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Proton Pump Inhibitors in Gastroesophageal Reflux in Pretems: A Review

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REVIEW ARTICLE

ABSTRACT

Objectives

Gastroesophageal reflux is primarily physiological in newborns, especially in prematures less than 34 weeks of gestation. Recently there has been a surge in the use of anti reflux medications especially proton pump inhibitors to treat significant reflux in newborns the rewards of which are questionable and hence their use needs to be addressed

Material and Methods

A PubMed search was done using the key words “gastroesophageal reflux”[all fields] and “preterm”[all fields] and/or “term” [all fields] and/or “newborn”[all fields]. The articles included were randomized trials, prospective studies, retrospective studies, review articles and observational studies.

Conclusion

As per current evidence, the risk to reward ratio of proton pump inhibitors does not favour it to be routinely recommended for treatment of gastroesophageal reflux in preterm newborns.

Key Words

Gastroesphageal reflux, Preterm, Newborn, Proton pump inhibitors

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INTRODUCTION

Gastroesophageal reflux is common in preterm infants with a reported incidence of 22% in babies below 34 weeks of gestation.[1] Gastroesophageal reflux occurs on an average of 3-5 times per hour but to what extent is it a clinical problem remains a question, as many babies may just be happy spitters. [2]

A number of factors may contribute to this scenario: relatively abundant milk intake, supine posture which promotes the passage of liquid gastric contents into oesophagus, immature oesophageal motility and poor oesophageal clearance.[3] Though primarily physiological due to above factors, significant gastroesophageal reflux in preterm infants may lead to failure to thrive[4] and prolonged hospital stay.[5]

Though the management of gastroesophageal reflux in newborns remains controversial, there has been a recent surge in empirical use of antireflux medications both during hospital stay and after discharge.[6] Pharmacological therapy such as H2 blockers have been associated with higher incidence of necrotizing enterocolitis[7], other infections (sepsis, pneumonia and UTI), and fatal outcome in VLBW.[8] Corvaglia et al in their study has demonstrated that of all the gastroesophageal reflux episodes in newborns, 76% were due to non acid reflux as compared to 24% due to acid reflux.[9] However, most pharmacological therapies act on acid reflux and thereby the risk to reward ratio may not be beneficial.

This review aims to bring together evidence on potential benefits and adverse effects of proton pump inhibitors, a common class of antireflux medication, in gastroesophageal reflux in preterms.

MATERIAL AND MEDTHODS

The data and material collected by A PubMed search done using the key words “gastroesophageal reflux”[all fields] and “preterm”[all fields] and/or “term” [all fields] and/or “newborn”[all fields]. The articles included were randomized

trials, prospective studies, retrospective studies, review articles and observational studies.

DISCUSSION

Proton pump inhibitors act as blockers of gastric proton pump which catalyses the final phase of acid secretary process, hindering both basal and stimulated acid secretion by parietal cells.

Since the therapeutic failure of H_2 blockers, use of proton pump inhibitors has significantly increased over the last ten years.[10] Apart from esomaprazole, none of the proton pump inhibitors are approved for use in infants (<one years of age). Esomaperazole has recently gained the indication for the short term treatment of erosive oesophagitis in infants from one to twelve months. Data with regards to proton pump inhibitors use in newborns is scant let alone in premature babies. Omari et al administered omeperazole in preterms at a dose of 0.7mg/kg/dose noted a significant decrease in acid gastroesophageal reflux frequency and of overall degree of oesophageal acid exposure, however there was no clinical benefit in the studies population.[11] Another study by Orenstein et al assessed the efficacy of lansoperazole versus placebo on a large cohort of term and preterm newborns (symptomatic infants) showing no significant advantage in symptoms due to gastroesophageal reflux such as crying, regurgitation, refusal to feed, back arching, wheezing etc.[12] On the other hand a higher incidence of lower respiratory tract infection was observed in the study group. Recently, another study by Omari et al to assess the effectiveness of esomeprazole in both term and preterm newborns showed acid bolus reflux episodes were reduced on therapy (median 30 vs 8, P < .001), as was the reflux index (mean % time esophageal pH < 4, 15.7% vs 7.1%, P < .001).[13]The number of gastroesophageal reflux symptoms recorded over 24 hours was also lower on therapy (median 22 vs 12, P < .05). However, as the sample size was small (26 infants) and the study was not placebo controlled the results need to be studied further.[13] Kierkus et al in a recent study using pantoprazole at a dose 1.2mg/kg have reported improved acid gastroesophageal reflux and median clearance time in an open label study after five consecutive daily dosage and was generally well tolerated for 6 weeks, though more than half of cohort showed anemia, hypoxia and constipation was observed. Since, preterms were not separately studied in the study, the results cannot be extrapolated to this group.[14]

Proton pump inhibitors can cause delay in gastric emptying,[15] inhibit neutrophil migration[16] and decrease gastric mucosal activity.[17] It should be noted that gastric pH physiologically decreases with increase in gestation.[18] Accordingly a higher incidence of intragastric bacterial infection has been reported in association with proton pump inhibitors therapy.[19] Hence, administering proton pump inhibitors to preterms who already have a lower pH may make them more susceptible for infections such as NEC. More et al in a recent systematic review showed that inhibitors of gastric acid secretion are associated with significantly increased risk of NEC (odds ratio [OR]: 1.78, 95% confidence interval [CI]: 1.4, 2.27, p < 0.00001).[20]

As most of the studies with respect to gastroesophageal reflux have not studied preterms separately from term newborns and since of the evidence available, majority deals with both H2 blockers and proton pump inhibitors (both in effects and side effects), further studies are needed before proton pump inhibitors can be recommended in this age group for the treatment of gastroesophageal reflux.

CONCLUSION

As per current evidence, the risk to reward ratio of proton pump inhibitors does not favour it to be routinely recommended for treatment of gastroesophageal reflux in preterm newborns. Further trials need to be undertaken to ascertain their role in gastroesophageal reflux in preterm population with regards to mortality, chronic lung disease, infections (especially NEC) and duration of hospital stay.

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