Editorial PCCM

Title: Enteral feeding in post-operative cardiac surgical infants – how fast should we go?

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Although most would agree that infants and children should be enterally fed after cardiac surgery, when this is initiated and how quickly it should be advanced remain unclear. A survey of European practices in 2017, showed that a third of units routinely started enteral feeds (EF) within 12-24 hours post-surgery, however this was infant or condition-specific [1]. More concerningly, relatively few units (39%) had written guidance for feeding postoperatively. A pilot randomized study in 2018 [2] compared trophic EF within 4-6 h post op versus no EF until 48h after surgery in infants <5kg with cyanotic congenital heart disease with increased pulmonary blood flow, undergoing CHD surgery. They found a significantly reduced length of ventilation in fed infants, with no significant differences in other outcomes. Similar results were noted by Sahu et al [3] in their RCT of 50 infants <6 months of age undergoing cardiac surgery, finding lower length of ventilation and length of stage in early enterally fed children. However, critical illness in general and cardiopulmonary bypass, are known to induce a systemic inflammatory response [4]. Hypoxia, reperfusion injury and other associated factors pose concerns for clinicians for the risk of gut mucosal ischaemia, potentially made worse by the stress of enteral feeding [5]. Therefore, more studies in this patient group are warranted.

In this issue of Pediatric Critical Care Medicine, Floh et al [6] report the results of a randomized pilot study of rapid escalation to EF (FF) (reaching 50 kcal/kg/d goal feeds by 27 hours) compared to standard feeding practice (SF), (reaching similar goal feeds by 63 hours) in a single Canadian CICU. It is unclear why this energy goal was chosen and applied to all infants regardless the phase of critical illness, when the ASPEN (2017) guidance recommends aiming for 2/3 of the target goal by the end of the first week [7]. Their primary objective was to examine the relationship between inflammation, insulin resistance, and clinical outcomes following pediatric cardiopulmonary bypass (CPB) surgery. They included only infants <6 months of age undergoing CHD surgery with cardiopulmonary bypass (CPB) excluding premature infants, not suitable for EF or undergoing cardiac transplantation. Their hypothesis was that increasing feeds early in the postoperative course decouples the association between systemic inflammation and insulin resistance and their study was analysed by intention-to-treat. One limitation was the subjectivity of 'feeding readiness on post op day 1' was determined at the discretion of the attending physician on the day. A strength is that a standardised algorithm was used to consistently define and manage feeding intolerance.

Blood samples (for glucose, cortisol, insulin and inflammatory cytokines (IL-1α, IL6, IL8, IL10 and TNFα) were taken at induction, completion of CPB, arrival in the CCU and every 12 hours following CPB for a maximum of 96 hours. Enteral and parenteral nutrition (PN) delivery was recorded at each of these sampling times.

Recruitment was problematic for this study as half of consented patients had to be excluded because they were deemed too sick (n=14) to feed or too well (n=19) by the treating physician to avoid hunger, and the nurses often liberalised the feeds in these well children (causing protocol violations). With two (8%) patients in the FF group and 3 (12%) patients in the SF group non-compliant with the study protocol; all of these patients received higher volume feeds than ordered. They found those randomized to faster feeds (FF) received a higher volume of feeds at 48h, unsurprisingly, but surprisingly, did not achieve full feeds faster than the standard feed (SF) group This is indeed surprising and may reflect the small sample size in this pilot study, which was not powered to detect this difference. The energy delivery from EN was higher in FF only at 48 hours and were similar in all other time points. Interestingly, no significant difference was found in the numbers of children who received supplemental PN but, PN was initiated after 24 hours in SF and 48 hours in FF (p=0.8); the role of PN initiation timing could be questioned in this critical care population.

In terms of postoperative inflammation, the pattern of cytokine expression was almost identical between groups with the exception that from 72 hours, patients in the FF arm had lower IL-8 than those in the SF arm. No consistent relationship was found between insulin resistance and cytokine concentrations in either study arm, but multivariate analysis revealed that feeding strategy modified the relationship.

The authors acknowledge the limitations of this pilot study and their problems with recruitment and crossover. Despite the lack of statistical significance found, they conclude that data from this study suggests the potential that faster EN escalation early in the CICU course *may* confer clinical benefits through modification of the relationship between inflammation and adverse events.

This study highlights the difficulties in conducting randomized trials in complex populations like this, and some mixed method feasibility work would have bene useful here [8]. The protocol deviations from nurses liberalizing feeds in 'well children' is a point in case, which could have been anticipated with more multidisciplinary (specifically nursing) involvement in study design.

A further important point to reinforce here, is that energy target delivery in this population is often compromised due the frequent interruptions to feeding, for common procedures such as chest closure. Future considerations may be the use of post-pyloric feeding in this patient group to allow for feeding during common procedures that require 'fasting'. Finally, this study also suggests that

clinicians may be 'too cautious' in enterally feeding these infants, when in fact higher volumes of feed are tolerated well, with few adverse effects. However, we still do not know whether in some groups of children a more delayed EF goal may be beneficial. These results need to be confirmed in a larger study, with better control of EN delivery to ensure adequate separation between both arms. The optimal timing and advancement of enteral feeding remains unclear and warrants further research.

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