Case report

Ranitidine Combined With Omeprazole for Symptomatic Relief of Severe GERD in Infants: A Case Report

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Abstract

Gastro esophageal reflux (GER), a common problem in infancy, is defined as the passage of gastric contents into the esophagus. Gastro esophageal reflux disease (GERD) includes troublesome symptoms or complications associated with GER. Unresponsive severe GERD to conservative and medical management may lead to fundoplication and surgery. There are no reports of combined therapy with two groups of acid suppressants and prokinetics to prevent fundoplication in severe infantile GERD. This is a case report of severe GERD unresponsive to conservative treatment of GERD who responded well to combined therapy of ranitidine and omeprazole. This therapeutic protocol prevented surgery in this case with no complication.

Introduction

GER, defined as passage of gastric contents into the esophagus, is a normal physiologic process that occurs throughout the day in healthy infants, children, and adults [1]. In infants GER is common and most often manifests as regurgitation and vomiting. Although 70%-85% of infants have regurgitation within the first 60 days of life, they become symptom free in 95% of cases by one year of age [2]. The prevalence of GERD is ranging from 8.5% in Eastern Asia to 10-20% in Western Europe and North America [3]. Episodes of transient relaxation of the lower esophageal sphincter and inappropriate adaptation of the sphincter tone to changes in abdominal pressure are the main pathophysiology of GERD [4].

GERD occurs when GER produces troublesome symptoms like recurrent vomiting, weight loss or poor weight gain, Irritability, hematemesis, dysphagia (feeding refusal), apnea, wheezing or stridor, hoarseness, cough and abnormal neck posturing (Sandifer sign) in infants [1,5].

The treatment options to manage infants with GERD include feeding changes, positioning therapy, prokinetic agents and acid suppressants [1,5]. Therapy for GERD in infants always begin with anti-reflux positioning, thickening of milk and using hypoallergic regimen. In infants who do not respond to these conservative therapies, treatment with prokinetics and acid suppressants is required. The acid suppressants agents including histamine-2 receptor antagonists (H2RAs) and proton pump inhibitors (PPIs) work in different ways. H2RAs act to decrease acid secretion by inhibiting the histamine-2 receptor on the gastric parietal cells [6]. PPIs deactivate the H+, K+ -ATPase pumps [7]. PPIs have been used after a therapeutic failure of H₂ blockers in some clinical trials in infants [5,8].

Abbreviations

GER: Gastro Esophageal Reflux; GERD: Gastro Esophageal Reflux Disease; H2RAs: Histamine-2 Receptor Antagonists; PPIs: Proton Pump Inhibitors

Case Report

A 10-day-old boy was referred to the neonatal clinic of this center with irritability, rumination, regurgitation and projectile vomiting of 10 times a day. He was exclusively breastfed and diagnosed to be a GERD case clinically by the neonatologist. His physical examination was normal with no abdominal distention. There was no sign of high intracranial pressure. His lab data including CBC, diff, biochemical indices and urine analysis were normal. Urine culture was negative. The abdominal X-ray was normal. According to his abdominal sonography, there was no organomegaly, hydronephrosis, pyloric spasm or stenosis and abnormal position of superior mesenteric vessels, but moderate to severe gastroesophageal reflux was reported.

Unresponsive GERD was defined ≤50% improvement in symptoms after each step of treatment. The duration for response to each step of treatment was considered one to two weeks according to the type of treatment.

In the first step of treatment, antireflux positioning (keeping upright for 20-30 minutes after breast feeding and then left lateral positioning) was started for him. His mother was practiced not to overfeed the infant, increase the frequency of feedings and feed him upright for 20-30 minutes after breast feeding and then left lateral positioning. There was no sign of high intracranial pressure. His lab data including CBC, diff, biochemical indices and urine analysis were normal. Urine culture was negative. The abdominal X-ray was normal. According to his abdominal sonography, there was no organomegaly, hydronephrosis, pyloric spasm or stenosis and abnormal position of superior mesenteric vessels, but moderate to severe gastroesophageal reflux was reported.

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the infant with low breast milk volumes. She was also practiced to thicken her expressed breast milk (1 tablespoon of dry rice cereal per ounce of breast milk) [4]. After breast milk thickening, the times of vomiting were not reduced but the severity of symptoms was declined at the end of the first week.

In the second step, hypoallergenic regimen was recommended for his mother. This step of treatment made no improvement in the symptoms of the patient. In the third step, ranitidine was administered with an optimum neonatal dose of 2mg/kg three times a day. After starting ranitidine, irritability was subsided and the frequency of vomiting and regurgitation were reduced to 7-8 times a day. In the fourth step, metoclopramide was administered that decreased the number of vomiting to 6-7 times a day.

In the fifth step, ranitidine was changed to omeprazole with a dose of 0.7 mg/kg twice daily and then 1.5mg/kg twice daily. This medical substitute improved the patient’s vomiting to 5-6 times a day.

After taking consent, the two acid suppressants were administered together. This time the number of vomiting was reduced to 2-3 times a day with lower severity.

The symptoms recurred with interruption of each one of mentioned medicines until 7 month of age. At that time ranitidine was omitted from his regimen.

At 8 month of age, metoclopramide was stopped with no recurrence of symptoms. When he was 9 month old, omeprazole was omitted from his medical regimen too. Now the patient is 18 month old. He has been symptom free for nine months.

There was a history of severe GERD in his sister. Her symptoms were also treated with the same regimen as her brother. Her symptoms did not recur after 12 months of age.

**Discussion**

GERD is a common disease during infancy especially in the first year of life.

It is one of the most common reasons for referrals to pediatricians or pediatric gastroenterologists. In GERD, troublesome symptoms (e.g. frequent vomiting, poor weight gain, irritability, and respiratory symptoms) complicate the physiologic GER [3, 9]. Factors such as prematurity, positive family history of GERD, neurologic impairment, medicines (e.g. sedatives, muscle relaxants) and malformations of GI tract are known to increase the risk of GERD [10].

The main goal of GERD treatment in infants is relieving symptoms, adequate growth, and preventing GERD-related complications. Acid suppressants, including histamine-2 receptor antagonists (H2RAs) and proton pump inhibitors (PPIs) are the mainstay of GERD treatment in pediatrics [1, 9].

Recently PPIs have been used in pediatric GERD and erosive esophagitis [11]. Oral PPIs have been increasingly used in children <12 months old for treatment of GERD during the last few years worldwide. According to a cohort study of USA, using PPIs have been increasing 7.5fold in infants aged 0-12 months from 1999 to 2004 and from 31.5% in 1999 to 62.6% in pediatrics in 2005 [12, 13]. PPIs have longer duration of action, more inhibition of meal-induced acid secretion and fewer complications, so they are superior over H2RAs that decrease acid secretion by inhibiting H2 receptors on gastric parietal cells [9]. Furthermore, tachyphylaxis and a decline in acid suppression may develop after repeated administration of H2RAs [14].

There are small clinical trials in a subset of adult patients that suggest some patients may benefit from a bedtime dose of an H2RA in addition to twice daily PPI. These include those who do not obtain relief with a twice daily PPI regimen and those with severe esophagitis, Barrett’s esophagus, or extra-esophageal disease, in whom tight control of acid secretion is required [15-16]. In our knowledge, there has been no case report or clinical trial of combination therapy (H2RA and PPIs) in severe GERD of infancy.

In the present case, the conservative therapy just helped to decrease the severity of symptoms.

Starting ranitidine and metoclopramide increased cure rate to 30%-40% in the patient. After changing ranitidine to omeprazole, the symptoms decreased by about 50%. Administering the two acid suppressants made the patient, symptom free by about 70%-80%. H2RAs and PPIs are both acid depressants but act in two different ways. In this case, combination of ranitidine and omeprazole with average doses helped the infant become symptom free by about 70%-80% without increasing complications. The growth indices of our patient were measured every month. The patient had normal catch-up growth and his mother was satisfied with improving the patient’s symptoms under the two acid suppressants regimen plus metoclopramide and antireflux positioning.

There was no complication during ranitidine plus omeprazole therapy with mentioned dosages. This regimen could prevent surgery and fundoplication in this infant.

**Conclusion**

This study showed that administration of omeprazole combined with ranitidine is more effective in improving symptoms of GERD than administrating each antisuppressant alone. This combined therapy could prevent fundoplication in this infant with severe GERD.

**References**


