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SCIENTIFIC LETTER

Paracetamol for Patent Ductus Arteriosus Closure: High Osmolality of Enteral Form and Spontaneous Intestinal Perforation

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To the Editor: Efficacy of oral and intravenous paracetamol for hemodynamically significant patent ductus arteriosus (hsPDA) is comparable to older agents; with lesser complications [1]. It becomes imperative for clinicians to be aware of problems that may be associated with it. We report a case of intestinal perforation after oral paracetamol for hsPDA. We believe that the osmolality of the formulation may be partially responsible.

Baby S was delivered at 28 wk with 850 g weight for abnormal umbilical artery dopplers. Parenteral nutrition was initiated and standard feed regimens were followed (mother's own milk). On day 6 she reached 100 ml/kg/d of feeds. On day 7, echo confirmed the presence of hsPDA. Standard recommended dose of oral paracetamol 15 mg/kg/dose (Calpol drops 100 mg/ml, Glaxosmithkline) every 8 h for 3 d was administered by orogastric tube with the scheduled feeds. Around 36 h later, she developed abdominal distension and bilious aspirates. Inotropes were required. X-ray evidence of free air in the peritoneum required a bedside peritoneal drain insertion. Laporotomy done 48 h later revealed multiple large perforations in the descending colon, with rest of the bowel uncompromised. Colostomy was performed. Subsequently, feeds could be escalated up to 90 ml/kg/d. Alas on day 26 of life, she developed features of sepsis. Blood culture was reported positive for *Serratia marsescens*. Inspite of appropriate antibiotics and intensive care, baby succumbed on day 28 of life.

Safety studies of paracetamol for hsPDA have focused on reporting the expected hepatoxicity, with elevated bilirubin and hepatic enzymes typically occurring 3 to 5 d into the course [2]. Indian studies have reported no serious adverse events [3]. A recent study has noted 20% incidence of spontaneous intestinal perforation (SIP). It is difficult to evaluate the relationship between paracetamol and necrotising enterocolitis or SIP [4].

Drug osmolality is an often overlooked pharmacokinetic aspect, when therapy is instituted enterally. A literature review of the topic revealed shocking revelations of extremely high osmolality of several drugs that are quite often used in neonatal practice. Osmolality of 330–350 mOsm/kg H_2O is considered appropriate for enteral administration. Oral paracetamol was found to have osmolality above 7000 mosm/kg H_2O [5].

Further use of these medications may need attention to formulations suitable for use in preterm neonates.

Compliance with Ethical Standards

Conflict of Interest None.

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