

EFFICACY AND SAFETY OF DOXYLAMINE AND PYRIDOXINE

in Treating Nausea and Vomiting During Pregnancy



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INTRODUCTION

Nausea and vomiting during pregnancy (NVP), often referred to as "morning sickness," is one of the most common and debilitating symptoms experienced by pregnant women. Affecting up to 70%–80% of pregnancies, NVP can significantly impair maternal well-being, daily activities, and quality of life (1). In severe cases, it may progress to hyperemesis gravidarum, a condition associated with dehydration, electrolyte imbalances, and hospitalization (2).

The etiology of NVP is multifactorial, involving hormonal, genetic, and environmental factors, making its management complex and patient-specific (3). While mild cases may resolve without intervention, moderate to severe symptoms often necessitate medical treatment to improve maternal comfort and nutritional status.

Doxylamine and pyridoxine (vitamin B6) combination therapy is an established first-line treatment for NVP due to its safety profile and efficacy (4, 5). Doxylamine, an antihistamine, reduces nausea by blocking histamine receptors, while pyridoxine mitigates symptoms through its role in neurotransmitter synthesis (6). Despite its long history of use and FDA approval for NVP, barriers to its widespread adoption, including concerns about safety, patient adherence, and prescribing practices, persist in various healthcare settings (7).

Given the prevalence of NVP and the significant burden it imposes, evaluating the real-world efficacy and safety of doxylamine-pyridoxine therapy is essential. This study aims to assess healthcare providers' awareness, perceptions, and prescribing patterns regarding this combination, contributing to evidence-based improvements in maternal care (4).

RATIONALE OF THE STUDY

The high prevalence of NVP underscores the need for effective, safe, and accessible treatment options that can alleviate symptoms and improve quality of life for pregnant women. While doxylamine and pyridoxine combination therapy is recognized as a first-line treatment, variations in its clinical use and perceptions among healthcare providers indicate a gap in knowledge and implementation.

This study seeks to address these gaps by evaluating clinicians' experiences and opinions regarding the efficacy, safety, and practical application of doxylamine and pyridoxine in managing NVP. By identifying barriers to its use and opportunities for optimizing patient outcomes, the findings aim to enhance clinical practices and inform guidelines for treating NVP.

STUDY OBJECTIVE

The primary objective of this study is to evaluate the real-world efficacy and safety of doxylamine-pyridoxine therapy for NVP. Specific aims include:

- **Assessing Clinician Awareness and Familiarity:** Determine clinicians' understanding of the mechanisms, benefits, and safety profile of doxylamine-pyridoxine therapy.
- **Evaluating Prescribing Patterns:** Identify current prescribing trends for NVP treatment and factors influencing therapy selection.
- **Analyzing Effectiveness and Safety:** Examine clinicians' perceptions of the effectiveness and tolerability of doxylamine-pyridoxine in diverse patient populations.
- **Exploring Patient Demographics:** Identify demographic and clinical factors influencing the use of doxylamine-pyridoxine, including severity of symptoms, gestational age, and comorbidities.

- **Identifying Barriers and Opportunities:** Investigate challenges to adopting doxylamine-pyridoxine therapy and explore strategies to improve its utilization and accessibility.

METHODS

The study employed a survey-based method, utilizing a structured questionnaire distributed among healthcare professionals involved in the management of nausea and vomiting during pregnancy (NVP). The aim was to gather data on the efficacy and safety of doxylamine-pyridoxine therapy in NVP management. The methodology includes the following components:

The questionnaire will include sections on:

- Clinician familiarity with doxylamine-pyridoxine therapy.
- Current prescribing practices and alternative treatments for NVP.
- Perceived efficacy and safety of doxylamine-pyridoxine in clinical practice.
- Factors influencing prescribing decisions and barriers to its use.
- Patient characteristics (e.g., gestational age, symptom severity) considered during treatment planning.

The survey will be reviewed and validated by experts in obstetrics and maternal-fetal medicine to ensure relevance and accuracy.

Participant Recruitment:

The study will target obstetricians, gynecologists, and general practitioners across healthcare settings in India. Participants will be recruited based on their experience in managing NVP and their willingness to contribute to the study.

Data Collection:

Responses will be collected electronically and in person over a three-month period. The survey will be designed to maximize participation by ensuring ease of completion and guaranteeing respondent confidentiality.

Data Analysis:

Quantitative methods will be used to analyze survey responses, identifying trends and patterns in awareness, prescribing practices, and perceived effectiveness. Descriptive statistics will summarize the data, while comparative analyses will explore variations based on clinician specialty, patient demographics, and treatment settings.

Ethical Considerations:

The study will adhere to ethical guidelines for research involving human participants. Informed consent will be obtained from all participants, and data will be anonymized to protect respondent confidentiality.

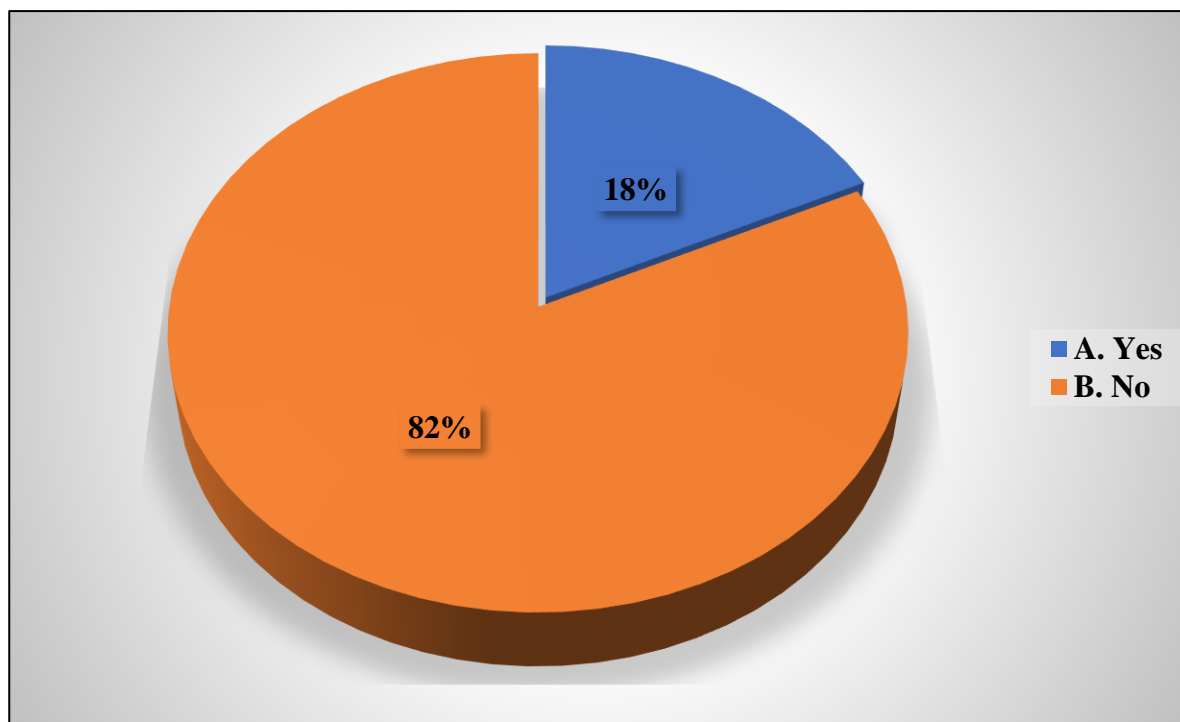
RESULTS

A total of 116 HCPs participated in the survey. Below is the summary of the responses.

1. Are you aware that Doxylamine and Pyridoxine is first-line treatment recommendation for nausea and vomiting during pregnancy as per the American College of Obstetricians and Gynecologists (ACOG)?

A. Yes

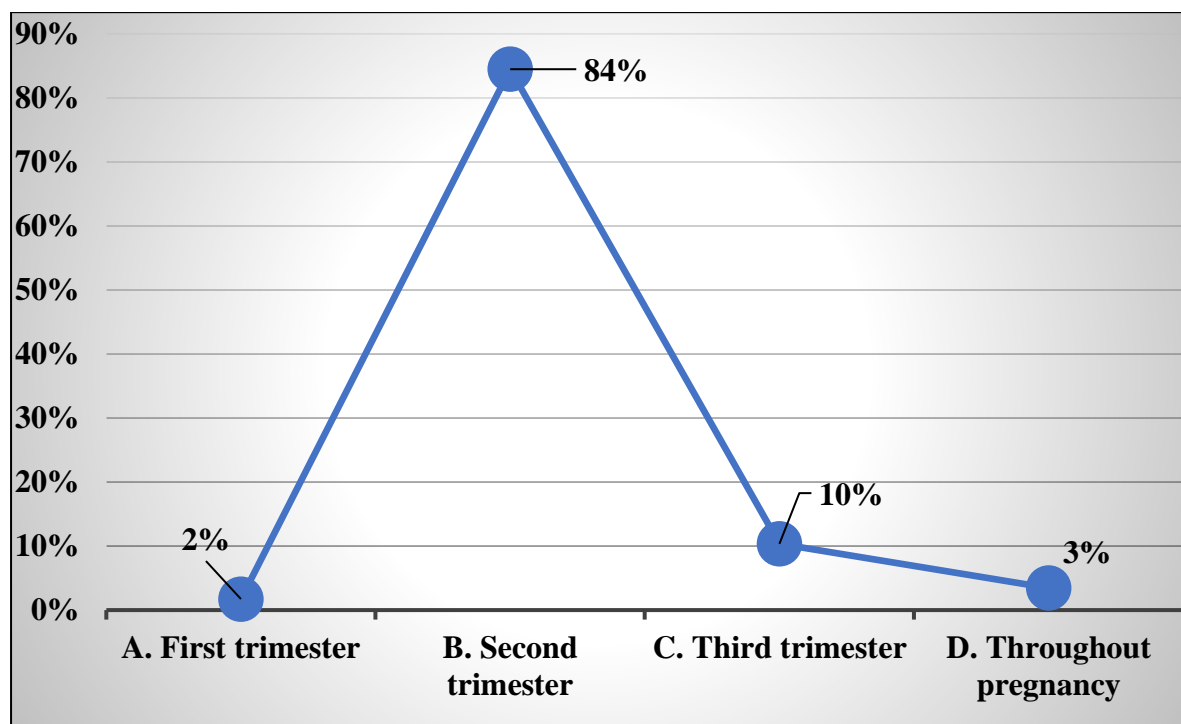
B. No



- **Yes (18%):** A small percentage of clinicians are aware that Doxylamine and Pyridoxine is the first-line treatment for nausea and vomiting during pregnancy as per ACOG.
- **No (82%):** The majority of clinicians are unaware of this recommendation.

2. In your clinical practice, at what stage of pregnancy do you most commonly prescribe Doxylamine and Pyridoxine?

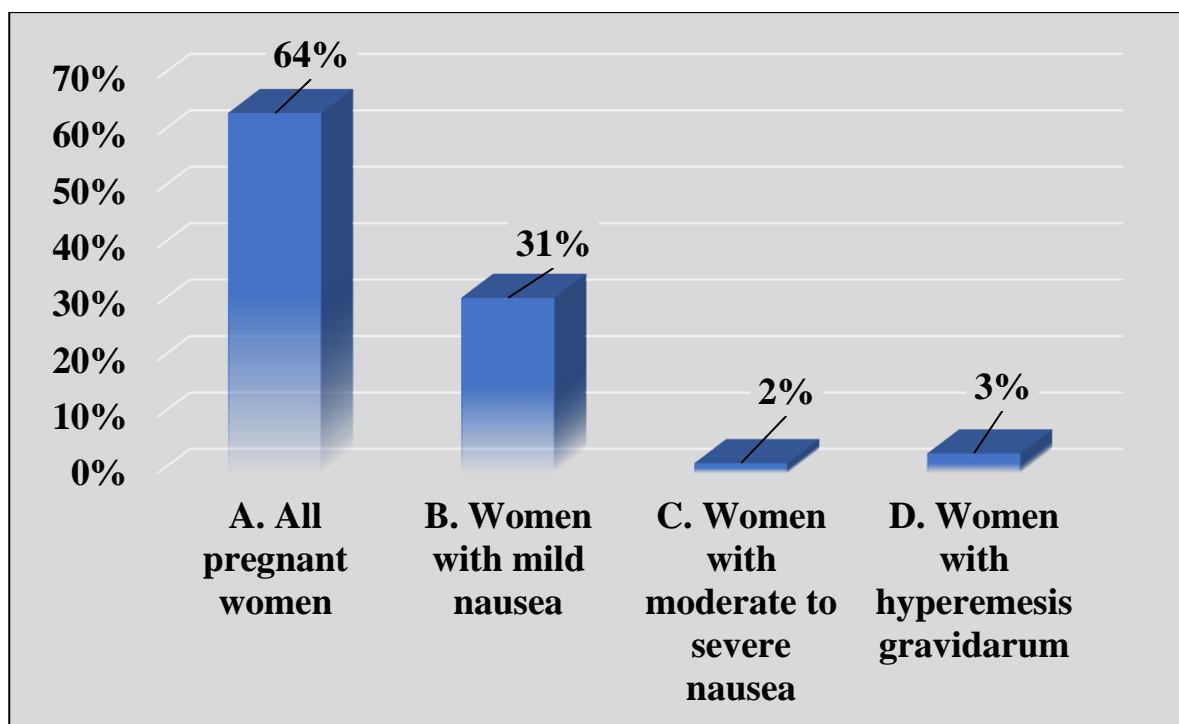
- A. First trimester
- B. Second trimester
- C. Third trimester
- D. Throughout pregnancy



- **First trimester (2%) & Throughout pregnancy (3%):** Very few clinicians prescribe Doxylamine and Pyridoxine during the first trimester & throughout pregnancy.
- **Second trimester (84%):** The majority of clinicians prescribe it during the second trimester.
- **Third trimester (10%):** Some clinicians prefer to prescribe it in the third trimester.

3. According to your opinion, which patient population is most suitable for Doxylamine and Pyridoxine therapy?

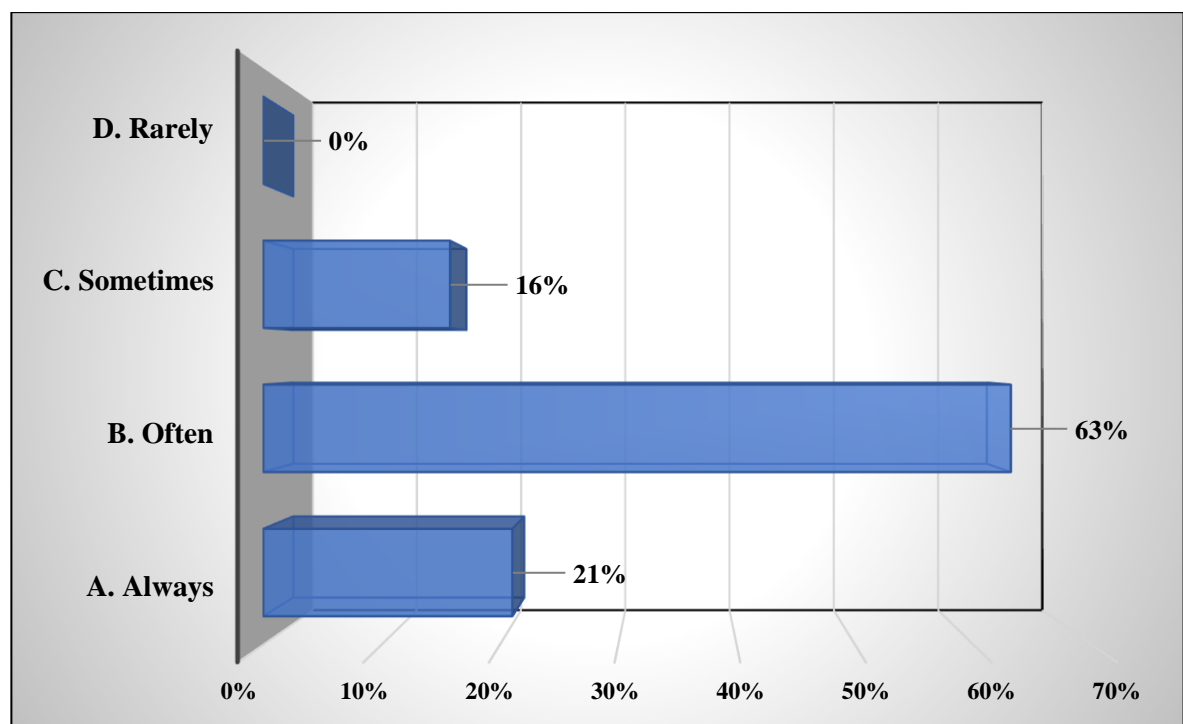
- A. All pregnant women
- B. Women with mild nausea
- C. Women with moderate to severe nausea
- D. Women with hyperemesis gravidarum



- **All pregnant women (64%):** The majority believe Doxylamine and Pyridoxine is suitable for all pregnant women.
- **Women with mild nausea (31%):** Many clinicians find it most suitable for women with mild nausea.
- **Women with moderate to severe nausea (2%) & Women with hyperemesis gravidarum (3%):** Very few recommend it for moderate to severe nausea & hyperemesis gravidarum cases.

4. In your clinical practice, how often do you prescribe Doxylamine and Pyridoxine in morning sickness during pregnancy?

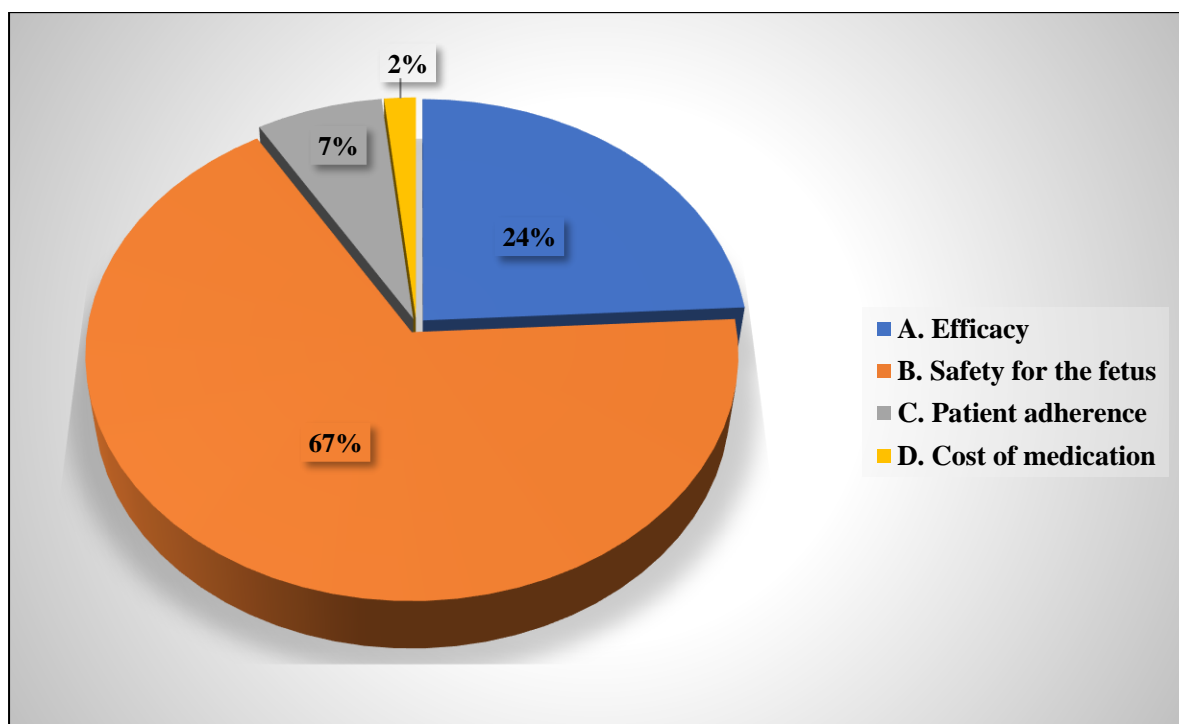
- A. Always
- B. Often
- C. Sometimes
- D. Rarely



- **Always (21%):** A smaller group of clinicians consistently prescribe Doxylamine and Pyridoxine for morning sickness.
- **Often (63%):** The majority frequently recommend it for managing morning sickness.
- **Sometimes (16%):** Some clinicians use it occasionally in their practice.
- **Rarely (0%):** No clinicians reported rarely prescribing it.

5. What is your primary concern when prescribing Doxylamine and Pyridoxine in pregnancy?

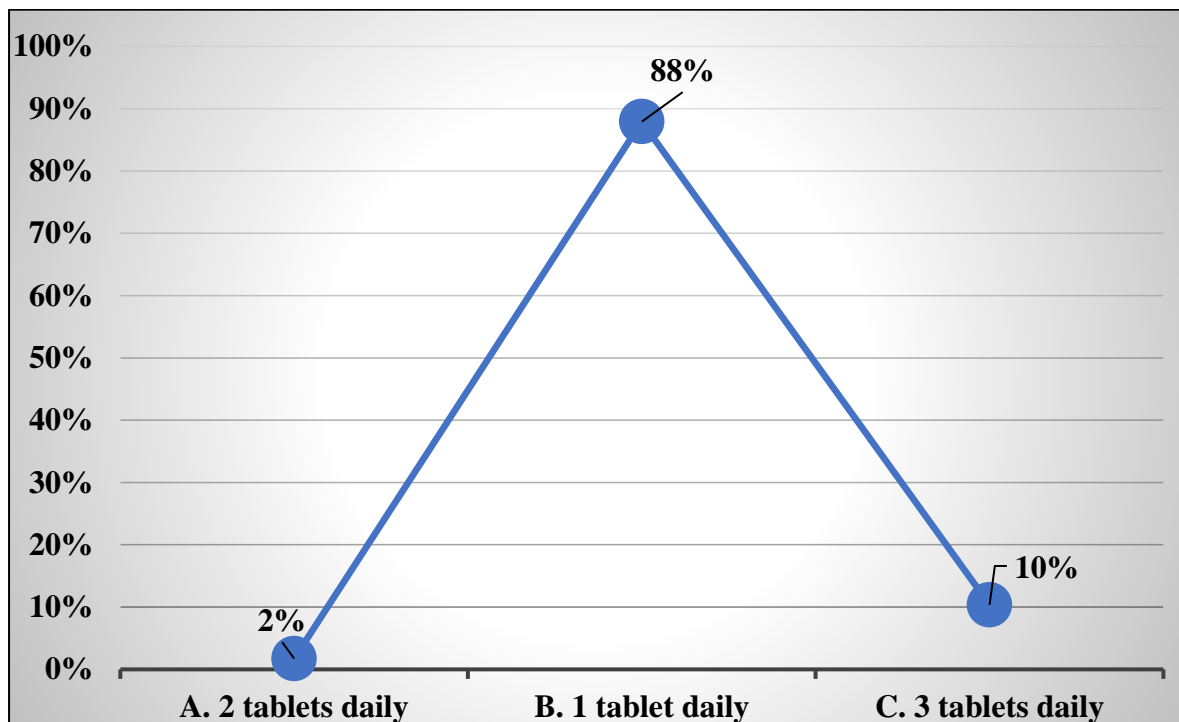
- A. Efficacy
- B. Safety for the fetus
- C. Patient adherence
- D. Cost of medication



- **Efficacy (24%):** A portion of clinicians are primarily concerned about the effectiveness of the medication.
- **Safety for the fetus (67%):** The majority prioritize fetal safety when prescribing Doxylamine and Pyridoxine.
- **Patient adherence (7%) & Cost of medication (2%):** A few clinicians consider patient adherence & cost of the medication as their main concern.

6. According to your opinion, what is the standard starting dose of Doxylamine and Pyridoxine for managing nausea and vomiting in pregnancy?

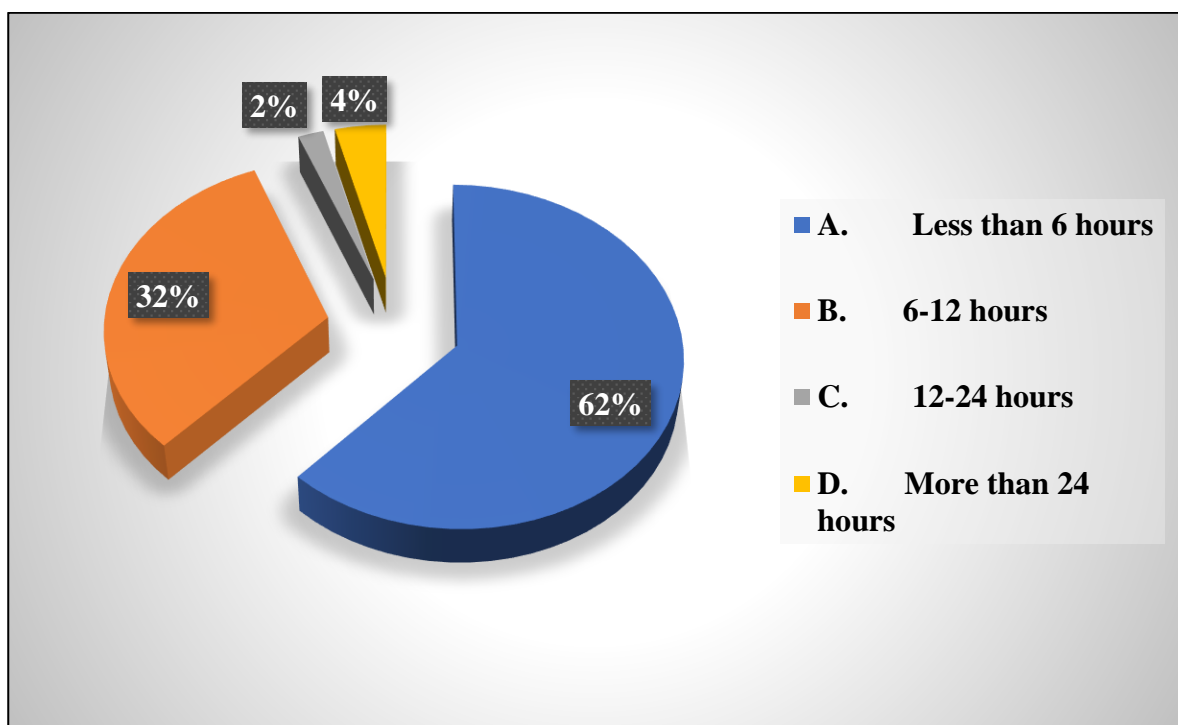
- A. 2 tablets daily
- B. 1 tablet daily
- C. 3 tablets daily



- **2 tablets daily (2%):** A very small percentage of clinicians consider 2 tablets daily as the standard starting dose.
- **1 tablet daily (88%):** The majority believe 1 tablet daily is the standard starting dose for managing nausea and vomiting in pregnancy.
- **3 tablets daily (10%):** Some clinicians suggest starting with 3 tablets daily.

7. In your clinical practice, which strength do you prefer for Doxylamine and Pyridoxine therapy for morning sickness in pregnancy?

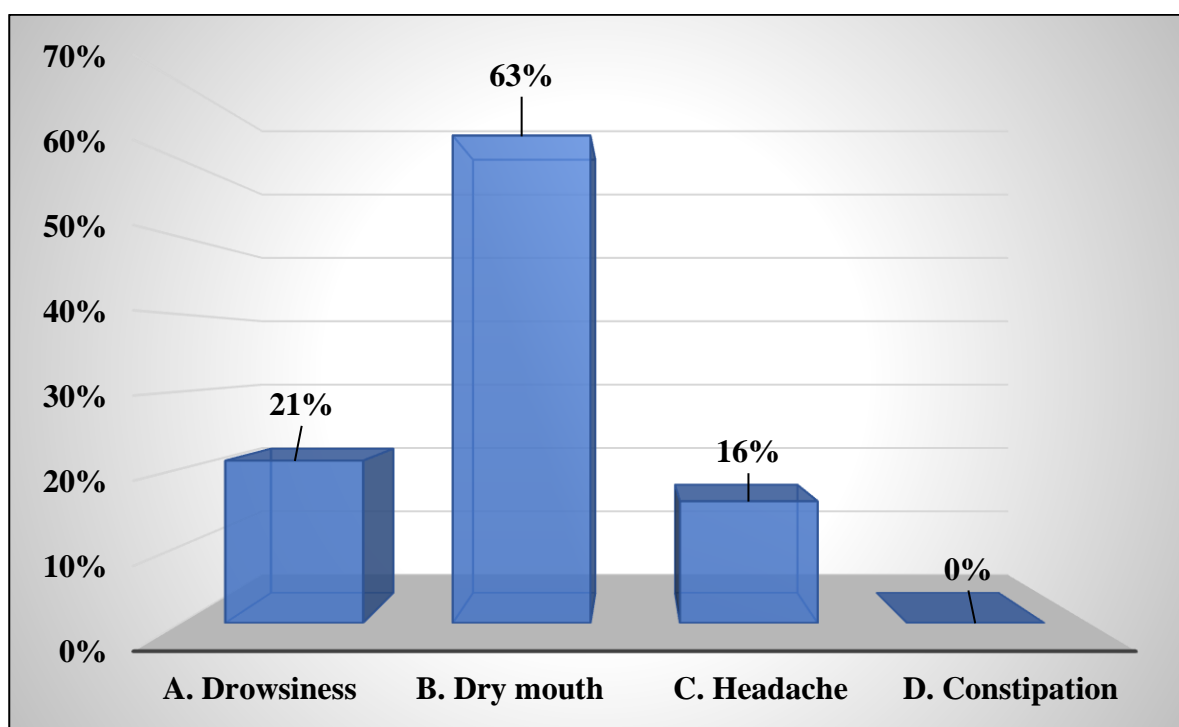
- A. Doxylamine Succinate USP 10 mg and Pyridoxine Hydrochloride (Vitamin B6) IP 10 mg Tablets
- B. Doxylamine Succinate USP 20 mg and Pyridoxine Hydrochloride (Vitamin B6) IP 20 mg Extended Release Tablets.



- **Doxylamine Succinate USP 10 mg and Pyridoxine Hydrochloride (Vitamin B6) IP 10 mg Tablets (18%):** A small percentage of clinicians prefer this lower strength combination.
- **Doxylamine Succinate USP 20 mg and Pyridoxine Hydrochloride (Vitamin B6) IP 20 mg Extended Release Tablets (82%):** The majority prefer this higher strength, extended-release combination for managing morning sickness during pregnancy.

8. In your clinical practice, what common side effect have you observed with Doxylamine and Pyridoxine therapy during pregnancy?

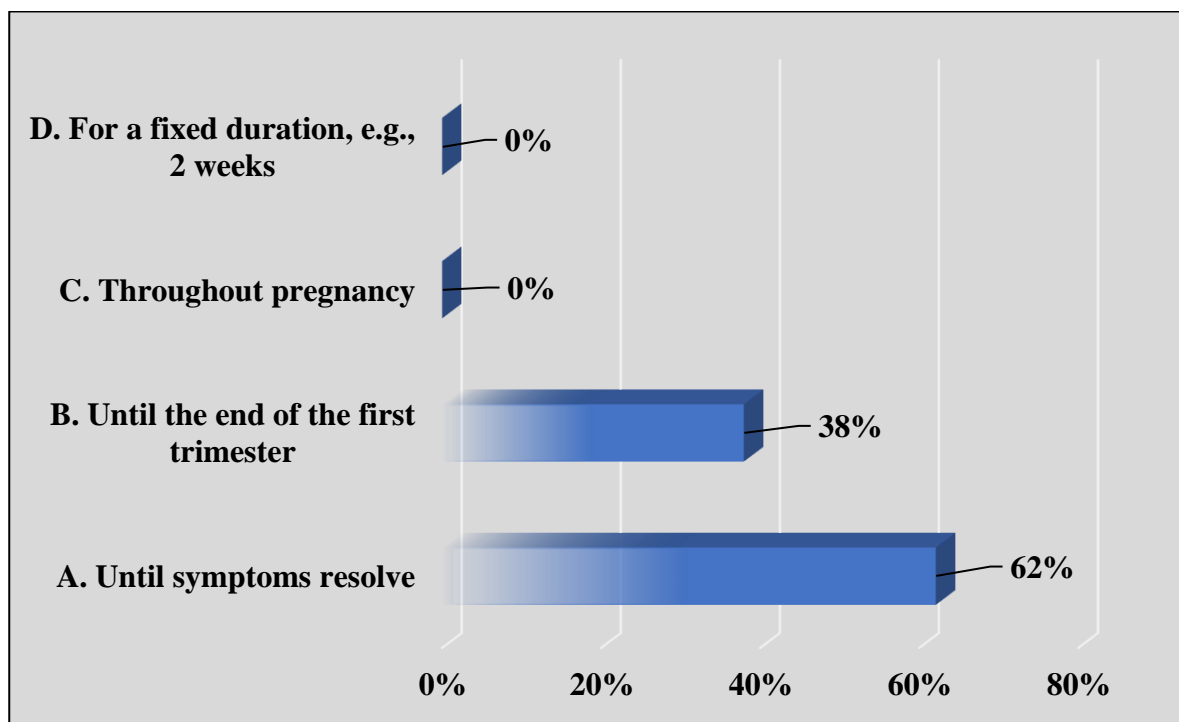
- A. Drowsiness
- B. Dry mouth
- C. Headache
- D. Constipation



- **Drowsiness (21%):** Some patients experience sleepiness as a side effect
- **Dry mouth (63%):** The majority report experiencing dry mouth
- **Headache (16%):** A smaller group reports headache
- **Constipation (0%):** No reports of constipation have been noted

9. In your clinical practice, how long do you typically continue Doxylamine and Pyridoxine therapy in your patients?

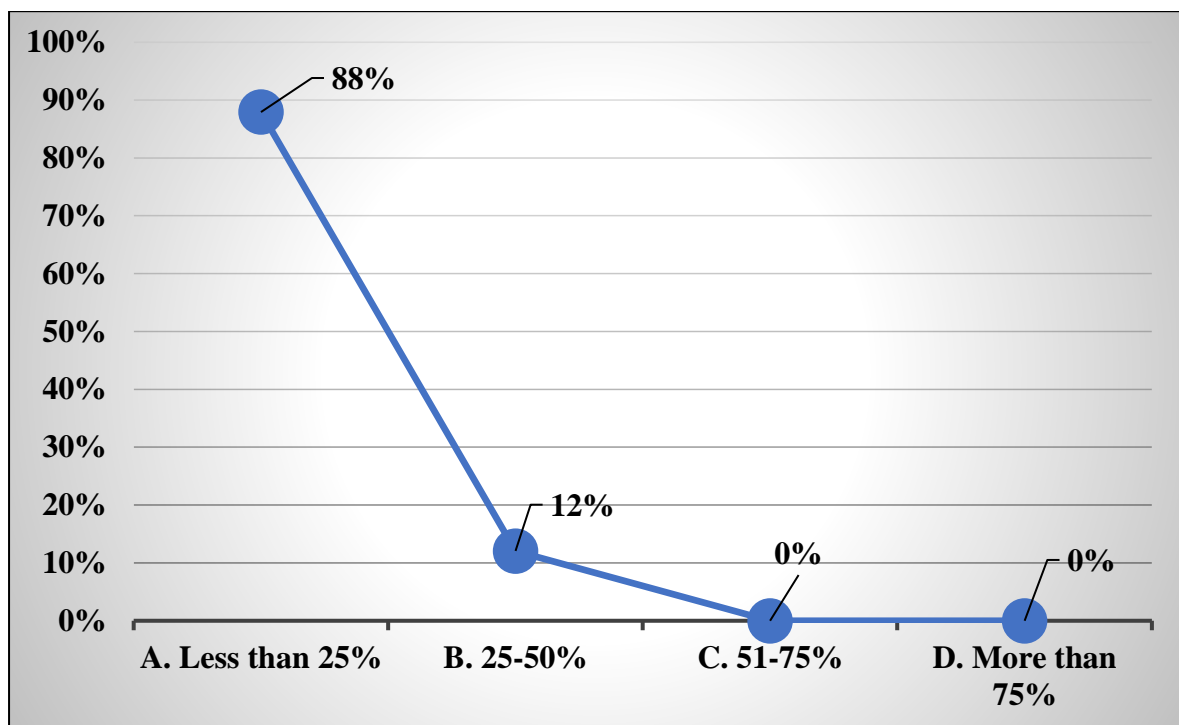
- A. Until symptoms resolve
- B. Until the end of the first trimester
- C. Throughout pregnancy
- D. For a fixed duration, e.g., 2 weeks



- **Until symptoms resolve (62%):** Most stop treatment when symptoms resolve, usually by the end of the first trimester.
- **Until the end of the first trimester (38%):** Some stop treatment by the end of the first trimester.
- **Throughout pregnancy (0%):** Rarely used beyond the first trimester.
- **For a fixed duration, e.g., 2 weeks (0%):** Duration is typically based on symptom resolution, not a set time.

10. In your clinical practice, what percentage of pregnant women report improvement in symptoms after starting Doxylamine and Pyridoxine?

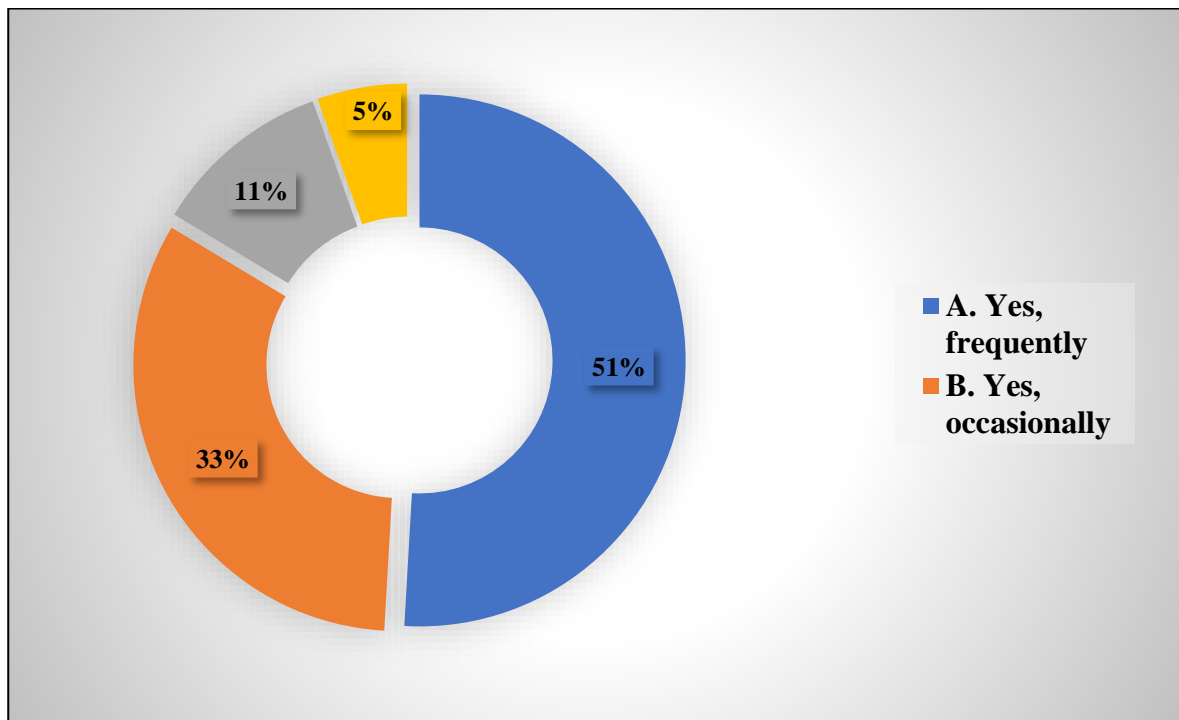
- A. Less than 25%
- B. 25-50%
- C. 51-75%
- D. More than 75%



- **Less than 25% (88%):** The majority of pregnant women report less than 25% improvement in symptoms after starting Doxylamine and Pyridoxine therapy.
- **25-50% (12%):** A smaller percentage of women report 25-50% improvement in symptoms.
- **51-75% (0%):** No patients report 51-75% improvement in symptoms.
- **More than 75% (0%):** No patients report more than 75% improvement in symptoms.

11. In your clinical experience, have you observed any cases where Doxylamine and Pyridoxine were ineffective?

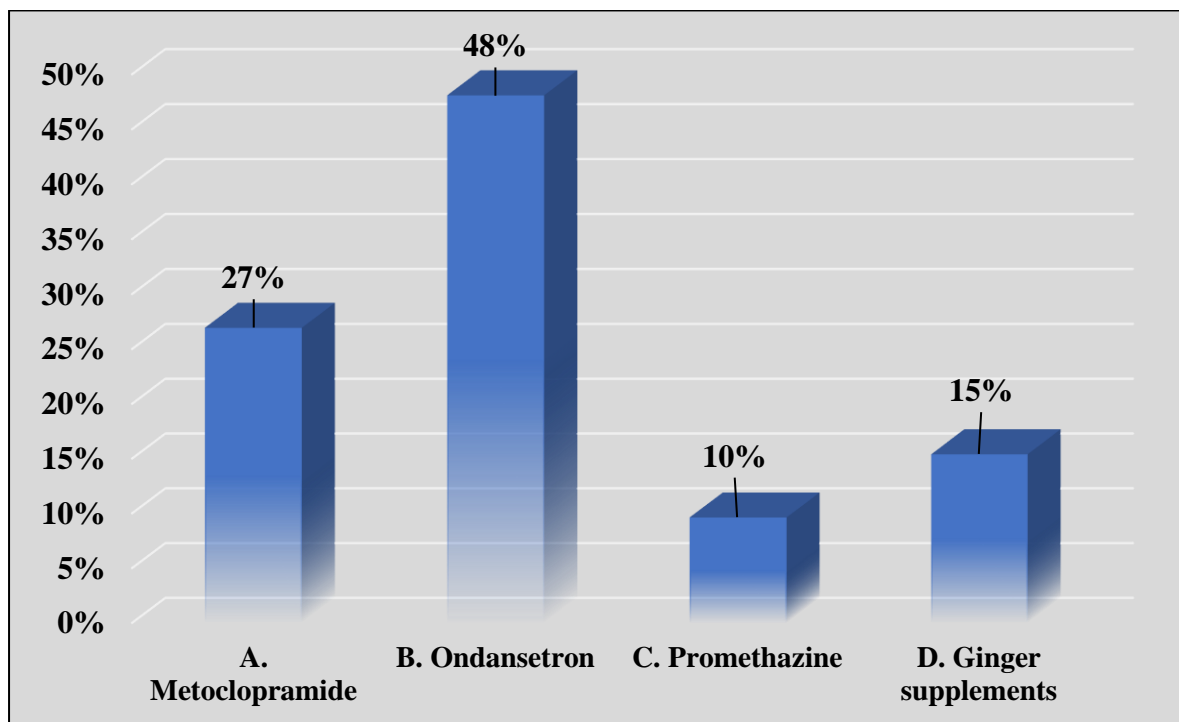
- A. Yes, frequently
- B. Yes, occasionally
- C. Rarely
- D. No



- **Yes, frequently (51%):** In the majority of cases, clinicians have observed that Doxylamine and Pyridoxine were ineffective in treating symptoms.
- **Yes, occasionally (33%):** A significant portion of clinicians report occasional ineffectiveness of Doxylamine and Pyridoxine.
- **Rarely (11%):** Few clinicians report rare instances where the therapy was ineffective.
- **No (5%):** Very few clinicians have not observed any cases of ineffectiveness with Doxylamine and Pyridoxine.

12. In your clinical practice, which alternative therapy do you consider if Doxylamine and Pyridoxine fail?

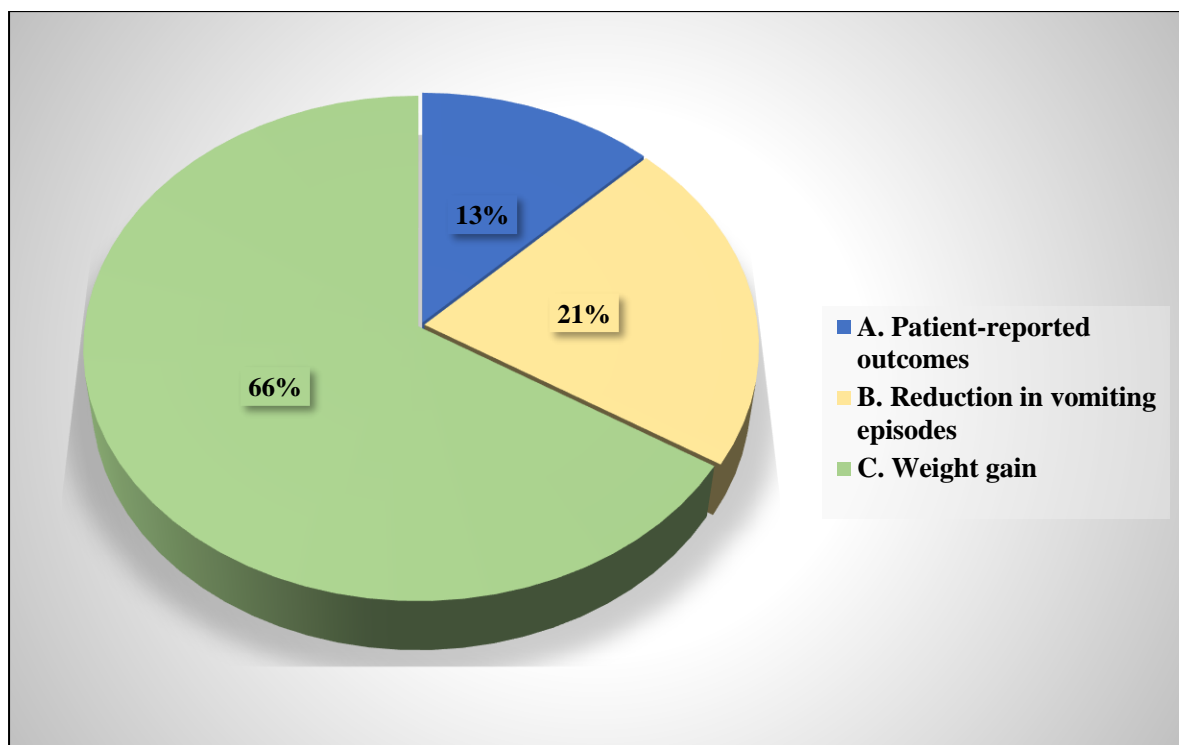
- A. Metoclopramide
- B. Ondansetron
- C. Promethazine
- D. Ginger supplements



- **Metoclopramide (27%):** Some clinicians opt for Metoclopramide as a second-line treatment.
- **Ondansetron (48%):** The majority of clinicians consider Ondansetron as an alternative therapy if Doxylamine and Pyridoxine fail.
- **Promethazine (10%):** Few clinicians consider Promethazine when first-line therapy is ineffective.
- **Ginger supplements (15%):** A smaller portion of clinicians recommend Ginger supplements as an alternative.

13. In your experience, how do you typically assess the effectiveness of Doxylamine and Pyridoxine therapy?

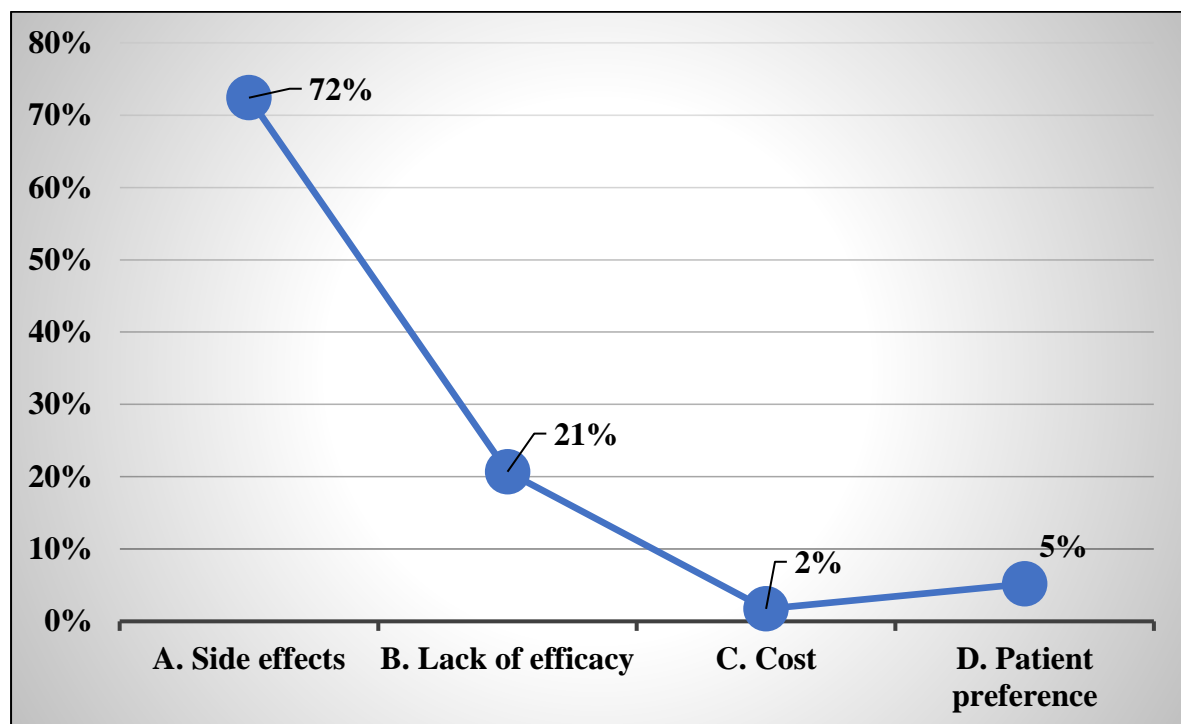
- A. Patient-reported outcomes
- B. Reduction in vomiting episodes
- C. Weight gain



- **Patient-reported outcomes (13%):** A smaller percentage rely on patient-reported outcomes, such as subjective symptom relief, to evaluate therapy effectiveness.
- **Reduction in vomiting episodes (21%):** Some clinicians assess effectiveness by tracking a decrease in vomiting episodes.
- **Weight gain (66%):** The majority of clinicians assess the effectiveness of Doxylamine and Pyridoxine therapy by monitoring weight gain, as it is a key indicator of improved nutritional status and symptom control.

14. In your experience, what is the most common reason for discontinuation of Doxylamine and Pyridoxine therapy?

- A. Side effects
- B. Lack of efficacy
- C. Cost
- D. Patient preference

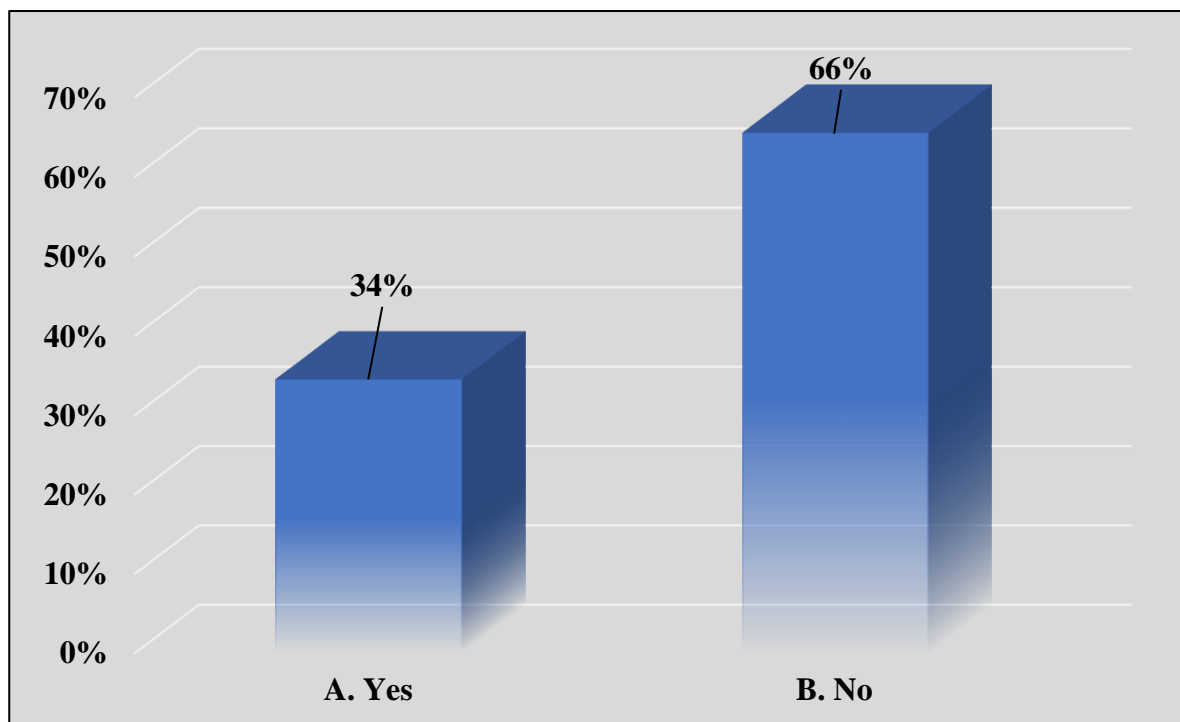


- **Side effects (72%):** The most common reason for discontinuation of Doxylamine and Pyridoxine therapy is side effects, such as drowsiness or other adverse reactions.
- **Lack of efficacy (21%):** Some patients discontinue therapy due to the lack of effectiveness in alleviating symptoms.
- **Cost (2%) & Patient preference (5%):** A small percentage of patients discontinue due to the cost of the medication & patient preference.

15. In your clinical practice, do you recommend any additional supplements or dietary changes along with Doxylamine and Pyridoxine?

A. Yes

B. No

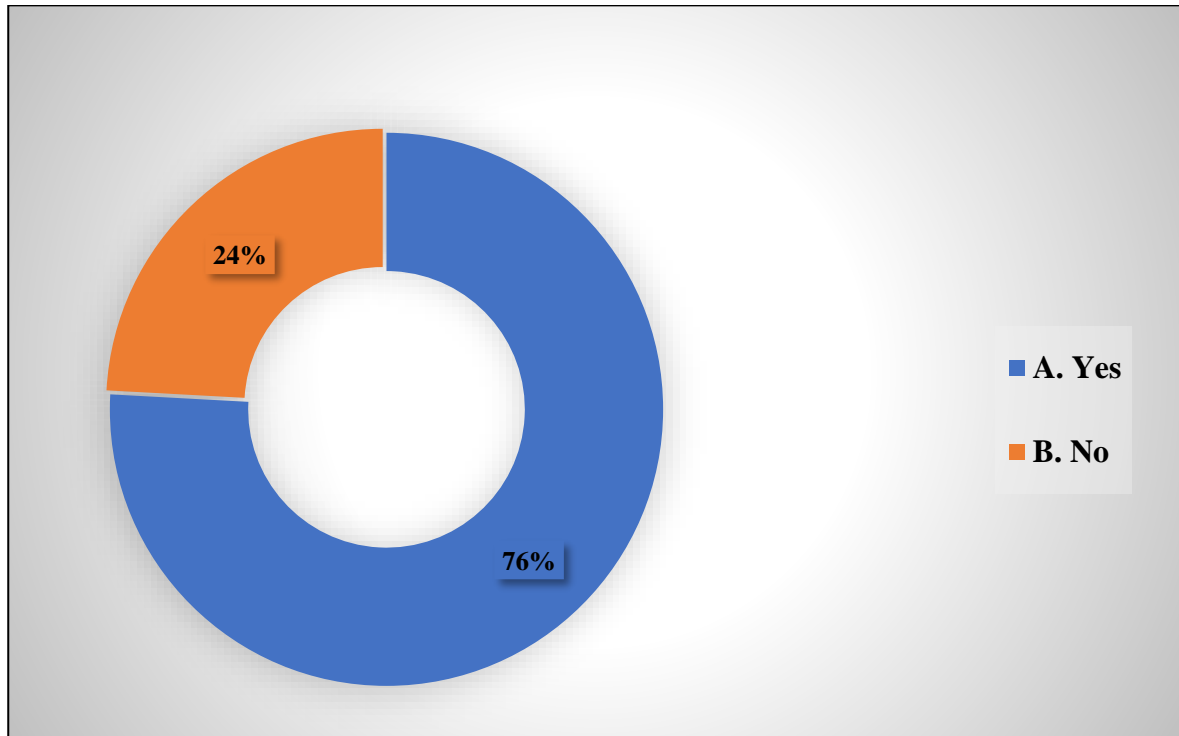


- **Yes (34%):** A portion of clinicians recommend additional supplements or dietary changes alongside Doxylamine and Pyridoxine to support symptom management and overall health.
- **No (66%):** The majority of clinicians do not routinely recommend additional supplements or dietary changes along with Doxylamine and Pyridoxine.

16. In your clinical practice, do you routinely recommend Doxylamine and Pyridoxine as first-line therapy for nausea and vomiting in pregnancy?

A. Yes

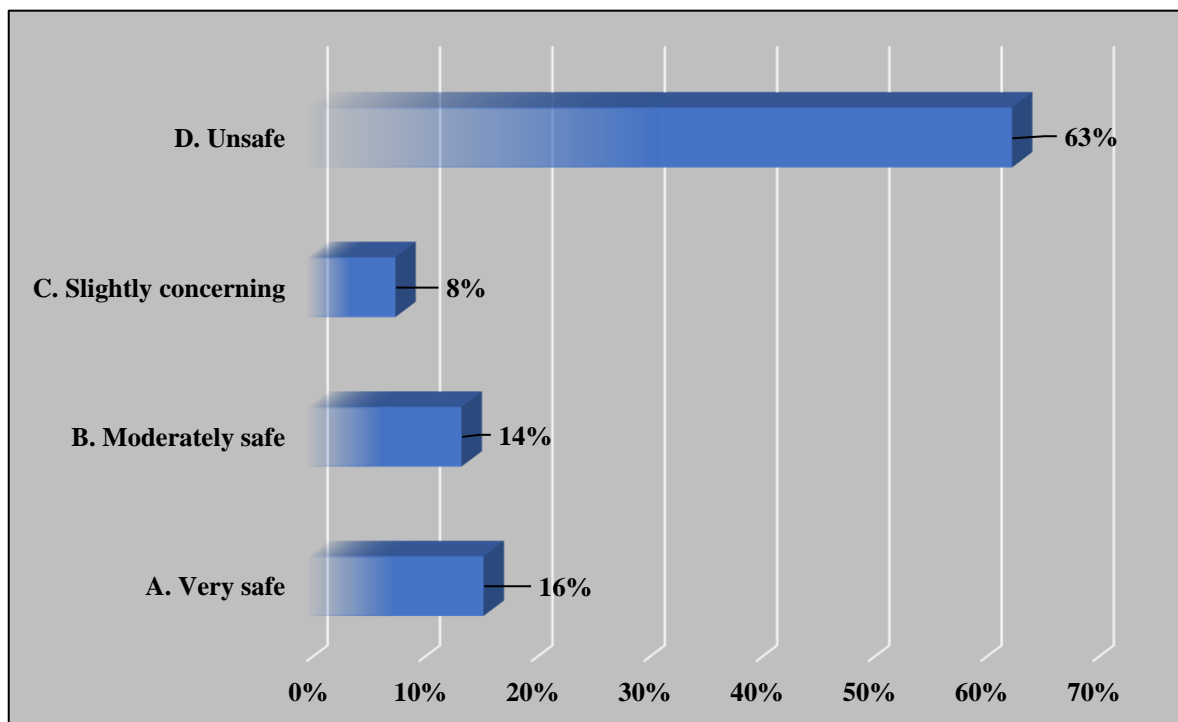
B. No



- **Yes, (76%):** The majority of clinicians routinely recommend Doxylamine and Pyridoxine as first-line therapy for nausea and vomiting in pregnancy.
- **No (24%):** A smaller percentage of clinicians do not recommend it as the first-line treatment.

17. What is your opinion on the safety profile of Doxylamine and Pyridoxine in pregnancy?

- A. Very safe
- B. Moderately safe
- C. Slightly concerning
- D. Unsafe

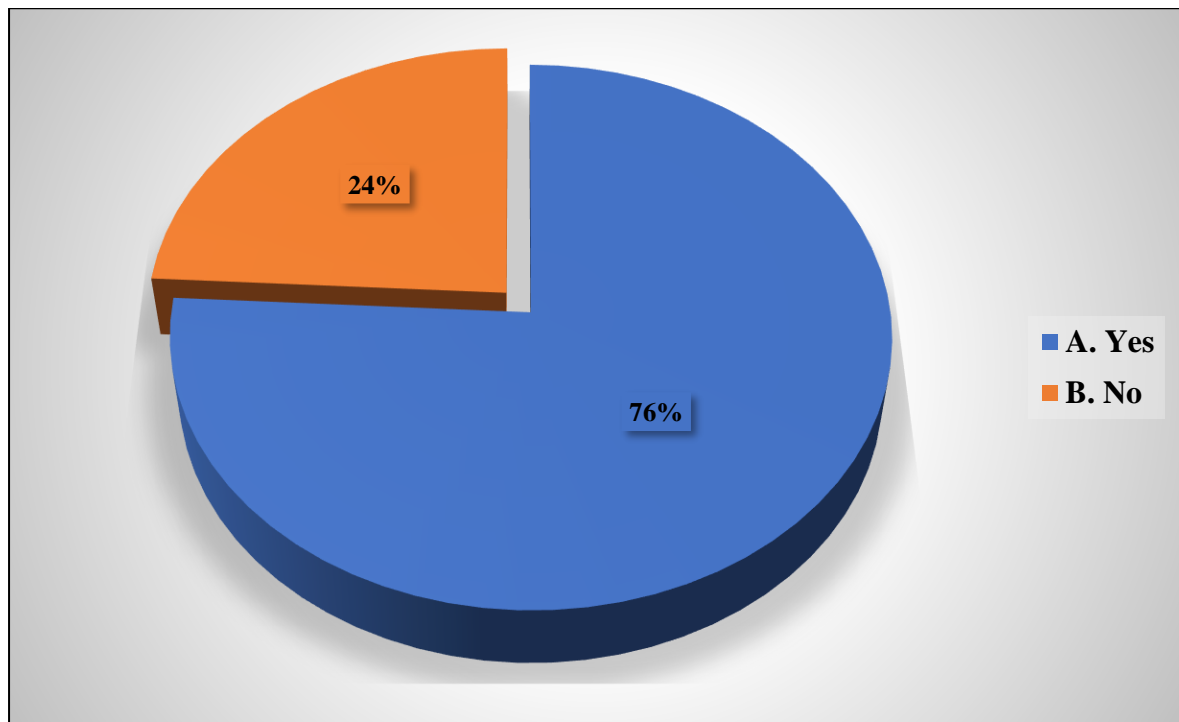


- **Unsafe (63%):** Most clinicians have safety concerns about Doxylamine and Pyridoxine in pregnancy due to potential side effects and limited long-term data.
- **Very safe (16%) & Moderately safe (14%):** Some clinicians consider Doxylamine and Pyridoxine safe for pregnancy due to their widespread use and available evidence.
- **Slightly concerning (8%):** Few clinicians find the safety profile of Doxylamine and Pyridoxine slightly concerning, possibly due to individual patient factors.

18. In your clinical practice, have you encountered any adverse effects related to the fetus with Doxylamine and Pyridoxine therapy?

A. Yes

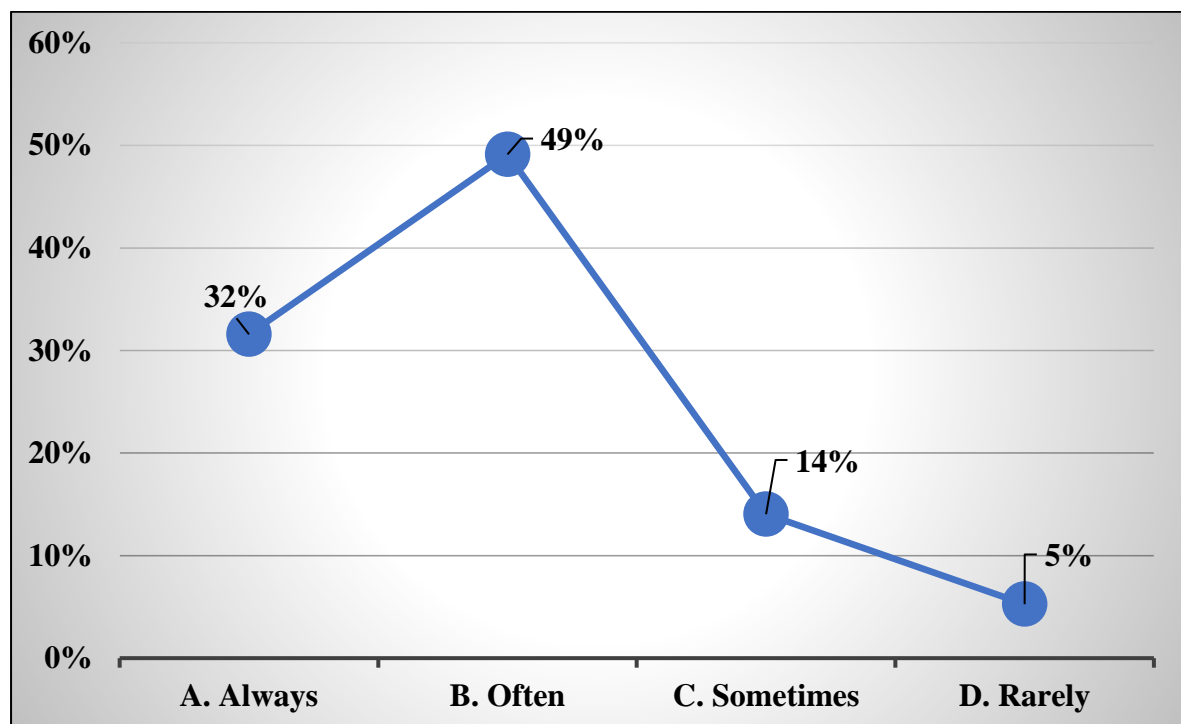
B. No



- **Yes (76%):** Most clinicians have encountered fetal adverse effects associated with Doxylamine and Pyridoxine therapy.
- **No (24%):** A smaller percentage of clinicians have not observed any fetal adverse effects.

19. In your clinical practice, do you consider patient preference when prescribing Doxylamine and Pyridoxine?

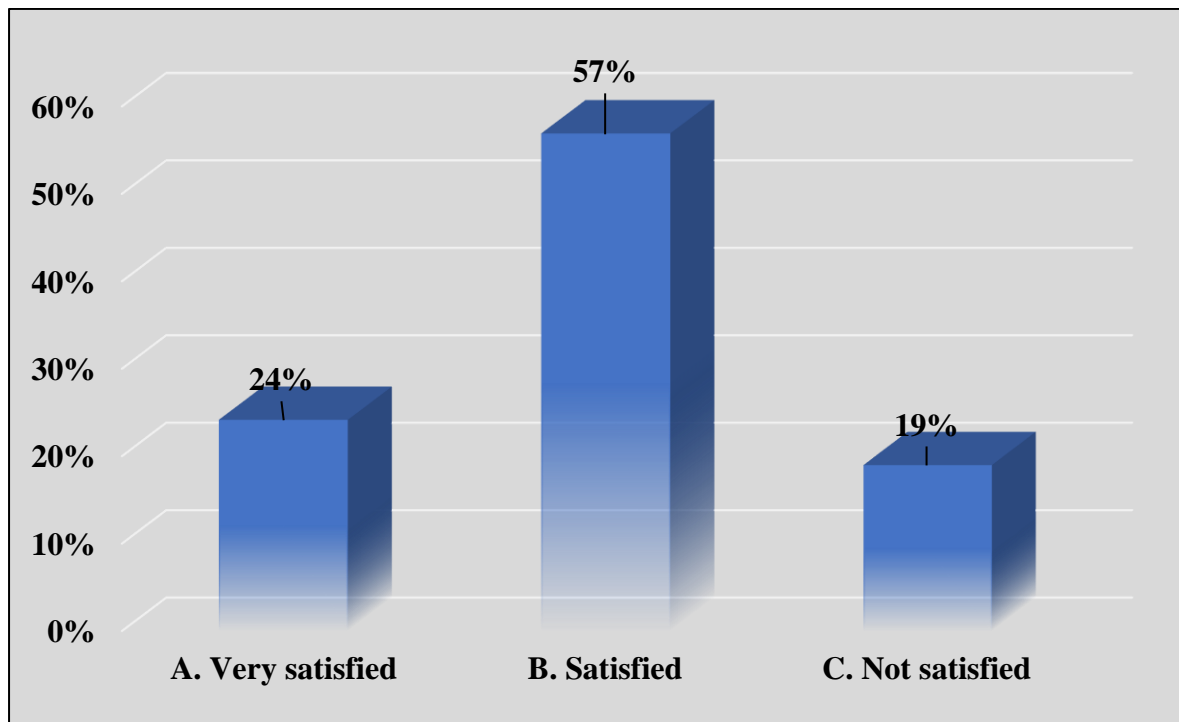
- A. Always
- B. Often
- C. Sometimes
- D. Rarely



- **Always (32%):** A significant portion of clinicians always take patient preference into account.
- **Often (49%):** Most clinicians often consider patient preference when prescribing Doxylamine and Pyridoxine.
- **Sometimes (14%):** Some clinicians consider patient preference occasionally.
- **Rarely (5%):** Few clinicians rarely factor in patient preference.

20. In your clinical practice, how satisfied are your patients with Doxylamine and Pyridoxine in morning sickness during pregnancy?

- A. Very satisfied
- B. Satisfied
- C. Not satisfied



- **Very satisfied (24%):** A smaller portion of patients report being very satisfied with the therapy.
- **Satisfied (57%):** The majority of patients are satisfied with Doxylamine and Pyridoxine for managing morning sickness during pregnancy.
- **Not satisfied (19%):** Some patients are not satisfied with the treatment's effectiveness or tolerability.

SUMMARY

This study provides valuable insights into the clinical practices and perspectives regarding the use of Doxylamine and Pyridoxine in managing nausea and vomiting during pregnancy.

- **Awareness of Recommendations:** A notable 82% of clinicians are unaware that Doxylamine and Pyridoxine is the first-line treatment for pregnancy-related nausea as per ACOG guidelines.
- **Prescribing Practices by Trimester:** Most clinicians (84%) prescribe it during the second trimester, with fewer recommending it in the first (2%) or third trimesters (10%).
- **Patient Suitability:** While 64% believe it is suitable for all pregnant women, others recommend it for mild nausea (31%) and rarely for severe cases or hyperemesis gravidarum (5%).
- **Usage Frequency:** The majority (63%) often prescribe Doxylamine and Pyridoxine for morning sickness, with 21% always doing so.
- **Concerns in Prescribing:** Fetal safety (67%) is the leading concern, followed by efficacy (24%), patient adherence (7%), and cost (2%).
- **Dosing Preferences:** Most clinicians (88%) start with 1 tablet daily, while others suggest 3 tablets (10%) or 2 tablets (2%).
- **Strength Preferences:** The extended-release combination of Doxylamine Succinate 20 mg and Pyridoxine Hydrochloride 20 mg is preferred by 82% of clinicians.
- **Side Effects:** Dry mouth (63%) and drowsiness (21%) are common, with no reports of constipation.
- **Treatment Duration:** Most clinicians (62%) stop therapy when symptoms resolve, often by the end of the first trimester.

- **Symptom Improvement:** Only 12% report moderate improvement (25–50%) in symptoms, with 88% noting less than 25% improvement.
- **Effectiveness Issues:** Frequently or occasionally ineffective in 84% of cases, according to clinicians.
- **Alternative Therapies:** Ondansetron (48%) is the preferred second-line treatment, followed by Metoclopramide (27%) and Ginger supplements (15%).
- **Evaluation of Effectiveness:** Weight gain (66%) is the primary measure of therapeutic success.
- **Reasons for Discontinuation:** Side effects (72%) and lack of efficacy (21%) are the most common reasons for stopping therapy.
- **Additional Recommendations:** Most clinicians (66%) do not recommend supplements or dietary changes alongside the therapy.
- **Routine Use:** Doxylamine and Pyridoxine are routinely recommended as first-line therapy by 76% of clinicians.
- **Safety Concerns:** Most clinicians (63%) find its safety profile in pregnancy concerning, with 76% having observed fetal adverse effects.
- **Patient Preference Consideration:** Clinicians often (49%) or always (32%) consider patient preference when prescribing.
- **Patient Satisfaction:** A majority (57%) report satisfaction with the therapy, although 19% are not satisfied.

DISCUSSION

The findings reveal significant gaps in awareness and variability in practice patterns for Doxylamine and Pyridoxine therapy. While widely prescribed, concerns about its safety and effectiveness remain prevalent. Weight gain is the most common measure of success, but patient satisfaction is mixed, and side effects lead to discontinuation in many cases.

CLINICAL RECOMMENDATIONS

- **Increase Awareness:** Launch educational programs to improve clinicians' understanding of Doxylamine and Pyridoxine therapy, including its recommended use, safety, and efficacy in managing nausea and vomiting during pregnancy.
- **Address Safety Concerns:** Provide updated and comprehensive safety data to alleviate clinician concerns, particularly around fetal outcomes.
- **Enhance Patient Satisfaction:** Encourage the incorporation of patient-centered approaches, including shared decision-making and considering individual preferences, to improve adherence and satisfaction.
- **Improve Guidelines and Standardization:** Develop and disseminate clear guidelines on dosing, duration, and monitoring of Doxylamine and Pyridoxine therapy.

CONSULTANT OPINION

Expert opinions on Doxylamine and Pyridoxine are divided. While many view it as a useful first-line option for managing nausea and vomiting in pregnancy, concerns persist about its safety profile and effectiveness. Continued research and transparent communication about benefits and risks are recommended to address these concerns and optimize its role in clinical practice.

MARKET OPPORTUNITIES

The growing demand for safe and effective treatments for nausea in pregnancy presents several opportunities:

- **Educational Campaigns:** Targeting clinicians with comprehensive information on the safety and efficacy of Doxylamine and Pyridoxine can enhance adoption.
- **Safety Data Dissemination:** Promoting research findings and long-term data to establish confidence in its use during pregnancy.
- **Alternative Solutions:** With many clinicians expressing dissatisfaction with current outcomes, there is an opportunity to explore and integrate complementary therapies or combination treatments.

MARKET POSITIONING

To better position Doxylamine and Pyridoxine as a preferred therapy:

- **Highlight Proven Benefits:** Emphasize its status as a first-line therapy supported by organizations like ACOG, ensuring clinicians understand its efficacy and safety profile.

- **Target Key Demographics:** Focus marketing and education efforts on obstetricians, gynecologists, and general practitioners who frequently manage pregnant patients.
- **Leverage Patient Advocacy:** Partner with patient groups to share real-life success stories, enhancing credibility and patient awareness.
- **Foster Trust through Transparency:** Address safety concerns proactively by providing robust clinical evidence and clear communication, building confidence among clinicians and patients.

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