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COMMENT

A perspective on the potential side effects of paracetamol use in the treatment of PDA

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Dear Editor;

We have read the contemporary study by Gover A and colleagues with much interest.[1] In the study, infants with patent ductus arteriosus (PDA) were treated with either oral or intravenous paracetamol and the treatment results were compared. Oral paracetamol treatment was shown to have a higher rate of PDA closure. In light of these results, the researchers concluded that the oral application of paracetamol should be preferred over intravenous as the first-line treatment for PDA.

Over the past decade, the use of paracetamol in the treatment of PDA has become widespread.[2] Several studies involving preterm infants have reported milder side effects and higher rates of PDA closure with paracetamol treatment as compared to other agents such as ibuprofen and indometacin. These findings have encouraged clinicians in neonatal intensive care unit to use paracetamol for PDA treatment.

However, as is the case for the use of any drug, clinicians should carefully consider the potential side effects of paracetamol use in preterm infants.

An adverse effect associated with paracetamol use in preterm infants is preterm intestinal perforation, which occurs due to oral administration of paracetamol.[3] Many analgesic and antipyretic drugs exhibit a high osmolality because they contain sweeteners and may not be suitable for use by preterm infants as they are produced for the pediatric age group. Research has speculated that these preparations may cause intestinal perforations in preterm infants.[3] In the contemporary study by Gover A and colleagues, the oral paracetamol preparation used and mentioned in the methodology was not described in terms of osmolality and whether it was diluted or not; the study reported 1 diagnosed case of intestinal perforation. However, this case had received intravenous paracetamol treatment.

According to our clinical experiences, oral paracetamol should be diluted with a 1–3/5 ratio before use due to the high osmolality. Nevertheless, the ideal solution is the production of an oral paracetamol preparation that exhibits suitable pharmacological properties and is specifically designed for use by preterm infants. The same situation is applicable to oral ibuprofen preparations.

Acute liver failure is another potential adverse effect of paracetamol use in preterm infants. Hepatotoxicity is an extremely rare adverse effect in preterm infants, even with high dose paracetamol administration.[4] In the literature, there are 3 reported cases of hepatotoxicity due to intravenous paracetamol administration.[5,6] In the study by Gover A and colleagues, there were no reported cases of hepatotoxicity in both groups. No study has described a case of hepatotoxicity due to oral paracetamol use; thus, oral treatment may be favored over other methods of administration.

The literature contains extremely limited data pertaining to the long-term effects of paracetamol use in preterm infants. Nevertheless, there are no associated neurodevelopmental risks according to short-term observational data. There is a need for extensive research on the long-term effects of paracetamol use in preterm infants.[7]

Gover A and colleagues' study on oral paracetamol use contains compelling results that are encouraging for neonatalogists. Nevertheless, the need for an oral paracetamol preparation specifically developed for preterm infants is clear. In addition, the short and long-term potential side effects of every novel drug must be precisely established for safe application. By addressing these points, we wanted to share the potential problems clinicians might face with paracetamol use and put an emphasis on the possible solution.

With much respect,

DATA AVAILABILITY

I read and accept to data availability rules of Pediatric Research.

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COMPETING INTERESTS

The author declares no competing interests.

ADDITIONAL INFORMATION

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