



Crying babies: Can proton pump inhibitors help?

CLINICAL QUESTION

In infants (≤ 1 year) with crying/irritability attributed to feeds, do proton pump inhibitors (PPIs) improve symptoms over placebo without additional harms?

BOTTOM LINE

PPIs do not improve crying, fussiness, irritability, or regurgitation attributed to feeds. However, PPIs may increase the risk of serious adverse effects (e.g., respiratory tract infections) from 2.5% on placebo to 12% at 4 weeks.

EVIDENCE

- Results statistically significant unless indicated. Randomized, controlled trials (RCTs) on infants retrieved from systematic reviews in the last ten years since no meta-analyses available.¹⁻⁵
- Two placebo-controlled RCTs of PPIs; four-week duration:^{6,7}
 - 162 infants (median age: 4 months) crying within 1 hour of $\geq 25\%$ of feeds; lansoprazole (0.2-1.5mg/kg/day):⁶
 - $\geq 50\%$ reduction in feedings with crying episode(s)/duration of episodes: 54% in each group.
 - Crying, regurgitations, stopped feedings, feed refusal, back arching: No differences.

- Serious adverse events (e.g., respiratory tract infections): 12% versus 2.5% (placebo), number needed to harm (NNH)=10.
 - 30 infants (mean age: 5 months) with frequent crying and reflux confirmed on biopsy/pH monitoring; omeprazole (10-20mg/day):⁷
 - Crying/fussing (minutes/24 hours): No difference.
 - Irritability (0-10 visual analogue score, lower=better): No difference.
- No placebo-controlled RCTs of histamine-2 receptor antagonists.
 - Head-to-head comparisons versus PPI: No difference.⁸
- Four withdrawal RCTs (8-268 infants, 1-11 months): Open-label treatment with rabeprazole,⁹ esomeprazole,¹⁰ pantoprazole,¹¹ or famotidine¹² x 1-4 weeks; responders/compliers randomized to blinded continued drug or placebo. At 4-5 weeks:
 - Vomiting, regurgitation, irritability, feeding difficulties, symptoms scores, adverse effects: No differences.⁹⁻¹¹
 - Weight: No difference.⁹
- Limitations: Most RCTs industry funded.^{6,9-12}

CONTEXT

- Frequent effortless regurgitation of feeds is common in early infancy (affecting ≥40%).¹³
- Regurgitation accompanied by distress symptoms (e.g., crying, back arching, irritability) have traditionally been attributed to gastroesophageal reflux disease. While PPIs improve esophageal pH in infant RCTs,⁷ they do not improve symptoms.
- Guidelines recommend against empiric trials of acid-suppressing drugs for crying/distress or regurgitation.^{13,14} Parents can be reassured that frequent regurgitation can be normal and frequently settles (90% have resolution at age ≤1 year).¹³

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