



Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jped surg



Review Articles

Early enteral feeding after pediatric abdominal surgery: A systematic review of the literature ☆☆☆☆



Douglas Greer ^{a,*}, Yasiru G Karunaratne ^a, Jonathan Karpelowsky ^{b,c}, Susan Adams ^{a,d}

^a Department of Pediatric Surgery, Sydney Children's Hospital, Randwick, NSW, Australia
^b Discipline of Child & Adolescent Health, Sydney Medical School, University of Sydney, NSW, Australia
^c Department of Pediatric Surgery, Children's Hospital at Westmead, Sydney, NSW, Australia
^d University of New South Wales, Randwick, NSW, Australia

ARTICLE INFO

Article history:
Received 26 March 2019
Received in revised form 7 August 2019
Accepted 25 August 2019

Key words:
Early feeding
Early enteral nutrition
Children
Pediatric
Postoperative
Fasting

ABSTRACT

Introduction: Traditionally enteral nutrition has been delayed following abdominal surgery in children, to prevent complications. However, recent evidence in the adult literature refutes the supposed benefits of fasting and suggests decreased complications with early enteral nutrition (EEN). This review aimed to compile the evidence for EEN in children in this setting.

Methods: Databases Pubmed, EmBase, Medline and reference lists were searched for articles containing relevant search terms according to PRISMA guidelines. First and second authors reviewed abstracts. Studies containing patients less than 18 years undergoing abdominal surgery, with feeding initiated earlier than standard practice, were included. Studies including pyloromyotomy were excluded. Primary outcome was length of stay (LOS). Secondary outcomes included time to full enteral nutrition, time to stool and postoperative complications.

Results: Fourteen articles met inclusion criteria – five on neonatal abdominal surgery, three on gastrostomy formation and six on intestinal anastomoses. There were three randomized control trials (RCTs), five cohort studies, four historical control trials, one nonrandomized trial and one case series. Nine studies showed a decreased LOS with EEN. Most studies which reported time to full enteral nutrition showed improvement with EEN; however, time to stool was similar in most studies. Postoperative complications were either decreased or not statistically different in EEN groups in all studies.

Conclusion: Studies to date in a limited number of procedures suggest EEN appears safe and effective in children undergoing abdominal surgery. Although robust evidence is lacking, there are clear benefits in LOS and time to full feeds, and no increase in complications.

Level of evidence: IV

© 2019 Published by Elsevier Inc.

Contents

1.	Materials and methods	1181
1.1.	Search strategy	1181
1.2.	Inclusion and exclusion criteria.	1181
1.3.	Study selection	1181
1.4.	Data extraction and management.	1181

Abbreviations: EEN, Early Enteral Nutrition; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; LOS, Length of Stay; RCT, Randomized-control Trial; PN, Parenteral Nutrition; ERAS, Enhanced Recovery After Surgery; NGT, Nasogastric Tube; NJT, Nasojejunum Tube; TAT, Transanastomotic Tube; NHMRC, National Health and Medical Research Council; EBM, Expressed Breast Milk; IBD, Inflammatory Bowel Disease.

☆ Funding: No external funding.

☆☆ Conflicts of interest: The authors have no conflicts of interest.

★ Author's contribution statement: Drs Karpelowsky and Adams acted as supervisors, and assisted with data interpretation, and manuscript writing and editing. Dr Greer conceptualized the review, determined search criteria and manuscript eligibility, extracted the data, and wrote the manuscript. Dr Karunaratne determined manuscript eligibility and assisted with data extraction. All authors have approved of the final manuscript.

* Corresponding author at: Department of Pediatric Surgery, Sydney Children's Hospital, Randwick, NSW, Australia, 2031. Tel.: +61 2 9382 1787.

E-mail address: douglas.greer@health.nsw.gov.au (D. Greer).

2.	Results	1182
2.1.	Inclusion	1182
2.2.	Risk of bias in included studies	1182
2.3.	Explanatory variables.	1183
2.3.1.	Grouping according to procedure	1183
2.4.	Definition of EEN.	1183
2.5.	Route and type of feeding.	1184
2.6.	Outcomes	1185
2.6.1.	Primary outcome: length of stay	1185
2.7.	Secondary outcomes	1185
2.7.1.	Time to full enteral nutrition	1185
2.7.2.	Time to stooling.	1185
2.7.3.	Duration of parenteral nutrition.	1185
2.7.4.	Postoperative abdominal distention, ileus and vomiting	1185
2.8.	Other complications	1185
3.	Discussion	1185
4.	Limitations.	1186
5.	Conclusion	1186
	References	1186

Historically, prolonged fasting after abdominal operations has been considered necessary to prevent nausea, vomiting and anastomotic complications [1]. The duration of postoperative fasting is variable but can range from 0 to 5 days depending on the operation [1]. The ramifications of this period of fasting are not insignificant and may include prolonged length of stay, increased use of parenteral nutrition (PN), social effects and significant costs to the health system [2,3]. In neonates and infants there are additional issues with delayed feeding including cholestatic jaundice, sepsis, delayed gut development, and metabolic disease [4].

In recent years interest has increased in the concept of early enteral feeding (EEN) in abdominal surgery. Data from clinic trials in adults have shown that this is not only safe, but may reduce the duration of postoperative ileus and length of stay after a variety of operations [5–9]. Studies in animal models also suggest that early feeding may improve wound healing and anastomotic strength and reduce morbidity from sepsis [10–13].

Most of the clinical research into the beneficial effects of early feeding has occurred in adult patients. In infants, there is conclusive evidence in favor of early feeding after one operation – pyloromyotomy. This has changed practice such that many centers now advocate for feeding within 4 h, with a significant reduction in length of stay [14–18]. However, evidence regarding the safety and benefits of EEN in the recovery from other abdominal procedures in children is less common.

EEN is also a core element of “enhanced recovery after surgery” (ERAS) and other fast-track protocols [19]. Although in its early stages, interest in ERAS in the pediatric surgery setting is increasing and initial results have been promising [20,21]. Given this interest, it is vital that the evidence for the various individual elements of these protocols, including EEN, is robust.

The purpose of this study was to identify and review the literature regarding early feeding after pediatric abdominal surgery, in order to assess safety and any potential benefits.

1. Materials and methods

The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline.

1.1. Search strategy

A search of electronic databases Pubmed, MedLine and EMBASE was performed from May to June 2018. Search terms used were ‘enteral feeding’ AND ‘postoperative’ AND ‘children’, and ‘oral feeding’ AND

‘postoperative’ AND ‘children’. Reference lists from included articles were also reviewed for relevant studies.

1.2. Inclusion and exclusion criteria

Studies were included if the main focus was early enteral feeding in children aged 0–18 years undergoing abdominal operations. ‘Abdominal operation’ was defined as a procedure where the abdominal compartment was entered – either by open incision or laparoscopically – and excluded nonsurgical gastrointestinal interventions such as endoscopic and radiological procedures such as percutaneous gastrostomy (PEG). Studies in languages other than English, on nonhuman subjects and persons more than 18 years, or where separate analysis of children in a combined adult/pediatric study was not possible, were excluded as were review articles without patient data. Studies were excluded if patients were not grouped according to timing of enteric intake, or where the route of feeding was other than oral, gastric tube (NGT), jejunal tube (NJT), transanastomotic (TAT) tube or by gastrostomy. Studies where the effect of EEN could not be independently assessed owing to concurrent interventions were also excluded. This included studies of EEN as part of more comprehensive ERAS protocols. Owing to the high level of evidence already available, studies on feeding post pyloromyotomy were not included.

1.3. Study selection

Titles and abstracts of all articles identified using search criteria were reviewed by the first and second authors (DG and GK) independently, and duplicates and irrelevant studies removed. Full texts of the remaining articles were reviewed by DG and GK for inclusion criteria. Where disagreement occurred, inclusion was based on consensus. Screening of reference lists was performed by DG.

1.4. Data extraction and management

Selected articles were classified by study type and National Health and Medical Research Council (NHMRC) [22] level of evidence. Explanatory variables extracted included demographics (age, gender), operative characteristics (type of operation and indication where provided) and feeding characteristics (route, type of feeding, timing). Outcomes analyzed included length of stay (LOS), time to full enteric intake, time to stool, days of PN, postoperative vomiting and distension or ileus. Complications extracted were anastomotic leak, wound infection, wound dehiscence, small bowel obstruction and total complications.

Table 1
Articles excluded after full text review.

Article	Reason for exclusion
Hofmeester et al [23]	Review article
Vrecenak et al [24]	Variables other than timing of feed not controlled for (multiple ERAS elements used)
Bishay et al [25]	Patients not grouped according to timing of feeds (grouped according to duration of PN)
Abatanga et al [26]	Patients not grouped according to timing of feeds (grouped according to duration of nasogastric tube insertion)
Pearson et al [27]	Review article
Sholadoye et al [28]	Patients not grouped according to timing of feeds (patients grouped according to age for analysis)
Mattioli et al [29]	Variables other than timing of feed not controlled for (multiple ERAS elements used)
Cavusoglu et al [30]	Variables other than timing of feed not controlled for (perioperative management not consistent between groups)
Rove et al [31]	Variables other than timing of feed not controlled for (multiple ERAS elements used)
Suri et al [32]	Route of feeding other than oral or NG/OG/TAT (percutaneous jejunostomy feeds)

ERAS, Enhanced recovery after surgery; NG, nasogastric; OG, orogastric; TAT, transanastomotic tube.

2. Results

2.1. Inclusion

There were 24 articles that met criteria for full text review. Of these, 10 [23–32] were subsequently excluded, with reasons summarized in Table 1. This left 14 articles [33–46] for analysis (Fig. 1). Included articles are summarized in Table 2, including NHMRC level of evidence, grouping according to procedure, patient characteristics. Outcomes are summarized in Table 3.

There were three randomized control trials (RCT) (II) [35,41,46], one nonrandomized experimental trial (III-2) [45], five retrospective cohort studies (III-2) [33,34,36,38,40], four trials with historical controls (III-3) [37,39,42,43] and one case series (IV) [44] (Table 2).

2.2. Risk of bias in included studies

Retrospective cohort studies, which included Jiang [33], Jiang [34], Aljahdali [36], Rosenfeld [38], and Jensen [40], were the most common. This study design carries an inherent risk of selection bias, as subtle differences between groups can skew results, especially considering their

retrospective nature. They are also susceptible to information bias as the source of data and process of collecting it may differ between groups. As it is not possible in these studies to blind the assessment of outcome, there is also a risk of detection bias.

Prospective trials using historical controls were the second most common study type and included Walter-Nicolet [37], Sunstrom [39], Yadav [42], and Sangkhathat [43]. Like all nonrandomized trials, there is a risk of bias owing to patient selection especially so because the control arm is not contemporaneous. The use of historical controls may also make confounding factors such as other variations in treatment difficult to measure. As with cohort studies, neither participants nor assessors can be blinded to grouping leading to a risk of performance and detection bias.

Ekingen [35], Amanollahi [41], and Davila-Perez [46] were all randomized-control trials. Ekingen randomized consecutive neonates undergoing abdominal surgery, and further grouped these patients based on the presence of an intestinal anastomosis. These patients represented a diverse range of pathologies. This, along with the lack of detail regarding the specific patient characteristics of each group, leads to a risk of selection bias and thus limited generalizability. Amanollahi allowed for exclusion from the trial based on surgeon-assessed difficulty

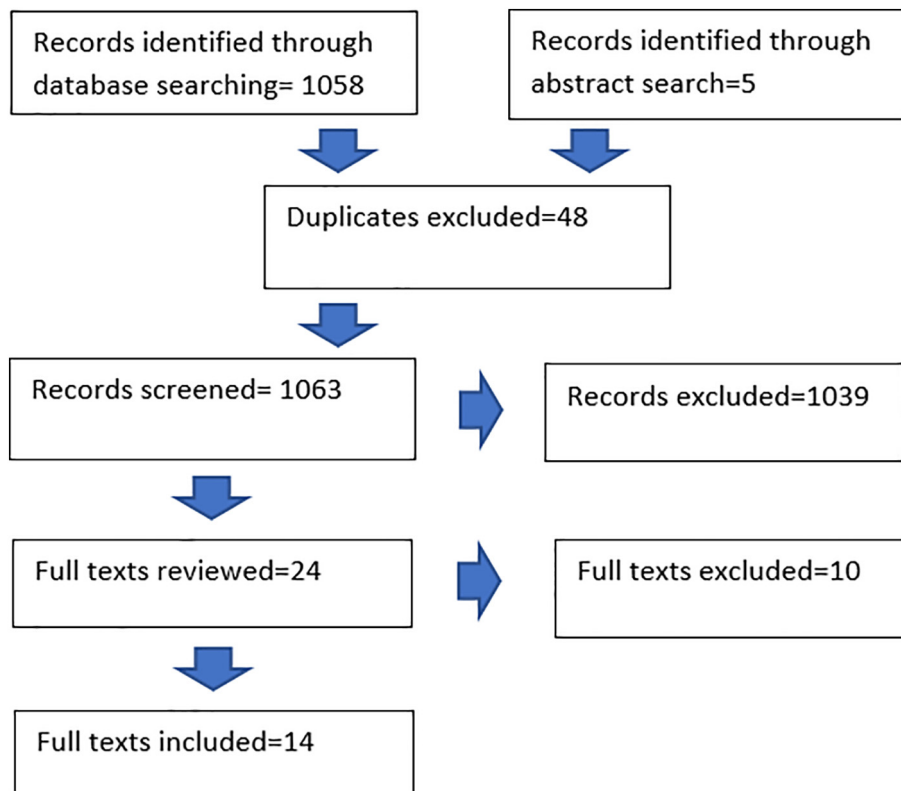


Fig. 1. Flowchart of systematic review results.

Table 2
List of included articles.

	Article	Level of Evidence [37]	Patient characteristics			Operation performed	Feeding details		
			Total number	Number controls	Age at operation, mean (range/SD)		Timing	Route	Type
Neonates	Jiang et al [33]	III-2	120		2.9 (1–6) d	Repair congenital intestinal malformations	48 h	NJT	Formula
	Jiang et al [34]	III-2	46		4.5 (2–12) d	Partial gastrectomy	48 h	NJT	Formula
	Ekingen et al [35]	II	56		8.3 (1–40) d	Laparotomy with/without intestinal anastomosis	12 h	NG	EBM
	Aljadhali et al [36]	III-2	570		N/S	Closure of gastroschisis	0–21 d	Oral/NG	Formula/EBM
	Walter-Nicolet et al [37]	III-3	73		3 (1–7) h	Closure of gastroschisis	5 d	Oral/NG	EBM
Gastrostomy	Rosenfeld et al [38]	III-2	156		5 (0.3–9) y	Laparoscopic gastrostomy	<24 h	Gastrostomy	Formula/EBM/Electrolyte solution
	Sunstrom et al [39]	III-3	65		3.4 (3.95) y	Laparoscopic gastrostomy	8 h	Gastrostomy	Formula/EBM/Electrolyte solution
	Jensen et al [40]	III-2	536		7 (2–28) m	Laparoscopic or open gastrostomy	6 h	Gastrostomy	Formula/EBM/Electrolyte solution
Intestinal Anastomosis	Amanollahi et al [41]	II	67		17.4 (24.6) m	Laparotomy with small bowel–small bowel anastomosis	24 h	Oral	Clear fluids then progress
	Yadav et al [42]	III-3	62		43.3 (38.5) m	Closure of ileostomy/colostomy	24 h	Oral/NG	Fluids as tolerated, then progress
	Sangkhathat et al [43]	III-3	64		11.5 (1–124) m	Closure of colostomy	24 h	NS	Clear fluids then progress
	Mamatha et al [44]	IV	32		12 (0.1–192) m	Any anastomosis distal to duodenum	24 h	Oral	Fluids as tolerated, then progress
	Shang et al [45]	III-2	575		3.8 (1.7) y	Any intestinal anastomosis	24 h	Oral	Diet as tolerated
	Davila-Perez et al [46]	II	60		41 (63) m	Any elective intestinal anastomosis	24 h	Oral	Fluids as tolerated, then progress

EEN, early enteral nutrition; SD, standard deviation; EBM, expressed breast milk; h, hours; d, days; m, months; y, years.

of anastomosis, also risking selection bias. As blinding of patients and assessors to group allocation was not possible in these studies, they also have a risk of performance and detection bias. None of these studies reported on loss to follow-up or group crossover.

Shang [45] was the only nonrandomized experimental trial, where patients were allocated to EEN or control based on surgeon preference. This introduces a potential source of bias by skewing population characteristics. The potential for bias owing to inability to perform blinding was also present in this study.

The case series by Mamatha [44] suffers from potential information and reporting bias owing to its retrospective nature and the absence of a control group.

2.3. Explanatory variables

2.3.1. Grouping according to procedure

Papers fell broadly in to three groups: abdominal operations in neonates [33–37], formation of gastrostomy [38–40] and operations involving intestinal anastomoses [41–46].

Two of the studies on neonatal abdominal surgery were by Jiang — one on digestive tract malformations (including atresias and duplication cysts) [33] and one on partial gastrectomy [34]. Ekingen [35] studied any neonate undergoing laparotomy with or without intestinal anastomosis, including congenital atresias, gastroschisis, diaphragmatic hernias, anorectal malformations and aganglionosis. The final two studies by Walter-Nicolet [37] and Aljadhali [36] studied gastroschisis exclusively.

Three articles related specifically to gastrostomy formation. Rosenfeld [38] and Sunstrom [39] exclusively included laparoscopic gastrostomy. Jensen [40] included open, laparoscopic and PEG. The PEG patients were excluded from our analysis as per the selection criteria. Prevalence of a concurrent antireflux procedure varied between papers—21% underwent concurrent fundoplication in the study by Rosenfeld [38] and 15% in the one by Sunstrom [39]. In Jensen's study [40], 25% underwent some sort of concurrent procedure but the type was not specified. No study conducted subgroup analyses of those undergoing a concurrent procedure.

The remaining six studies included children with intestinal anastomoses at various levels [41–46]. Shang [45] included patients with any intestinal anastomosis, while Davila-Perez [46] included only patients having an elective intestinal anastomosis and Mamatha [44] reported on children having any intestinal anastomosis distal to the ligament of Treitz, excluding neonates. Amanollahi [41] studied those with bowel resection and an intestinal anastomosis. Yadav [42] and Sangkhathat [43] studied intestinal anastomosis in the setting of stoma closure.

2.4. Definition of EEN

In prospective studies, EEN was described according to the time postoperatively at which feeding was initiated, rather than being determined by other physiological parameters. This duration differed markedly across studies ranging from 6 h to 5 days. Where there were controls and in retrospective series, most were commenced on enteric intake according to clinician discretion based on clinical progress, ranging from one to more than 20 days.

In the neonatal section, EEN, where defined, ranged from eight hours to five days. The earliest was Ekingen [35] where feeding in the EEN group was started between 8 and 20 h postoperatively, with a mean of 12 h. The control group was fasted until there was documented resolution of ileus, defined as passage of flatus or stool. Both studies by Jiang [33,34] initiated feeding at 48 h postoperatively in the EEN group, while the control group was fed once NGT aspirates had become nonbilious. Ekingen [35] started feeding in the EEN group at between 8 and 20 h postoperatively, with a mean of 12 h. The control group was fasted until there was documented resolution of ileus, defined as passage of flatus or stool. Walter-Nicolet [37] started feeding at postoperative day 5 in the EEN group. The control group was historical, and feeding was initiated when there was clinical resolution of ileus, at physician discretion. The retrospective cohort study by Aljadhali [36] did not specify the exact timing of enteric feed introduction but divided patients into four groups based on days postoperatively until first enteric intake: Group 1 (before day 7), Group 2 (between day 8–13), Group 3 (between day 14–20), and Group 4 (after day 21). Feeding was oral or by NGT.

Table 3
Summary of findings comparing EEN to control.

		LOS	Time to full feeds	Time to stool	Length of PN	Distension	Vomiting	Ileus	Anastomotic leak	Bowel obstruction	Wound dehiscence	Wound infection	Total complications
Jiang et al [23]	EEN	17.1 d*	15.2 d*	46.1 h	X	X	X	X	X	1.4%*	X	X	X
	Control	23.4 d*	19.1 d*	48.4 h	X	X	X	X	X	12%*	X	X	X
Jiang et al [24]	EEN	12.2 d	7.3 d	50.1 h*	X	0*	X	X	X	X	X	X	X
	Control	17.3 d	7.5 d	69.4 h*	X	18.2%*	X	X	X	18.2%	X	X	X
Ekingen et al [25]	EEN (anastomosis)	12 d*	8.4 d*	35.8 h*	X	42.4%	15.5%	X	X	X	X	0	X
	Control (anastomosis)	21.4 d*	15.4 d*	59.8 h*	X	30.4%	21.7%	X	X	X	X	8.6%	X
	EEN (no anastomosis)	9.6 d	6.3 d	25.3 h*	X	42.4%	15.5%	X	X	X	X	0	X
	Control (no anastomosis)	14.1 d	9.3 d	52.2 h*	X	30.4%	21.7%	X	X	X	X	8.6%	X
Aljadahli et al [26]	0-7d	55 d*	X	X	38 d*	X	X	X	X	X	X	6%*	X
	8-14d	39 d*	X	X	28 d*	X	X	X	X	X	X	6%*	X
	15-21d	54 d*	X	X	39 d*	X	X	X	X	X	X	17%*	X
	>21d	102 d*	X	X	80 d*	X	X	X	X	X	X	24%*	X
Walter-Nicolet et al [27]	EEN	40 d	31 d	4 d	X	X	X	X	X	X	X	X	X
	Control	54.5 d	32 d	6 d	X	X	X	X	X	X	X	X	X
Rosenfeld et al [28]	EEN	2.1 d*	X	X	X	X	23.1%	X	X	X	X	0	X
	Control	3.1 d*	X	X	X	X	11.9%	X	X	X	X	8.4%	X
Sunstrom et al [29]	EEN	2 d*	X	X	X	X	X	X	X	X	X	7.7%	X
	Control	2 d*	X	X	X	X	X	X	X	X	X	7.7%	X
Jensen et al [29]	EEN (Open)	1 d*	18.3 h*	X	X	X	4.6%	X	X	X	X	0	5.6%
	Control (Open)	5 d*	51.1 h*	X	X	X	7.7%	X	X	X	X	9.5%	5.1%
	EEN (Laparoscopic)	1 d*	17.4 h*	X	X	X	5.1%*	X	X	X	X	0.2%	3.6%
	Control (Laparoscopic)	6 d*	58.3 h*	X	X	X	6.6%*	X	X	X	X	2.3%	3.6%
Amanollahi et al [31]	EEN	5.2 d*	X	3.7 d*	X	2.7%*	X	X	2.7%	X	X	X	10.8%
	Control	8.3 d*	X	4.4 d*	X	23.3%*	X	X	3.3%	X	X	X	6.7%
Yadav et al [32]	EEN	7.2 d*	62.3 h*	44 h	X	10%	16%	X	0	X	0	6.5%*	64.5%
	Control	9.5 d*	196 h*	49 h	X	3%	13%	X	3%	X	3%	29%*	93.5%
Sangkhathat et al [33]	EEN	4.5 d*	X	32.8 h*	X	X	2.9%	X	X	X	X	X	X
	Control	6.1 d*	X	48 h*	X	X	3.3%	X	X	X	X	X	X
Mamatha et al [34]	EEN	3 d	30 h	X	X	X	X	X	X	X	X	X	X
Shang et al [35]	EEN	7.4 d*	X	3.1 d*	2.3 d*	16.1%	X	33%*	1.2%	14.8%	4.3%	8.6%	8.3%*
	Control	9.2 d*	X	3.8 d*	3.2 d*	13.3%	X	40.8%*	3.5%	19.6%	3.5%	7.5%	17.3%
Davila-Perez et al [36]	EEN	6 d	2.1 d*	1.6 d	X	13%	X	X	6.7%	X	X	10%	X
	Control	9.8 d	5 d*	2.6 d	X	13%	X	X	6.7%	X	X	26.7%	X

LOS, length of stay; PN, parenteral nutrition; EEN, early enteral nutrition; h, hours; d, days; X, not reported.

* denotes a statistically significant difference.

With regards to laparoscopic and open gastrostomy formation, all defined EEN as well within 24 h postoperatively. Jensen [40] was the earliest – with both laparoscopic and open groups starting at less than six hours in the intervention groups, and after six hours in the controls. Sunstrom [39] started feeding at 8 h postoperatively or on the morning of Day 1 for the EEN group. The control group was historical and timing for feeding for this group was not specified. Rosenfeld [38] was the least specific – dividing patients into groups based on postoperative day when feeding was initiated: day 0, or day 1 and after.

Of those studies of EEN after intestinal anastomosis, all but one initiated feeding at or before 24 h in the EEN group. Amanollahi [41] initiated feeding at 24 h postoperatively while the control group started feeding after 5 days. Yadav [42] also started at 24 h postoperatively in the EEN group and in the historical control group with return of bowel activity, at clinician discretion. Sangkhathat [43] fed patient within 24 h in the EEN group and used a historical control group, where feed was started with clinical resolution of ileus. Mamatha [44] started feeding within 24 h of operation and there was no control group. Shang [45] allowed patient in the EEN group within 24 h postoperatively and the control group at 3 days. The one exception to feeding within 24 h was Davila-Perez's study [46] which defined EEN as any time before postoperative day 5, with a minimum of 24 h. The control group was fed after five days.

2.5. Route and type of feeding

Feeding was either oral [36,37,41,42,44–46], via NGT [35–37,42], via NJT [33,34], via gastrostomy [38–40], or not specified [43]. Initial feed type in the EEN group consisted of clear fluids in one study [43], any

fluid as tolerated in three [42,44,46], expressed-breast milk (EBM) or formula in five [33–37], and diet according to age in one [45]. Type of nutrition for all three studies on gastrostomy was formula, EBM, or electrolyte solution but proportions were not specified [38–40]. There was less detail available regarding the type and rate of feeding in controls.

In the neonatal papers, two studies out of five – both by Jiang [33,34] – started clear fluids before EBM/formula while the others went straight to milk feeds. Jiang [33,34] used an NJT, with patients initially fed 5% glucose solution before transitioning to formula or EBM in control and EEN groups. Ekingen [35] started with EBM via NGT for both groups. Aljadahli [36] and Walter-Nicolet [37] also used formula or EBM via NGT or orally in all patients.

In all three papers dealing with gastrostomy formation [38–40] patients were fed via the gastrostomy. None of the authors specified whether oral feeding was permitted in addition to gastrostomy.

In the papers on EEN after intestinal anastomosis, only two of the six studies specified starting with clear fluids [41,43]. Amanollahi [41] allowed oral clear fluids after 24 h in the EEN group, then diet as tolerated by 48 h. The type and route of nutrition for the control group were not specified. Patients in the EEN group in the study by Yadav [42] were fed milk after 24 h orally or via NGT. The control group was fed orally but the type of enteral nutrition was not specified. Sangkhathat [43] did not specify a route for either group. Infants less than two years old were given water within 24 h followed by formula, then *ad libitum* breast-feeds once tolerating sufficient formula and in non-breast-fed infants soft food on day 3 postoperatively. Children more than two years old were given water on the first postoperative day then diet was increased as tolerated. Patients in the study by Mamatha [44] were fed orally starting with a liquid diet then increased. Shang [45] and

Davila-Perez [46] also fed patients orally starting on a liquid diet then upgraded. Neither study specified the feeding regimen in the control group.

2.6. Outcomes

2.6.1. Primary outcome: length of stay

All 14 studies reported LOS. Of the 13 papers with comparative controls nine showed a statistically significant decrease in length of stay in the EEN group [33,35,38–43,45]. Aljahdali [36] (gastroschisis) demonstrated a statistically significant improvement in LOS in group 2 – 39 days – compared to 55 days in Group 1, 54 days in Group 3, and 102 days in Group 4 ($p < 0.05$). Jiang (neonatal partial gastrectomy) [24], Walter-Nicolet (gastroschisis) [27], and Davila-Perez (intestinal anastomosis) [36] all demonstrated a trend toward decreased LOS in the EEN group; however this did not reach statistical significance.

2.7. Secondary outcomes

2.7.1. Time to full enteral nutrition

Eight studies reported time to full enteral nutrition [33–35,37,40,42,44,46] with six showing a significant difference between EEN and control groups.

Three papers in the neonatal surgery group – Jiang (intestinal atresia) [33], Ekingen (various neonatal operations) [35], and Walter-Nicolet (gastroschisis) [37] – demonstrated a significant decrease in time to full enteral nutrition in the EEN groups ($p < 0.05$, $p = 0.01$, and $p < 0.01$) respectively). Jiang's second paper on neonatal partial gastrectomy [34] showed a small improvement which did not reach statistical significance.

Jensen [40] was the only gastrostomy study which reported time to full enteral feeding. It showed a decrease in the EEN group for both laparoscopic and open approaches: 17.4 h vs 58.3 h ($p < 0.01$) and 18.3 h vs 51.1 h ($p < 0.01$) respectively.

Yadav [42] and Davila-Perez's [46] papers on EEN following intestinal anastomosis both showed significantly shorter time to full feeds in the EEN group: 62.3 vs 196 h, $p < 0.01$, and 2.1 vs 5 days ($p < 0.01$) respectively. Mamatha's uncontrolled case series [44] reported a mean time to full feeds of 30 h (range 16–60).

2.7.2. Time to stooling

Time to stool was reported by nine studies [33–35,37,41–43,45,46] with a significant reduction in the EEN group shown in five [34,35,41,43,45]. In neonates, a historical control trial on gastrectomy [34] and an RCT on various laparotomies [35] both demonstrated a significantly decreased time to first stool in the EEN group ($p < 0.05$ and $p = 0.02$ respectively). The same trend, although not significant, was observed in other historical control trials on intestinal atresia [33] and on gastroschisis [37].

Amanollahi [41], Sangkhathat [43], and Shang [45] demonstrated significantly decreased time to stool in older children undergoing intestinal anastomosis in the EEN group ($p = 0.02$, $p < 0.01$, and $p = 0.04$ respectively). The same trend was observed by Yadav [32] and Davila-Perez [36] but was not statistically significant.

2.7.3. Duration of parenteral nutrition

Only two papers reported on duration of PN [36,45]. A cohort study on gastroschisis [36] showed lowest duration of PN in Group 2, followed by Group 1, Group 3, then Group 4 ($p < 0.05$). A nonrandomized study of various intestinal anastomoses [45] showed a significant decrease in duration of PN in the EEN group: 2.3 vs 3.8 days ($p = 0.02$).

2.7.4. Postoperative abdominal distention, ileus and vomiting

Six papers reported on postoperative distention [34,35,41,42,45,46], two of which found reduced distention in the EEN group [34,41]. A historical control trial in neonatal intestinal atresia [34] demonstrated an incidence of 0% in the EEN group compared to 18% in the control

group ($p < 0.05$). An RCT in pediatric intestinal anastomoses [41] found an incidence 3% in the EEN group compared to 23% in controls ($p = 0.01$). The remainder found no significant difference.

Only one study – a nonrandomized trial of EEN following intestinal anastomosis – commented specifically on postoperative ileus [45] after intestinal anastomoses. It showed a significantly lower incidence in the EEN group: 33% vs 41% ($p = 0.01$).

Five studies reported the incidence of postoperative vomiting, with no study demonstrating a significant difference [35,41,42,45,46].

2.8. Other complications

Various other complications were reported in 11 papers including anastomotic leak, bowel obstruction, wound infection, wound dehiscence, and overall complications.

No difference was found in the incidence of anastomotic leak between EEN and control in the four studies which reported on it [41,42,45,46]. Three studies reported on postoperative bowel obstruction. A study on neonates undergoing laparotomy for congenital intestinal malformations [33] reported a significantly decreased incidence of bowel obstruction: 1.4 vs 12% ($p < 0.05$). The other two on partial gastrectomy in neonates [34] and intestinal anastomoses [45] showed no significant difference.

Eight authors reported wound infection rates [35,36,38–40,42,45,46]. Seven of these showed a decreased incidence in the EEN group of which two reached statistical significance [36,43]. The study on gastroschisis by Aljahdali [36] showed an incidence of 6% in Groups 1 and 2 compared to 17% in Group 3 and 24% in Group 4 ($p < 0.05$). A historical control trial on stoma closure [42] also showed a significantly decreased incidence in the EEN group: 6.5% vs 29% ($p = 0.02$). The eighth paper reporting on wound infection [45] found a slightly higher incidence in the EEN group which was not statistically significant.

Neither of the two papers looking at wound dehiscence showed a statistically significant difference [42,45]. Four papers reported total complications [39,41,42,45]. The study by Shang [45] showed a significant reduction in the EEN group: 8.3% vs 17.3% ($p < 0.05$), and the other three showed no difference. No study demonstrated an adverse effect attributable to EEN.

3. Discussion

This review demonstrates that existing literature supports the value of early enteral feeding in pediatric patients undergoing abdominal surgery. A decrease in length of stay was demonstrated in most of the studies, along with a decrease in time to full enteral nutrition. Although several studies demonstrated improvement in rates of wound and anastomotic complications this was not shown consistently. Importantly, however, no adverse effects of EEN were demonstrated. Contrary to historic assumptions, no study showed a significant increase in postoperative ileus, distension, or vomiting in the EEN group and several studies showed EEN may decrease the incidence of these complications.

The theoretical benefits of EEN have been demonstrated in animal models of intestinal anastomoses, with an increase in anastomotic and wound strength along with collagen deposition by as much as double with EEN compared to controls [10–12]. Clinical benefits in adults have been extensively reported. A meta-analysis by Lewis et al concluded that EEN was associated with a significant reduction in LOS, wound infection, pneumonia, and overall infection, along with a trend towards a decreased incidence of anastomotic leak, and overall mortality [6]. While the incidence of vomiting was noted to be higher in EEN groups, the rate of NGT insertion was not significantly different [6]. Safety has also been demonstrated in adult colorectal surgery and in gynecological surgery [5,7–9].

In the pediatric setting, the place of EEN in postoperative care following pyloromyotomy has been confirmed. Two systematic reviews with meta-analyses of RCTs by Graham [14] and Sullivan [17] both

showed decrease LOS and no associated increased vomiting compared to delayed or structured feeding protocols [14,17]. Both authors recommended the use of postoperative ad libitum feeding regimens for infants having pyloromyotomy for pyloric stenosis, introduced after 4 h. This practice was demonstrated by both reviews to decrease LOS and was not associated with increased vomiting compared to delayed or structured feeding protocols.

ERAS, integrating EEN, has been demonstrated to be effective in many disciplines of adult surgery, including colorectal, urology, and thoracic surgery [49–52]. Interest in the application of ERAS protocols in pediatric surgery is increasing, as demonstrated in a survey of pediatric surgeons by Short and colleagues [48]. Short also demonstrated a significant reduction in LOS, narcotic doses, intravenous fluids, and time to regular diet in pediatric patients undergoing colorectal surgery [53]. Early studies to examine its effectiveness in inflammatory bowel disease (IBD) have also shown promising results. Rove et al have shown a trend towards decreased LOS in pediatric urology [31].

Studies of EEN as part of pediatric ERAS protocols were excluded from this review because of the difficulty separating the effect of individual components of ERAS on patient outcomes. In addition, stand-alone evidence for EEN, as a component of ERAS, provides context for interpretation of future research in ERAS in pediatric surgery. Thus, its separate evaluation in this review was warranted, and has established its place in potential future fast track protocol.

4. Limitations

The findings of this review are limited by the quality of included studies as outlined in the risk of bias section. There were only two RCTs, precluding a meta-analysis, and the definition of early feeding was broad. In addition, the cohorts, the range of operations and the definition of other explanatory and outcome variables were not directly comparable between papers. The diversity in the studied populations, ranging from premature neonates to adolescents, also makes generalizability difficult. The studies were also not powered to detect subtle changes in the incidence of postoperative complications.

5. Conclusion

This review supports the benefits of EEN across the pediatric spectrum, with decreased LOS and time to full feeding in neonates, infants and children. Importantly, no adverse effects of EEN have been demonstrated. The benefits of EEN are likely to be amplified by inclusion in evidence-based ERAS protocols with health economic and social benefits. Confirming this will require further well-designed clinical trials.

References

- Mattei P, Rombeau J. Review of the pathophysiology and management of postoperative ileus. *World J Surg*. 2006;30:1382–91.
- Mythen M. Postoperative gastrointestinal tract dysfunction. *Anesth Analg*. 2005;100:196–204.
- Kehlet H, Holte K. Review of post-operative ileus. *Am J Surg*. 2001;S3–S10.
- Dunn L, Hulman S, Weiner J, et al. Beneficial effects of early hypocaloric enteral feeding on neonatal gastrointestinal function: preliminary report of a randomized control trial. *J Pediatr*. 1988;112:622–9.
- Reissman P, Teoh TA, Cohen SM, et al. Is early oral feeding safe after elective colorectal surgery? A prospective randomised control trial. *Ann Surg*. 1995;222:73–7.
- Lewis S, Egger M, Sylester P, et al. Early enteral feeding versus 'nil by mouth' after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. *Br Med J*. 2001;323:773–9.
- Ortiz H, Armendariz P, Yarnoz C. Is early postoperative feeding feasible in elective colon and rectal surgery? *Int J Color Dis*. 1996;11:119–21.
- Stewart B, Woods R, Collopy B, et al. Early feeding after elective open colorectal resections: a prospective randomised control trial. *Aust NZ J Surg*. 1998;68:125–8.
- Steed HL, Capstick V, Flood C, et al. A randomized controlled trial of early versus "traditional" postoperative oral intake after major abdominal gynecologic surgery. *Am J Obstet Gynecol*. 2002;186:861–5.
- Tadano S, Terashima H, Fukuzawa J, et al. Gastrointestinal: early postoperative oral intake accelerates upper gastrointestinal anastomotic healing in the rat model. *J Surg Res*. 2011;169:202–8.
- Kiyama T, Onda M, Tokunaga A, et al. Effect of early postoperative feeding on the healing of colonic anastomoses in the presence of intra-abdominal sepsis in rats. *Dis Colon Rectum*. 2000;43:54–8.
- Moss G, Greenstein A, Levy S, et al. Maintenance of GI function after bowel surgery and immediate enteral full nutrition. I. Doubling of canine colorectal anastomotic bursting pressure and intestinal wound mature collagen content. *J Parent Ent Nutr*. 1980;4:535–8.
- Windsor A, Kanwar S, Li A, et al. Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis. *Gut*. 1998;42:431–5.
- Graham K, Laituri C, Markel T, et al. Review article: a review of postoperative feeding regimens in infantile hypertrophic pyloric stenosis. *J Pediatr Surg*. 2013;48:2175–9.
- St Peter S, Tsao K, Sharp S, et al. Predictors of emesis and time to goal intake after pyloromyotomy: analysis from a prospective trial. *J Pediatr Surg*. 2008;43:2038–41.
- Wheeler R, Najmaldin A, Stoodley N, et al. Feeding regimens after pyloromyotomy. *Br J Surg*. 1990;77:1018–9.
- Sullivan K, Chan E, Vincent J, et al. Feeding post-pyloromyotomy: a meta-analysis. *Pediatr*. 2016;137:1–11.
- Adibe O, Nichol P. Ad libitum feeds after laparoscopic pyloromyotomy: a retrospective comparison with a standard feed. *J Laparoendosc Adv Surg Tech*. 2007;17:235–7.
- Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Brit J Anaesth*. 1997;78:606–17.
- Short H, Heiss K, Burch K, et al. Implementation of an enhanced recovery after surgery protocol in pediatric colorectal surgery. *J Pediatr Surg*. 2018;53:688–92.
- Reissman M, Dingemann J, Wolters M, et al. Fast-track concepts in pediatric surgery: a prospective study in 436 infants and children. *Langenbeck's Arch Surg*. 2009;394:529–33.
- National Health and Medical Research Council. *NHMRC levels of evidence and grades for recommendations for guideline developers*. Canberra: National Health and Medical Research Council; 2009
- Hofmeester M, Draaisma J, Versteegh H, et al. Perioperative nutritional management in congenital perineal and vestibular fistulas: a systematic review. *Eur J Pediatr Surg*. 2015;25:389–96.
- Vrecenak J, Mattei P. Fast-track management is safe and effective after bowel resection in children with Crohn's disease. *J Pediatr Surg*. 2014;49:99–102.
- Bishay M, Lakshminarayanan B, Arnaud A, et al. The role of parenteral nutrition following surgery for duodenal atresia or stenosis. *Pediatr Surg Int*. 2013;2013:191–5.
- Abatanga F. Nasogastric tube use in children after abdominal surgery—how long should it be kept in situ? *West Afr J Med*. 2012;31:19–23.
- Pearson K, Hall N. What is the role of enhanced recovery after surgery in children? A scoping review. *Pediatr Surg Int*. 2017;33:43–51.
- Sholadoye T, Suleiman A, Mshelbwala P, Ameh E. Early enteral feeding following intestinal anastomosis in children is safe. *Afr J Pediatr Surg*. 2012;9:113–6.
- Mattioli G, Palomba L, Avanzini S, et al. Fast-track surgery of the colon in children. *J Laparoendosc Adv Surg Tech*. 2009;19(Suppl. 1):S7–9.
- Cavusoglu Y, Karaman A, Afsarlar C, et al. Ostomy closures in children: variations in perioperative care do not change outcome. *Indian J Surg*. 2015;77(Suppl. 3):1131–6.
- Rove K, Brockel M, Saltzman A. Prospective study of enhanced recovery after surgery protocol in children undergoing reconstructive operations. *J Pediatr Urol* 2018;14:252e.1–252e.9
- Suri S, Eradi B, Chowhary S, et al. Early postoperative feeding and outcome in neonates. *Nutrition*. 2002;18:380–2.
- Jiang W, Lu X, Xu X, et al. Early enteral feeding for upper digestive tract malformation in neonates. *Asia Pac J Clin Nutr*. 2015;24:38–43.
- Jiang W, Zhang J, Geng Q, et al. Early enteral nutrition in neonates with partial gastrectomy: a multicentre study. *Asia Pac J Clin Nutr*. 2016;25:46–52.
- Ekingen G, Ceran C, Guvenc B, et al. Early enteral feeding in newborn surgical patients. *Nutrition*. 2005;21:142–6.
- Aljhdali A, Mohajerani N, Skarsgard E. Effect of timing of enteral feeding on outcome of gastroschisis. *J Pediatr Surg*. 2013;48:971–6.
- Walter-Nicolet E, Rousseau V, Kieffer F, et al. Neonatal outcome of gastroschisis is mainly influenced by nutritional management. *J Pediatr Gastroenterol Nutr*. 2009;48:612–7.
- Rosenfeld E, Mazzolini K, deMello A, et al. Postoperative feeding regimens after laparoscopic gastrostomy placement. *Laparoendosc Adv Surg Tech*. 2017;27:1203–8.
- Sunstrom R, Hamilton N, Fialkowski E. Minimizing variance in pediatric gastrostomy: does standardized perioperative feeding plan decrease cost and improve outcomes? *Am J Surg*. 2016;211:948–53.
- Jensen A, Renaud E, Drucker N, et al. Why wait: early enteral feeding after pediatric gastrostomy tube placement. *J Pediatr Surg*. 2018;53:656–60.
- Amanollahi O, Azizi B. The comparative study of the outcomes of early and late oral feeding in intestinal anastomosis surgeries in children. *Afr J Pediatr Surg*. 2013;10:74–7.
- Yadav P, Choudhury R, Grover J, et al. Early feeding in pediatric patients following stoma closure in a resource limited environment. *J Pediatr Surg*. 2013;48:977–82.
- Sangkhatat S, Patrapinyokul S, Tadyathikom K. Early enteral feeding after closure of colostomy in pediatric patients. *J Pediatr Surg*. 2003;38:1516–9.
- Mamatha B, Alladi A. Early oral feeding in pediatric intestinal anastomosis. *Indian J Surg*. 2015;77(Suppl. 2):S670–2.
- Shang Q, Geng Q, Zhang X, et al. The impact of early enteral nutrition on pediatric patients undergoing gastrointestinal anastomosis: a propensity score matching analysis. *Medicine*. 2018;97:e0045.
- Davila-Perez R, Bracho-Blanchet E, Galindo-Rocha F, et al. Early feeding vs 5-day fasting after distal elective bowel anastomoses in children. *A Randomized Controlled Trial*. *Surg Sci*. 2013;4:45–8.

- [48] Short H, Taylor N, Thakore M, et al. A survey of pediatric surgeons' practices with enhanced recovery after children's surgery. *J Ped Surg.* 2018;53:418–30.
- [49] Wilmore D, Kehlet H. Management of patients in fast-track surgery. *Brit Med J.* 2001;322:473–6.
- [50] Gustaffson U, Scott M, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) society recommendations. *World J Surg.* 2013;37:259–84.
- [51] Williams J, McConnel G, Allender J, et al. One year results from the first US-based Enhanced Recovery after Cardiac Surgery (ERAS Cardiac) Program. *J Thorac Cardiovasc Surg.* 2018;157:1881–8.
- [52] Azhar R, Bochner B, Catto J, et al. Enhanced recovery after urological surgery: a contemporary systematic review of outcomes, key elements, and research needs. *Eur Urol.* 2016;70:176–87.
- [53] Short H, Heiss K, Burch K, et al. Implementation of an enhanced recovery protocol in pediatric colorectal surgery. *J Pediatr Surg.* 2018;53:688–92.