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Mini Review

Pharmacotherapy of Gastroesophageal Reflux Disease in Children

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Abstract

Background: Gastroesophageal reflux disease (GERD), once a domain of adults only, is now being frequently diagnosed beyond first year of life. However, therapeutic approach to its pharmacological management remains debatable.

Objective: Putting into perspectives the current concepts with our own observations in the drug therapy of GERD in pediatric practice.

Design: Review of recent English medical literature with authors' own experience in the field.

Salient Features: High index of suspicion followed by a therapeutic trial employing an anti-reflux should precede diagnostic test(s) as and when indicated. H_2 receptor antagonists, preferably ranitidine, should be the drug of first choice in children. A prokintic, preferably metoclopramide, is helpful in cases where abdominal distention and bloating are predominant. The more potent H2 receptor antagonist, cisapride as also the proton pump inhibitors should be reserved for difficult cases not responding to aforesaid approach.

Conclusions: First line treatment of pediatric GERD largely revolves around ranitidine, a H2 antagonist. Metoclopramide, a prokinetic, is helpful as an add-on in case of predominant bloating and abdominal distention. Proton pump inhibitors are now picking up as the preferred choice.

Keywords: Gastroesophageal Reflux Disease (GERD); H_2 Receptor Antagonists; Metaclopramide; Omeprazole; Pantaprozole; Prokinetics; Proton-Pump Inhibitors (PPIs); Ranitidine

Introduction

Gastroesophageal reflux disease (GERD), once dubbed as an entity encountered nearly exclusive in adults, is now being frequently diagnosed in pediatric practice thanks to awareness and high index of suspicion on the part of the professionals [1,3-5]. In neonatal and early infancy, what we usually come across is physiologic gastroesophageal reflux (GER) that usually responds to conservative measures such as positional therapy and/or altered feeding regimen. Beyond first year, most cases belong to the actual GERD*[1,3-5]. The incidence of GERD has a tendency to increase as the child grows into the toddler, preschool, prepubescent and adolescent years.

According to Mohan., *et al.* [6], gastroeso hageal reflux (GER) is an age-related phenomenon in infancy. In older children, it is usually related to life style and usually labelled GERD. By and large GERD is a clinical diagnosis, usually not warranting specific investigations. In a group of select cases, where local pathology is strongly

suspected, such investigations as upper GI endoscopy may be carried out.

This mini review proses to provide a state-of-thr art update on pharmacotherapy pf GERD in infancy and childhood along with authors own experience in the field.

Overview

Pharmacotherapy of (GERD) has revolved around antacids, prokinetics, H_2 receptor antagonists and proton pump inhibitors (PPIs) over the past few decades [1, 4-6]. Table 1 presents the salient features of the commonly employed agents in these therapeutic groups.

Drug	Dose	ADRs/special comments
Prokinetics Metaclopramide	0.6-1.6 mg/kg/day (maximum 60 mg/day)	Extrapyramidal manifestations somnolence, nervousness, asthenia, gynecomastia, lactorrhea, diarrhea, motor restlessness.
Cisapride	0.5 mg/kg/day in 2-3 divided doses	Crampy abdominal pain, diarrhea light-headedness, mild headache, slight blurred vision, fever, prolonged QT interval. Cardiac arrhythmias, sudden death. ECG monitoring mandatory.
H2 receptor antagonist Ranitidine	3-6 mg/kg/day in 2-3 divided doses	Headache, constipation, diarrhea. Kidney and liver function impairment
Proton pump inhibitors Omeprazole,	0.7-3.3mg/kg/day	Abdominal discomfort, constipation, dizziness, headache, hoarseness, tachycardia, bruising; thrombocytopenia, leukopenia
Lansaprazole,	0.6-1.6 mg/kg/day (maximum 60 mg/day)	Abdominal discomfort, vomiting, constipation, dizziness, headache, hoarseness, tachycardia, bruising
Pantaprozole	0.4-0.8 mg/kg/day (maximum 40 mg/day)	Abdominal discomfort, constipation, dizziness, headache, stuffy nose, sore throat

Table 1: Commonly used drugs in pediatric GERD: Salient features [1,8].

Antacids

Antacids, containing aluminium, magnesium, calcium, or some combination of these substances, are conventionally available as tablets and liquids. These provide short-lived relief in varying gastric problems by neutralizing acid in stomach. At present, antacids are more or less outdated as far as their use in GERD is concerned.

Prokinetics

Prokinetics enhance gastrointestinal motility by increasing the frequency of contractions in the small intestine as a result of activation of a wide range of serotonin receptors. Besides GERD, these are used to treat irritable bowel syndrome, gastritis, gastroparesis, and functional dyspepsia.

Metoclopramide is of help in cases with dominant abdominal distension. However, a more potent prokinetic, cisapride, is quite effective. But, its use may cause serious cardiovascular adverse drug reactions (ADRs) including long Q-T interval, fatal arrhythmias and sudden death. The clinical and ECG monitoring is, therefore, mandatory. These considerations have become a “roadblock” in the routine use of cisapride in GERD even in adults. As a matter of fact, following adverse reports in 2000 in the USA and Europe, use of cisapride got restricted to a limited access program supervised by a pediatric gastroenterologist.

H_2 receptor antagonists

H_2 receptor antagonists, also called H_2 blockers, are a sort of anti-histamins that block the action of histamine at the level of histamine H_2 receptors of the parietal cells in the stomach. As a result, the production of histamine and, therefore, acid in stomach is cut down. Over and above GERD, these agents are employed in the treatment of reflux esophagitis and peptic ulcer, as also for the prevention of stress ulcers. Earlier, they surpassed the antacids. In recent years, they are being surpassed by proton-pump inhibitors (PPIs) that are found to be more effective at both healing and alleviating symptoms of ulcers and reflux esophagitis than the H_2

receptor antagonists. These are an advance over prokinetics in treatment of GERD. Both cimetidine and ranitidine are effective. However, cimetidine is now out of favour because of higher CNS and antiandrogen ADRs. The third drug of this group, fomatadine, does not have a significant role in pediatric GERD.

Proton pump inhibitors

PPIs are known for causing a pronounced and long-lasting reduction of stomach acid production. PPIs are most effective in both healing and alleviating symptoms of GERD. Nevertheless, until recently, these were less frequently recommended in pediatric GERD because of the risk of serious ADRs and limited experience in children [1]. Now, their use is picking up.

Our own approach

Ranitidine, in our experience, should be the preferred first line drug for the pediatric GERD [1-5,9].

This H_2 receptor antagonists, is a sort of anti-histamine that blocks the action of histamine at the level of H_2 receptors of the parietal cells in the stomach. As a result, the production of histamine band is cut down. This leads to reduction of acid in the stomach.

Over and above the GERD, ranitidine is effective in reflux esophagitis and peptic ulcer. Furthermore, it is useful in prevention of stress ulcers.

Initially we use dose of 1-2 mg/kg/dose 2-3 times daily. Later, this dose is doubled up. Once the stable control is attained in around 4 weeks, a single daily dose may suffice. The agent is supplied as tablet (150 and 300 mg) and syrup (75 mg/5 ml). The daily dose may be given as a single dose, in divided doses twice or thrice daily depending on the individual merits of the case and as advised by the attending pediatrician or gastroenterologist. For a gratifying outcome, it should be given before breakfast, lunch or dinner.

In a single daily dose regimen, it is best given in the morning.

In twice daily regimen, the two doses are given 12 hours apart, i.e., morning and evening.

In thrice daily regimen, it is given in the morning, afternoon and evening 6-8 hours apart.

The dose needs to be reduced in poor renal and hepatic function.

In our experience, ranitidine is by and large well tolerated and a safe drug. However, infrequently, ADRs like nausea, vomiting, diarrhea, headache, light-headedness, rash, insomnia and fatigue may be encountered. Mercifully, these ADRs are usually transient, disappearing after a few days therapy.

In a child with porphyria, ranitidine may precipitate an attack. It is, therefore, best avoided in these patients.

Drug interactions include iron salts, ketaconazole and itraconazole.

A world about the so-called “combination drug therapy” in GERD. At times, in difficult cases, a prokinetic may be employed in combination with a H2 receptor antagonist or PPI. We do come across children suffering from GERD along with a disturbing abdominal distention and bloating. Addition of a prokinetic proves of value in these children. Our preference is for metaclopramide.

We are of the opinion that PPIs should be kept in reserve for cases that fail to respond to therapy with H2 receptor antagonists and prokinetics.

In our limited experience of using cisaprde under strict monitoring on a few children with GERD and severe constipation, we did not come across any such serious ADR as prolonged QT interval, arrhythmias or sudden death. We strongly feel that renewed work on cisapride from this angle needs to be initiated to reach a logical conclusion if indeed this important drug really deserves the condemnation that was tagged with its use in the pasr.

Conclusion

In conclusion, first line treatment of pediatric GERD largely revolves around ranitidine and pentaprozole, Cisapride needs to be reserved for refractory cases only.

Take home massages

- GERD is being increasingly diagnosed beyond first year of life.
- Though diagnostic modalities are available, high index of suspicion followed by a therapeutic trial should precede such

test(s) as and when indicated.

- A H2 receptor antagonistans or PPI should be the drug of choice in children
- A prokinetic, preferably metoclopramide, is helpful in cases where abdominal distention and bloating are predominant.
- PPIs and
- Cisapride should be reserved for difficult cases do not fail to show response to aforesaid approach.

Conflict of Interest

None.

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