

FROM THE FAMILY PRACTICE INQUIRIES NETWORK

What medications are safe and effective for heartburn during pregnancy?

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■ EVIDENCE-BASED ANSWER

Ranitidine is the best-studied agent effective for treatment of heartburn in pregnancy. Some antacids are effective, but it may be prudent to avoid them in the first trimester until better safety studies are published. Although sucralfate, metoclopramide, and the proton pump inhibitors are probably safe in pregnancy, there are no data about their efficacy. (Grade of Recommendation: B [limited randomized controlled trials of short duration and small sample size])

■ RECOMMENDATIONS FROM OTHERS

Standard texts suggest that antacids¹ or histamine (H₂) blockers² be used as first-line agents for reflux. Burrow and Duffy³ recommend a stratified approach with antacids followed by H₂-blockers, reserving the use of proton pump inhibitors for the more severe cases.

■ EVIDENCE SUMMARY

Heartburn affects 30% to 50% of pregnancies and occurs primarily in the second and third trimesters.⁴ Lifestyle changes and dietary modification are recommended as initial measures for relief of symptoms.

Antacids

Each of the 3 identified placebo-controlled trials of antacid therapy had significant methodologic limitations. Aluminum phosphate more frequently produced complete relief of moderate to severe heartburn at 60 minutes compared with placebo ($P < .001$; number needed to treat [NNT] = 2.1 for mild heartburn and 20 for severe).⁵ Patients who received a combination of magnesium and aluminum hydroxide for 7 days had no more relief of symptoms than the placebo group.⁶ Atlay and colleagues⁷ found that sodium bicarbonate significantly reduced reflux symptoms compared with placebo ($P = .021$; NNT=6.0).

There are limited data regarding the safety of antacids during pregnancy. A single case-control study found a higher rate of congenital anomalies in children of women who took antacids in the first trimester (unadjusted odds ratio calculated from data=2.36; $P < .05$).⁸ This association was not detected when studied over the entire

pregnancy. The rate of malformations was not different for magnesium, aluminum, and bicarbonate. The association could well be due to recall bias or other systematic biases inherent in case-control methodology.

H2-Blockers

The only identified studies of H2-blockers evaluated ranitidine. A 4-week double-blind randomized control trial found that ranitidine 150 mg twice daily reduced patient symptoms by 44% over placebo ($P < .05$).⁹ This study was limited by its short duration (<1 month) and small sample size (N=30). A 2-week study that compared antacids plus ranitidine to antacids alone found a 52% decrease in symptoms in the ranitidine group and a 44% reduction in the antacid-alone group.¹⁰ Ranitidine, cimetidine, and famotidine are US Food and Drug Administration (FDA) pregnancy category B (no demonstrated risk).

Proton Pump Inhibitors

In nonpregnant adults, proton pump inhibitors are more effective than antacids and H2-blockers for gastroesophageal reflux disease (GERD). No cohort or control studies have been performed on their efficacy in pregnancy. On the basis of animal studies, omeprazole is a category C drug (potential benefit of use should outweigh potential risks). A cohort study of 113 women found no associated anomalies (relative risk=1.94; 95% confidence interval, 0.36-10.36).¹¹ Pantoprazole, lansoprazole and rabeprazole are category B medications.

Other Agents

Metoclopramide and sucralfate have been used in nonpregnant adults with GERD. Although both are category B, there are no data about their effectiveness for heartburn during pregnancy.

CLINICAL COMMENTARY

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Heartburn along with morning sickness and back pain frequently diminishes the joy of pregnancy. Simple nonpharmacologic solutions such as frequent small meals, remaining upright after eating, and elevating the head of the bed will often suffice. The traditional use of agents in their order of development (antacids, H2-blockers, then proton pump inhibitors) finds some justification in this review for selected agents. Particularly enlightening was the rationale for specific agents: aluminum phosphate has efficacy as an antacid; ranitidine is the only studied H2-blocker; and there are 3 FDA category B proton pump inhibitors (pantoprazole, lansoprazole, and rabeprazole). Specific recommendations for these agents would improve patient benefit with a minimum of therapeutic trials frustrating both patient and physician.

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