accompanying mood disorders. The women in these cases initiated therapy primarily after 10 weeks' (1 case report at 5 weeks') gestation and were most commonly started on oral mirtazapine 7.5 to 15 mg, with doses titrated as high as 30 to 45 mg daily (2 cases transitioned from intravenous to oral).[74–77] In 1 case report, signs of neonatal withdrawal were reported after birth; in this case the medication was continued until delivery because the neonate was born prematurely.[77]

Selective serotonin reuptake inhibitors (fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram) are effective for treatment of mood disorders in pregnancy and should be considered if concomitant mood disorders require treatment.[78]

Tricyclic antidepressants (amitriptyline, nortriptyline, and imipramine) have been used for many years for several conditions. Although studies involving more than 1000

patients have shown that tricyclic antidepressants are not teratogenic when used in the first trimester,[79] their narrow therapeutic index, life-threatening cardiotoxicity in overdose, and severe anticholinergic effects make them less appealing.

Drug interactions with NVP medications and mood-altering medications are common; the benefits and risks of using medication combinations when drug interactions exist should be assessed on an individual basis (e.g., corrected QT interval prolongation, extrapyramidal symptoms, serotonin syndrome).

HELICOBACTER PYLORI

H.P. is a Gram-negative bacterium that is significantly associated with many pregnancy-related disorders, including HG.[1,6,80,81] The presence of H.P. in gastric mucosal biopsy is the gold standard for diagnosing H.P. infection. However, easy, low-cost non-invasive diagnostic tests, such as serum antibody detection and stool antigen, are preferred during pregnancy.[1,4,6,80–82] Another less-used, non-invasive diagnostic test is the carbon-labeled urea breath test. The ionizing radiation dose involved in the carbon-labeled urea breath test is extremely low and is lower than the amount considered to be teratogenic. The best approach in pregnancy is to perform this when the benefits outweigh the risks.[1,80]

Considering the potential pregnancy-related complications from H.P. infection, pre-pregnancy eradication using triple therapy (proton-pump inhibitor with 2 antibiotics for 2 weeks) would still be the best approach if the condition is known before the pregnancy.[1,80] Although a combination of penicillin and erythromycin has been prescribed in a limited number of cases of H.P.-related NVP, there is still no definite safe therapy for H.P. infection in pregnancy.[1,80] Triple therapy treatment during pregnancy may be undertaken because each of the drugs in the triple therapy may be used in pregnancy if the benefits outweigh the risk.

CONCLUSION

NVP can and should be managed safely and effectively after other causes of nausea and vomiting have been ruled out. Adoption of an easy to use, objective and validated tool can be helpful to assess severity and treatment impact on NVP such as the pregnancy-unique quantification of emesis and nausea (PUQE) or modified PUQE – 24 scoring systems. Women who do not have an iron deficiency and are experiencing NVP can discontinue iron-containing PVs during the first trimester and substitute them with folic acid or adult or children's vitamins low in iron. Ginger and P6 acupressure are safe and readily available options for women. A pyridoxine monotherapy or a doxylamine/pyridoxine combination is recommended as first-line treatments because these agents have the greatest evidence to support efficacy and safety. MBCT may be considered as an adjunct therapy. Other drugs may also be used, primarily dimenhydrinate, in conjunction with the doxylamine/pyridoxine combination. When these are not optimally effective in relieving NVP symptoms, consideration should be given to dopamine antagonists (metoclopramide and phenothiazines). If possible, corticosteroid use should be avoided in the first 10 weeks of pregnancy, a critical period for oral cleft formation. H.P. colonization therapy treatment during pregnancy may be undertaken because each of the drugs in the triple therapy may be used in pregnancy if the benefits outweigh the risk.

The choice of pharmacological treatment for NVP is as important as the choice of when to start using it. All women with physical symptoms of NVP should be counselled early in their pregnancy on safe and effective treatments because their quality of life may be impaired even with mild to moderate impact.[4]

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