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ORIGINAL ARTICLE

Early Enteral Nutrition in Neonates Following Abdominal Surgery

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ABSTRACT

Introduction: Nil per oral (NPO)/nil by mouth has been the most commonly practiced convention in post-operative period. Misplaced fear of aspiration led to routine prescription of "NPO." Starvation leads to atrophy of the gut mucosa leading to decreased barrier effect of gut mucosa. This starvation-induced gut mucosal injury increases septic complications and mortality. The study aims at establishing the feasibility and effect of early enteral nutrition (EEN) in neonates following abdominal surgeries. **Materials and Methods:** A total of 260 cases formed the cohort of prospective cohort study, 79 in EEN - Group "A" and 181 in NPO - Group "B." Effect of EEN was evaluated with regard to outcome, hospital stay, surgical site infections (SSI), stress markers such as C-reactive protein (CRP), procalcitonin, tumor necrosis factor alpha (TNF α), and neonatal-predisposition, insult/injury, response, organ failure (Neo-PIRO) scores, intra-abdominal pressure (IAP) grade, tolerance of feeds, and time to first stool. Chi-square was the statistical method used. Epi info version 7 was the software used. **Results:** Group B had higher mortality (20.09%) than Group A ($P < 0.05$). 33.7 in Group B developed SSI, of which 90% were deep and intracavitary ($P < 0.05$). Hospital stay was less in Group A ($P < 0.05$). CRP and Neo-PIRO scores were less in Group A compared to Group B ($P < 0.05$). TNF-α expression and IAP scores were not statistically significant ($P > 0.05$). Procalcitonin levels were higher in Group B. Feeds were better tolerated in Group A. First stool appeared earlier in Group A than B. There was no difference in anastomotic leak in both the groups. **Conclusion:** EEN in neonates following abdominal surgeries is feasible, well tolerated reduces the hospital stay and mortality, and reduces SSIs, and early gut motility could be established.

Key words: Early enteral nutrition; Endogenous endotoxemia; Nil per oral

INTRODUCTION

Initiation of enteral feeds following abdominal surgeries has always been a matter of convenience, decided by comfort, and a practice handed over from generations. Fear of aspiration led to a situation where nil per oral (NPO)/nil by mouth became a standard post-operative instruction following abdominal surgeries in newborn. Advantages of early enteral nutrition (EEN) have been well documented [1,2]. Pediatric surgeons in general, neonatologist, and pediatricians in particular are averse to early feeding.

Starving the gut leads to atrophy of the mucosa and facilitates transluminal endotoxemia and bacteremia [1-4]. The food in the gut protects the gut mucosa and prevents endogenous endotoxemia, and bacteremia is a proven fact. The conventionally taught concept of NPO is not getting wiped off from the mindset of pediatricians and pediatric surgeons alike. We intended to study the feasibility of EEN in neonates following abdominal surgeries and to study the effects of EEN on outcome, surgical site infections (SSI), hospital stay, stress markers such as C-reactive protein (CRP), tumor necrosis factor alpha (TNF-α), procalcitonin, neonatal-predisposition, insult/injury, response, organ failure (Neo-PIRO) scores, intra-abdominal pressure (IAP) grades, time to first stool, tolerance of feeds, and anastomotic leak.

MATERIALS AND METHODS

A prospective cohort study was conducted from 2007 to 2016. A total number of 260 cases were recruited.

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Three of the eleven referring pediatricians were convinced of EEN. The cohort was divided into EEN Group "A" (n = 79) and NPO group "B" (n = 181). The various definitions used in the study were as follows:

1. EEN was defined as trophic or regular feeds any time after complete recovery from anesthesia before 24 h of surgery.
2. Feed intolerance was defined as gastric residue more than previous feed, bilious aspirate, and progressively increasing trend of IAP.
3. Gut priming was defined as administering expressed breast milk through nasogastric route at the rate of 1 ml/kg every 2h that was increased to 2–3 ml/kg when tolerated progressively.
4. Recovery from anesthesia was defined as adequate complete response to stimuli, normal cry, and consolability (FLACC scale) and maintaining saturation on room air with active reflexes.

Inclusion criteria were peritonitis (hollow viscous peritonitis, urinary peritonitis, biliary peritonitis, and meconium peritonitis), neonatal necrotizing enterocolitis, neonatal intestinal obstruction, and malrotation with volvulus neonatorum. Gut anastomosis was done in 47 and 71 cases in Groups A and B, respectively. Besides one patient with gastric volvulus, all others patients had small bowel anastomosis (ileo-ileal in ileal atresia, jejuno-jejunal in jejunal atresia, and duodeno-duodenal in duodenal atresia).

Exclusion criteria were all the neonates who were unstable (i.e., neonates with hypotension, lethargy, delayed capillary filling time >3 s., and poor neonatal reflexes/responsiveness) at the time of admission and those who died within 24 h.

Outcome parameters studied included SSI, hospital stay, sepsis stress markers such as CRP, procalcitonin, TNF α, Neo-PIRO scores, IAP grades (measured using intravesical route), time to first stool, tolerance of feeds, and anastomotic leak.

A blinded statistical analysis was done by a third-party statistician. Chi-square was the statistical tool used. Statistical software used was Epi Info 7.

Comparison of the outcomes in the two groups showed that 20.99% (n = 38/181) of Group B died, whereas only 13.92% (n = 11/79) died in Group A; the difference was statistically not significant (P > 0.05) (Table 1). SSI incidence in Group B was statistically more as compared to Group A (33.7% vs. 20.25%) (P < 0.05) (Table 1). Hospital stay was significantly less in Group A (P < 0.05) (Table 1). Correlation of stress markers such as CRP, TNF α, procalcitonin, and Neo-PIRO scores in the two groups has been depicted in Table 1. A significant correlation was seen with only CRP and Neo-PIRO scores (P < 0.05). There was no dif-

Table 1: Comparison of parameters between NPO and EEN groups

Parameters	EEN	NPO	*P*
Outcome	*n*=79	*n*=181	>0.05
Alive	68	143	
Dead	11	38	
SSI	*n*=16	*n*=61	<0.05
Superficial	8	9	
Deep fascia	4	39	
Intracavitary	4	13	
Hospital stay (days)			<0.05
<10	41	61	
11–20	12	48	
>21	15	24	
Stress markers			
TNF α			>0.05
<20 pg/ml	60	95	
>30 pg/ml	19	48	
CRP levels (%)			<0.05
<6 mg	52	61	
>6 mg	27	120	
Procalcitonin levels	*n*=55	*n*=61	
<2 ng/ml	39	22	
>2 ng/ml	16	39	
Neo-PIRO score			<0.05
<11	31	32	
12–24	31	71	
>25	17	78	
IAP score			>0.05
<10	21	51	
11–20	20	44	
21–25	17	55	
25–30	21	31	
Anastomotic leak	*n*=47	*n*=71	>0.05
Present	2	5	
Absent	45	66	

NPO: Nil per oral, EEN: Early enteral nutrition, SSI: Surgical site infections, TNF α: Tumor necrosis factor alpha, CRP: C-reactive protein, Neo-PIRO: Neonatal-pre-disposition, insult/injury, response, organ failure, IAP: Intra-abdominal pressure

ference in the expression of TNF-α and procalcitonin in both the groups. IAP grades did not differ significantly in both the groups ($P > 0.05$). First stool was earlier in Group A. Feeds were well tolerated in Group A. No case of aspiration as gut priming guided increments were followed. There was no difference between two groups in relation to anastomotic leak statistically.

DISCUSSION

Enteral nutrition was known from the 12th century and got stabilized in the 1960s [3] (Table 2). Enteral nutrition as a source of supply of substrate for enterocytes has been well established. EEN on newborns was shown to decrease post-operative sepsis [3-6]. The fear of aspiration, misplaced concepts of feed intolerance, and established mindset of NPO in all abdominal surgeries led to ignoring the scientific advances in understanding the role of food in maintaining the integrity of intestinal mucosa.

Starvation and its effects on intestine have been well established in literature. The role of gut as a source of sepsis and maintaining the coordination of other organs such as gut-liver, gut–lung, and gut–kidney cannot be overemphasized. The nutrition helps in maintenance of gut integrity. Gut integrity maintains overall coordinated function of other organs, facilitating early recovery from the stress of surgery, and reduced complications [1-3]. Keunen et al. [7] showed EEN in neonates and preterms help in brain growth and maturation. It also helps in establishing microbiome of gut bringing back colonic ecosystem to normal.

Starvation leads to disuse atrophy of villi, decrease disaccharide activity, decreased intestinal mucosa mass, and loss of DNA of enterocyte (Figure 1). This malfunctioning enterocyte leads to increase the permeability of intestinal mucosa to antigen and macromolecules. This starvation-induced gut mucosal injury leads to decrease the production of Vitamin K due to the absence of normal colonic flora. This also leads to decreased growth factors and bile acid metabolism. This compounded effect of starved gut and abnormal colonic bacterial environment leads to colonization of pathological bacteria and might lead to sepsis and sequelae. In addition, starvation leads to decreased immune cells of intestine gut-associated lymphoid tissue. This decreased gut immunity leads to increased uptake of toxins and decreased immune response to foreign antigen. This leads to bacterial translocation. Figure 1 clearly shows shortening of villi flattening of villi decreased translocation of IgA into the lumen from enterocyte and loss of tight junctions leading to bacteremia and endotoxemia. This is the crux of matter and is the scientific basis of the need of maintaining the integrity of gut mucosa. This forms the basis of EEN.

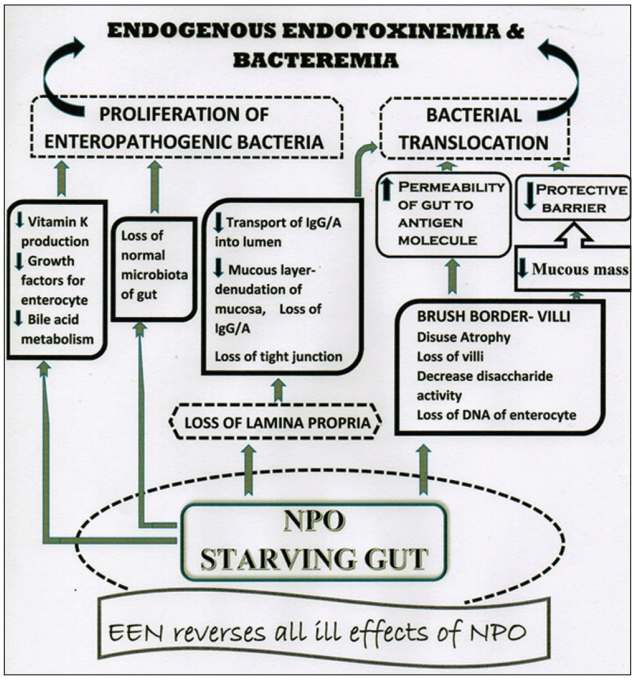

Figure 1: Mechanism behind early enteral nutrition

The type of feed, amount of feed, and rate of feed have been reasonably set in literature [8,9]. The present study has defined the gut priming as 1 ml/kg/every 2nd h breast milk when tolerated progressively increased to 2–3 ml/kg every 2 h.

Shores et al. [5] have suggested small volume breast milk and trophic feeds 10–20 ml/kg/day. The present study also followed the same guidelines and the feeds were well tolerated with no complication.

Ekingen et al. [10] showed improved outcome with early nutrition. The present study showed the mortality rates of 13% and 21% in Groups A and B, respectively. The difference was not statistically significant ($P > 0.05$).

Moore et al. [4] and Paul et al. [6] showed the evidence of decreased SSI with EEN. The present study showed similar results. There was a decreased incidence of deep facial SSI in EEN Group A as compared to NPO Group B ($P < 0.05$).

Many authors [5,6,10-13] have clearly shown reduced hospital stay with EEN. The present study also showed a positive effect of EEN on hospital stay. Reduced hospital stay in EEN Group A was statistically significant ($P < 0.05$).

Fujimoto et al. and Chellis et al. [14,15] have shown reduced Intensive Care Unit stay with EEN. Chellis et al. [15] have also shown that EEN was feasible, well tolerated, and cost effective in critically ill mechanically ventilated pediatric patients. The present study also confirms feasibility and tolerance of feeds.

Table 2: Literature regarding EEN in chronological order

Literature	Benefits
Moore et al. [4]	EEN reduces post-operative septic complications
Chellis et al. [15]	EEN is feasible well tolerated and cost effective in critically ill patients
Meurling [9]	Enteral route should be used as soon as possible or rather before. A few ml of breast milk can be given before the bowel starts to function.
Bauer et al. [16]	Significant increase in RBP and pre-albumin levels and reduced hospital stay with enteral nutrition
Luckey et al. [20]	Early post-operative feeding decreases post-operative ileus
Sangkhathat et al. [11]	EEN after colostomy closure stimulated early bowel movement and reduced hospital stay with no increased adverse effects
Ekingen et al. [10]	Early intra-gastric small volume breastfeeding well tolerated, helpful in increased wound healing and anastomosis strength decreases post-operative ileus and early first stool and reduced hospital stay. It increases splanchnic blood flow and stimulates gut immune system
Peter et al. [12]	EEN significantly reduces complication rates reduces
Chernoff [3]	Tube feeding - gut a route for nutrition since ancient times
Fujimoto et al. [14]	EEN shortens ICU stay
Shores et al. [5]	EEN well tolerated and faster achievement of 50% goal of calories
Paul et al. [6]	EEN is feasible safe, reduced post-operative complications and discomfort, and decreased hospital stay
Keunen et al. [7]	adequate nutrition crucial for brain development, improved immunological balance and subsequent decreased inflammation and beneficial effect through improved gut immune brain axis
Dutta et al. [8]	Feeding guidelines in VLBW babies and use of trophic feeds
Mamatha and Alladi [13]	Early first stool and decreased hospital stay with EEN
Jiang et al. [19]	EEN well tolerated with shorter hospital stay
Prasad et al. [17]	Low Neo-PIRO score with EEN

EEN: Early enteral nutrition, ICU: Intensive care unit, VLBW: Very low birth weight, Neo-PIRO: Neonatal-pre-disposition, insult/injury

Bauer et al. [16] studied retinol binding protein (RBP) and pre-albumin levels with EEN. They showed that EEN did improve post-operative nutrition by the way of significant increase in RBP and prealbumin. Fujimoto et al. [14] showed improvement in hepatic dysfunction by the way of decrease in bilirubin levels. Not many studies have shown the effect of EEN on stress markers such as CRP, procalcitonin, and TNF-α. The present study shows significant reduced CRP levels in Group A compared to Group B ($P < 0.05$). The expression of TNF α was not statistically significant ($P > 0.05$). Procalcitonin levels were higher in Group B when compared to Group A. It clearly shows the positive impact of EEN on stress by maintaining the integrity of gut mucosa.

The author had earlier published the novel grading system - Neo-PIRO for neonatal surgical infections [17]. When Neo-PIRO scores were compared between Groups A and B, scores were significantly higher in Group B as compared to Group A ($P < 0.05$).

Rise in IAP with post-operative feeding was evaluated in the present study by measuring intravesical pressures [18]. The fear of many that EEN adds to ileus was not supported by this study. It clearly showed decreasing trend in IAP scores and was statitically significant ($P < 0.05$).

Ekingen et al. [10] and others [13] showed early first stool with EEN. In the present study also, the average

time of first stool post-operatively was 38 and 70 h in Groups A and B, respectively.

Many others [6,10,15,19] have clearly showed that EEN is safe and well tolerated. The present study also concurs that there were no adverse effects of EEN. There was no case of aspiration as feed increments were strictly guided by gut priming.

A decreased incidence of anastomotic leak with enteral nutrition has been previously reported [10,13,15]. The present study did not show any difference between two groups ($P > 0.05$).

EEN with incorporation of probiotics and prebiotics is being tried by the authors now. The use of probiotics in reducing post-operative complications has been reported in literature [4-6,12]. EEN also facilitates early return of bowel movements [20] and thereby increases tolerance of feeds. Prokinetics may facilitate this effect of EEN. It is advised that one should not emphasis too much on the presence of bowels sounds on auscultation before starting feeds. This auscultation of bowel sounds may be fraught with observer's inadequacies in evaluating bowel sounds.

To conclude, EEN in neonates following abdominal surgeries is feasible and is well tolerated, EEN reduces the hospital stay, mortality, the duration of inotropes, ventilatory support, an dSSI and helps establishing early gut motility.

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