


Esomeprazole for the Treatment of GERD in Infants Ages 1–11 Months


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DỊCH VỤ 2


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BACKGROUND

- Gastroesophageal reflux (GER) is defined as the retrograde passage of gastric contents into the esophagus or extraesophageal regions, which affects approximately 50% of healthy infants ages 0 to 3 months.
- In a study involving 948 healthy infants 13 months or younger, 50% of those ages 0 to 3 months, 67% of those ages 4 months, and 21% of those ages 6 to 7 months regurgitated at least once daily
- In most infants, regurgitation decreases in frequency or resolves completely by 12 months of age.

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- Simple physiological reflux can lead to pathologic gastroesophageal reflux disease (GERD) when reflux produces adverse symptoms or characteristic histologic and/or endoscopically visible changes (eg, esophageal erosions).
 - Clinical symptoms of GERD in infants include recurrent vomiting, poor weight gain, irritability, dysphagia, discomfort, esophagitis and respiratory disorders.

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- One of the primary goals of acid suppressive therapy is to relieve symptoms that may be associated with esophageal inflammation and prevent other complications (eg, esophageal strictures, respiratory involvement).
 - Esomeprazole is the only PPI approved by the US Food and Drug Administration (FDA) for treating children 1 to 11 months old for erosive esophagitis caused by acid-mediated GERD and is available in oral and intravenous formulations.

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- Treatment of GERD in infants younger than 1 year has not been studied as extensively as in older children or adolescents, and the few clinical studies that have been conducted yielded conflicting findings.
 - The objective of the present study is to evaluate the efficacy and safety of esomeprazole in infants ages 1 to 11 months with signs and symptoms of GERD.

METHODS

Study Design and Patients

- This was a multicenter randomized, double-blind, placebo-controlled, parallel-group, treatment-withdrawal study conducted in 33 centers in the United States, France, Germany, and Poland.
- The study followed guidelines established by the FDA.


SELECT CRITERIA

- Infants ages 1 to 11 months: They had a clinical diagnosis of suspected GERD based on symptoms, endoscopically proven GERD, laboratory test results, diagnostic tests.
- Patients were required to have at least 1 of the symptoms of GERD.
 - Vomiting/regurgitation, irritability.
 - Cough, wheezing and/or stridor, labored breathing,
 - Respiratory symptoms triggered by feeding, feeding difficulties (food refusal, choking, hiccups for >1 hour/day).at least 2 times per week in a 4-week period.

- During the 2-week open-label phase, all of the patients received esomeprazole (Nexium) once daily orally according to body weight.
- After the open-label phase, infants were randomized 1:1 to double-blind treatment with esomeprazole (at the open-label dose) or placebo for up to 4 weeks.
- The primary endpoint was time to discontinuation owing to symptom worsening based on global assessments by the parent/guardian and physician. Adverse events were recorded.


RESULTS:


- Of the 98 patients enrolled, 81 (82.7%) experienced symptom improvement determined by physician global assessment (PGA) during open-label esomeprazole treatment.
- During the double-blind phase, discontinuation rates owing to symptom worsening were 48.8% (20/41) for placebo-treated versus 38.5% (15/39) for esomeprazole-treated patients (hazard ratio 0.69; $P=0.28$).

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- The time to discontinuation was significantly longer with esomeprazole than placebo (hazard ratio 0.24; P=0.01).
 - Numerical increase in the incidence of upper respiratory infection in patients treated with esomeprazole (6/39 patients) compared with placebo (4/41 patients).

DISCUSSION

- A majority (83%) of patients showed improvement in GERD symptoms within 2 weeks of starting openlabel esomeprazole therapy.
- The downward trend in symptom severity was greatest in the vomiting/regurgitation, crying >1 hour, and irritability symptom categories. .
- Esomeprazole was well tolerated.

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- These observations may indicate that infants with more severe symptoms (eg, more severe vomiting and irritability) are more likely to have GERD versus GER and thus may be better candidates for acid suppression treatment with PPI therapy.

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- In clinical studies of infants younger than 1 year, PPIs, including esomeprazole, have not demonstrated a statistical benefit in treating GER or GERD.
 - Possible explanations include the lack of an accurate diagnostic test to distinguish acid-related disorders from symptoms caused by allergy, motility problems.

CONCLUSION

- Esomeprazole was well tolerated and the oral suspension formulation was effective for delivery in this population.
- Infants with more severe vomiting and irritability may benefit from and be more appropriate candidates for PPI therapy.
- The discontinuation rate owing to symptom worsening did not differ significantly between infants receiving esomeprazole versus those receiving placebo.
- Improved diagnostic criteria in this age group are needed to identify infants with GERD who may benefit from acid suppression therapy.



THANKS FOR YOUR ATTENTION!