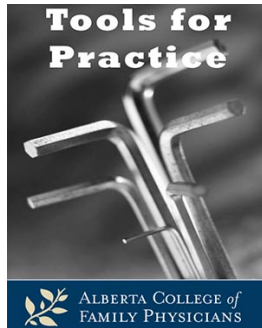


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Doxylamine and Pyridoxine for Nausea and Vomiting of Pregnancy: A review of “retch”ed evidence

Clinical Question: What is the safety and efficacy of doxylamine/pyridoxine (Diclectin®) in nausea and vomiting of pregnancy?

Bottom Line: Doxylamine/B6 appears safe short-term and may be slightly better than placebo in reducing nausea and vomiting in pregnancy (~1 point better on 15-point scale). B6 alone may have similar effect on nausea but other effects unclear. Results are at high risk of bias due to initially undeclared industry support and methodological concerns.

Evidence:

Safety:

- Five systematic reviews of 22-37 observational studies (17,000-50,000 pregnant women) exposed to antihistamines like doxylamine.¹⁻⁵ Many authors have industry affiliations.^{1,3-5}
 - No reliable effect on malformations with doxylamine.¹⁻⁵

Efficacy:

- Four systematic reviews:⁶⁻⁹ Not discussed as did not include largest Randomized Controlled Trial (RCT), published 2017.¹⁰
- 2017 publication of 1970s industry-sponsored (eight arm) RCT: 2,359 women of doxylamine, B6, and dicyclomine alone or in various combinations, or placebo, for seven days.¹⁰
 - Percent improvement from baseline for doxylamine/B6 versus placebo, statistically significant:
 - ≥Moderate undefined “effectiveness” (78% versus 57%).
 - Nausea (75% versus 52%); not vomiting.
 - Patients rated doxylamine/B6 better on nausea and vomiting.
 - B6 alone better than placebo for nausea (68% versus 52%), but not statistically better for vomiting, overall effectiveness or patient ratings.
 - Drowsiness: 5.6% versus 3% (placebo), Number Needed to Harm=38.
 - Limitations: Only 66% completed study, questionable data integrity, possible selective reporting.
- Industry-sponsored RCT (259 women) of doxylamine/B6 or placebo.¹¹

- ~1-point decrease in 15-point nausea/vomiting scale at day 15.
- No change in individual nausea, vomiting, retching scores.¹²
- US RCT (36 women) found ondansetron superior to doxylamine/B6 in reducing nausea (3 out of 10-point scale better) but not vomiting.¹³
 - Limitations: Used ½ dose doxylamine.
- Older studies less reliable.⁶

Context:

- Disclosed and undisclosed conflicts of interest raise concerns around some of the analysis and reporting of doxylamine/B6 research.¹⁴
- Cochrane review states “lack of high quality evidence to support any particular intervention”, including doxylamine/B6, B6 alone, metoclopramide, or ginger.⁶
- Guidelines recommend first-line: Antihistamines, phenothiazines (like prochlorperazine), or ginger (UK),¹⁵ B6 alone (US),¹⁶ or doxylamine/B6 (US, Canada).^{16,17}

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Disclosure:

Authors do not have any conflicts of interest to declare.

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