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# Peptide-based enteral formula vs a whole protein enteral formula after major intestinal surgeries in children

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## Abstract

**Background:** Malnutrition is a common finding after major abdominal surgeries especially after prolonged period of fasting in children. Enteral feeding is the commonest support way postoperatively for stimulating gut hormones, modulating immunity, and maintaining the barrier function of the intestinal mucosa.

Our aim was to compare the results and outcome regarding tolerance, nutritional status, and hospital stay following a postoperative diet of peptide-based enteral formula against a whole protein enteral formula after major intestinal surgeries in pediatric patients who had resection and re-anastomosis after intussusception.

**Results:** This is a prospective cohort study on two groups of patients with a total of 30 patients during the period between January 2019 and June 2020.

All patients in both groups underwent major intestinal surgeries (resection and re-anastomosis after intussusception). The first group received postoperative whole protein formula exclusively on the 3rd postoperative day while the other group received peptide-based formula exclusively on the same day.

Postoperative mean serum albumin and pre-albumin levels were significantly higher in peptide-based formula group compared to those who had protein-based formula as their initial feeds (P value < 0.05). The average hospital stay was also significantly shorter in the peptide group (P value < 0.05). Peptide formula was easily tolerated than protein formula in postoperative children who had major intestinal surgeries.

**Conclusion:** Peptide-based enteral formulas are better tolerated and more useful as regards nutritional status than whole-protein formulas in post-operative course of pediatric patients regarding clinical outcome and better economically with shorter hospital stay.

## Background

Malnutrition is a common finding after major abdominal surgeries especially after prolonged period of fasting in children. Enteral feeding is the commonest support way postoperatively for stimulating gut hormones, modulating immunity, and maintaining the barrier function of the intestinal mucosa. However, many drawbacks can occur with this type of feeding such as malabsorption, poor emptying, and hypoalbuminemia. Proteins are hydrolyzed

into small peptides in the small intestine by numerous transport mechanisms which make these peptides a good alternative to the standard protein formula [1].

Some studies advocated the use of peptide-based formula over the standard protein one because of less incidence of diarrhea with this formula [2, 3]. Others have reported that peptide-based formulas have no upper hand over standard formulas [4]. However, peptide-based formula has not been adequately investigated especially in children who had major intestinal surgeries. The major mechanism for absorption of dipeptides and tripeptides of protein digestion products across the brush border is

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absorption through proton-coupled oligopeptide transporters (POTs) [5–11].

Dietary proteins are converted into large peptides by gastric and pancreatic proteases in the gastrointestinal lumen and then undergo further hydrolysis into small peptides (80%) and free amino acids (20%) by various peptidases in the brush border membrane of the intestinal epithelium [12].

Few studies in literature have investigated the benefit of peptide-based formula in sick children. In our hospital, children who had major intestinal surgeries began to receive peptide formula since 2017 [13].

The aim of this study is to compare this peptide-based enteral formula with a standard protein formula in terms of tolerance, nutritional outcome, and hospital stay after abdominal surgery in children.

**Methods**

This prospective cohort study was conducted on two groups of patients with a total of 30 patients (15 patients in each group) during the period between January 2019 and June 2020.

We included in our study all patients who underwent intestinal surgeries (resection and re-anastomosis after intussusception); on the other hand, our exclusion criteria were any patients who presented with signs of peritonitis before surgery or presented intra operatively with bowel perforation and peritoneal soiling.

After surgery, the patients were divided into two study groups without randomization: group 1 received postoperative whole protein formula exclusively on the third postoperative day, while group 2 received peptide-based formula on the same day.

Both groups started feeding after surgery using the same protocol as regards the amount. Each patient received initially 20 cc/kg milk through nasogastric tube (NGT), and feeding was increased gradually till it reached 100 cc/kg after which solid diet was initiated, and the patient was discharged once it tolerated solid diet. Patients who presented with high NGT output > 1 ml/kg/day, vomiting, diarrhea, or significant abdominal distension were considered intolerant to feeding.

Blood samples were collected from all patients on the seventh postoperative day to detect albumin and pre-albumin levels. The average hospital stay was documented in all patients.

The collected data was revised, coded, tabulated, and introduced to a PC using Statistical Package for Social Science (SPSS 25). Data was presented, and suitable analysis was done according to the type of data obtained for each parameter.

Student T Test was used to assess the statistical significance of the difference between two study group means.

Mann-Whitney test (U test) was used to assess the statistical significance of the difference of a non-parametric variable between the two study groups.

Paired t test was used to assess the statistical significance of the difference between the two means measured twice for the same study group.

*P* value: level of significance

- *P* > 0.05: non-significant (NS)
- *P* < 0.05: significant (S)
- *P* < 0.01: highly significant (HS)

**Results**

A total of 30 patients were enrolled in this study, 15 patients in each group. The mean age of patients was 15 months ± 1.5 months.

All patients had abdominal surgery in the form of resection and re-anastomosis for ileocolic intussusception. All patients were given feeds following the same protocol. Both groups started feeding on the third postoperative day. Albumin and pre-albumin levels were measured in all patients on admission day and on the seventh postoperative day.

There were no major differences between the two groups regarding pre- and postoperative albumin levels (Table 1).

On the other hand, pre-albumin levels showed significant differences between the two study groups after surgery. Post-operative pre-albumin levels in patients who received whole protein formula (group 1) were

**Table 1** Pre- and postoperative albumin levels

		Group		Student t test	
		Peptide based	Whole protein		
		Mean ± SD	Mean ± SD	<i>P</i> value	Sig.
Preoperative albumin		3.51 ± 0.22	3.49 ± 0.21	0.733	NS
Post-operative albumin		3.09 ± 0.18	3.13 ± 0.17	0.610	NS
Paired t test	<i>P</i> value	< 0.001	< 0.001		
	Sig.	S	S		
Percent of change in albumin		– 11.81% ± 4.87%	– 10.26% ± 2.7%	0.291	NS

between 12 and 16 mg/dL compared to much higher levels detected in patients who received peptide-based formula (group 2) which were between 22 and 28 mg/dL (Table 2).

Postoperative mean pre-albumin was significantly higher in the peptide group (23.53) compared to the protein group which was only 14.13 (*P* value < 0.05) (Table 2).

As regards tolerance to feeding; patients who presented with high nasogastric output > 1 ml/kg/day, vomiting or significant abdominal distension was considered intolerant to feeding.

Ten out of the fifteen patients who had whole protein diet (group 1) showed intolerance and feeding had to be postponed for 24 h, while five patients in this group showed good tolerance to early feeding on the third postoperative day. On the other hand, patients on peptide-based formula (group 2) showed good tolerance to early feeding with no vomiting, distension, or diarrhea except for one patient who had vomiting with initiation of feeding, and feeding was postponed for 24 h with better tolerance on restarting.

Patients who received whole protein formula (group 1) showed longer hospital stay with average postoperative stay of 5 to 7 days and a mean of 6.33 days. While patients on peptide-based formula (group 2) showed shorter hospital stay with an average of 3–5 days and a mean of 4.53 days (*P* value < 0.05) (Table 3).

**Discussion**

Enteral nutrition care is an important issue in children, but it is more challenging in children who had major intestinal surgeries [14].

In our study, we are clarifying the role of postoperative nutrition as an important factor in the process of tissue recovery and catch up after surgery with subsequent more rapid postoperative recovery, and we are focusing on the choice of enteral feeding type used especially with patients who underwent intestinal surgeries with expected mucosal affection and subsequent absorption

problems due to the effect of derangement of intestinal permeability [14].

Several articles mentioned the role of early enteral feeding initiation in critically ill patients in general and its effect in the process of recovery [15].

A meta-analysis done by Doig GS et al. showed decreased mortality rates in critically ill adult patients with early enteral nutrition [15], while other studies clarified the same effect in adult patients with other critical conditions like pancreatitis [16].

The role of peptide diet formula in critical illness as an important factor for protein synthesis and tissue buildup in addition to its tolerance superiority and better absorption when compared to whole protein diet has been mentioned in several studies which showed its effect in adults after surgery [16, 17].

On the other hand, the data available in literature on the effect of peptide-based diet in children were all discussing its effect in medically affected children with no reference to its effect post-surgery [18, 19].

In our study, we found that peptide-based diet improved the process of protein synthesis showing raised levels of prealbumin after surgery in patients fed on peptide-based formula, with no significant change in post-operative albumin due to its longer half-life.

In comparison to our data, a randomized trial was done on adults by Heimburger et al., who demonstrated that 10 days of feeding with a peptide diet produced greater increase in serum proteins rapid-synthesis than did a whole-protein diet, especially between days 5 and 10 [13].

Also, we found that peptide-based formula shortened hospital stay almost to half of the period with protein diet, which may compensate for the high cost of peptide-based formula compared to whole protein formula and hence overcoming the economic obstacle against using peptide-based diet routinely in critically ill children.

The current study showed effectiveness of peptide-based formula in improving nutritional status of children

**Table 2** Pre- and postoperative pre-albumin levels

	Group		Student t test	
	Peptide based Mean ± SD Median (IQR)	Whole protein Mean ± SD Median (IQR)	P value	Sig.
Pre-operative prealbumin	13.53 ± 2.26	13.33 ± 2.02	0.801	NS
Post-operative prealbumin	23.53 ± 1.55	14.13 ± 1.51	< 0.001	S
Paired t test	<i>P</i> value	< 0.001	0.07	
	Sig.	S	NS	
Percent of change in prealbumin	62.5% (56.25–109.09%)	7.69% (0–18.18%)	< 0.001 (M)	S

M, Mann-Whitney test of significance

**Table 3** Average hospital stay in both groups

	Group		Student t test	
	Peptide based	Whole protein	P value	Sig.
Average hospital stay by days	Mean ± SD 4.53 ± 0.92	Mean ± SD 6.33 ± 0.98	< 0.001	S

especially after major abdominal surgeries. Peptide-based formulas, however, are more expensive compared to the standard whole protein diet. Another limitation of this study was its low number of admitted patients. Well-designed clinical trials are needed to survey the efficacy, tolerance, and cost-effectiveness of using peptide-based enteral formulas for abdominal surgery patients.

### Conclusion

We conclude that peptide-based formula is safe and tolerable in children having abdominal surgeries. Peptide-based formula is more effective than protein formula in improving nutritional status and increasing body proteins postoperatively. Hospital stay can be significantly shortened with the use of peptide-based formula.

### Abbreviations

POTs: Proton-coupled oligopeptide transporters; NGT: Nasogastric tube; SPSS 25: Statistical package for Social Science; NS: Non-significant; S: Significant; HS: Highly significant

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### Authors' contributions

MM and MS shared in writing, collecting, and analyzing the data. YG shared in writing and supervising the feeding protocol from the nutrition point of view. MS was the clinical supervisor and helped in editing this manuscript. I confirm that all authors have read and approved the manuscript.

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### Availability of data and materials

The data and material are available for review.

### Declarations

#### Ethics approval and consent to participate

This study was approved by the IRB of Surgery Department, Faculty of Medicine, Ain Shams University, with reference number 00006379. A written consent was obtained from a parent or guardian for all participants.

#### Consent for publication

Not applicable

#### Competing interests

There was no conflict of interest in this project.

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