Article type : Mini commentary

Corresponding author mail id :- abhide@sgul.ac.uk

Mini-commentary on BJOG-18-0043.R1: A randomized controlled trial of amnioexchange for fetal gastroschisis

Amnio-exchange for gastroschisis does not help, and may even harm

Amarnath Bhide

Fetal Medicine Unit

Lanesborough Wing, 4th Floor,

St. George's Hospital

Blackshaw Road, London SW17 0QT

Department of Clinical Medicine,

Faculty of Health Sciences, UiT-The Arctic University of Norway

Gastroschisis is a congenital defect associated with infant morbidity related to temporary or permanent damage to the intestines exposed to the amniotic fluid: long periods of parenteral feeding or bowel atresia necessitating bowel resection. In the accompanying study (Luton et al, BJOG-18-0043.R1), the authors explored if two-weekly amnio-exchange from 30 weeks till delivery reduced duration of ventilation and parenteral nutrition in fetuses with gastroschisis. The answer is that it does not. There may even be an excess of deaths in the treatment arm.

Why did the procedure failed to show any benefit? One possibility is that exposure to amniotic fluid has nothing to do with intestinal damage. This is unlikely, since there is evidence from animal work that removal of digestive secretions in the amniotic fluid reduced intestinal inflammation (Ashrafi et al, Pediatr Surg Int. 2008;24:421-4). However, a previous non-randomized study (Midrio et al, J Pediatr Surg. 2007;42:777-82) reported that serial amnio-exchanges did not modify the biochemical or inflammatory status of amniotic fluid nor did it prevent injury to the herniated gut.

The authors exchanged 'upto' 300 ml of amniotic fluid with normal Saline. The mean amniotic fluid volume is 777 ml and does not change appreciably between 22 and 39 weeks, although the 95% confidence interval was wide: 302 to 1997 ml (Brace R & Wolf E, Am J Obstet Gynecol. 1989;161:382-8). Therefore, less than 40% of amniotic fluid volume was replaced with 300 ml amnio-exchange. This may have been insufficient.

The effects of dilution of amniotic fluid with amnio-exchange was transient as shown by the authors, and a two-weekly interval may be too long. The authors nicely show that amniotic fluid digestive enzymes are elevated in gastroschisis as compared to controls. Even higher levels were seen with bowel atresia in the gastroschisis cohort. It is tempting to hypothesise that exposure of the intestines to amniotic fluid is the underlying cause of the bowel atresia. However, the converse may be true. Bowel atresia with resultant obstruction may lead to increased levels of digestive enzymes. Indeed, amniotic fluid gamma-glutamyl-transpeptidase (GGTP) and intestinal alkaline phosphatase (iALP) were elevated in cases with gastro-duodenal and small bowel obstruction (Muller et al, Prenat Diagn. 1994;14:973-9).

Out of the five intrauterine demises in the study cohort (n=34), two were thought to be linked to the procedure. One death was observed in the control arm. The difference was not statistically significant, but the study was underpowered to assess mortality. In any case, the excess death rate in the trial arm is worrying.

In summary, the findings of the current study do not support the practice of amnio-exchange (used similar to the protocol reported in this study) in order to reduce intestine-related morbidity for fetuses affected with gastroschisis. Units offering amnio-exchange need to re-think their practice. In the light of this study results, amnio-exchange for gastroschisis would now be deemed unethical outside of clinical trials.

Conflict of interest: The author is a former scientific editor of BJOG. A completed disclosure of interest form is available to view online as supporting information.