

# Does colostrum play a role in intestinal adaptation? A systematic review of literature

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# **Abstract**

Colostrum is a source of growth factors and nutrients aiding newborns in adaptation to extrauterine life. Its clinical use has been investigated as an immunological component to protect, especially preterm newborns, from early infectious complications. This article aims to investigate the current knowledge about the value of colostrum in enhancing mechanisms of intestinal adaptation in patients affected by Short Bowel Syndrome (SBS). A MEDLINE systematic search was conducted. Inclusion criteria were English language and post-operative colostrum administration in animals

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This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0). and humans undergoing bowel resection. From a total of 734, 10 full-text articles were included: 5 studies on animal models, 4 on humans affected by SBS, and 1 study on animal and paediatric populations. Intestinal adaptation was investigated through diverse clinical, morphological, and functional parameters. No clear benefits of colostrum were reported in both populations. Paucity of trials, limited study duration, and heterogeneous conditions led to poorly standardized results. Colostrum tolerability is an encouraging result, but the outcome of colostrum clinical use in short bowel has still to be determined. Further investigations are required to safely promote use of colostrum in nutritional programs. Standard parameters of intestinal adaptation would be required to evaluate the possible role of colostrum in the process.

#### Introduction

Short Bowel Syndrome (SBS) is a rare, multisystemic condition that results from the anatomical or functional loss of segments of the intestine. It leads to insufficient absorption of micro- and macronutrients due to reduced small intestinal length. SBS carries a poor prognosis and represents the leading cause of intestinal failure (IF). According to the American Society for Parenteral and Enteral Nutrition (ASPEN), pediatric IF is defined as "a reduction of functional intestinal mass below the level required to sustain life, necessitating parenteral support for at least 60 days within a 74-day period". Despite improvements in management over the years, mortality remains high, ranging from 30% to 50%. The malabsorptive state caused by insufficient bowel length presents numerous challenges.

Several strategies have been developed to improve nutritional status in these patients, with the ultimate goal of supporting growth and development. Surgical options, including autologous gastrointestinal reconstructive procedures, have proven safe and effective in increasing intestinal length.<sup>5</sup> Parenteral Nutrition (PN) is often essential to provide adequate caloric intake. However, PN carries serious risks, including central line-related complications.<sup>6</sup> One of the most severe long-term complications is Intestinal Failure-Associated Liver Disease (IFALD), which occurs in the absence of primary liver pathology. IFALD can progress to cirrhosis and portal hypertension, requiring liver or combined liver-intestine transplantation.<sup>7</sup>

Medical therapies have also been explored to promote Intestinal Adaptation (IA). Among them, Teduglutide, a GLP-2 analog, has shown promise.<sup>8</sup> IA includes a range of structural and functional modifications that aim to maximize absorption in the reduced gut. The process is not yet fully understood, and its timing varies.<sup>9-11</sup> Several hormones and growth factors are involved, including





Growth Hormone (GH), Glucagon-Like Peptide-2 (GLP-2), Epidermal Growth Factor (EGF), and Insulin-like Growth Factor (IGF). 12-13 IA is associated with mucosal hyperplasia, deeper crypts, and longer villi.

Enteral Nutrition (EN) plays a key role in triggering and sustaining IA.<sup>14</sup> In recent years, interest has grown in the potential use of colostrum. Colostrum is rich in immune and growth factors, hormones, and nutrients that support the newborn's transition to extrauterine life. Its clinical use has been studied as an immunological tool, particularly in reducing bacterial translocation and sepsis after abdominal surgery.<sup>15</sup>

Our goal is to improve intestinal rehabilitation strategies by exploring low-risk interventions. We reviewed the available literature on the potential role of colostrum in supporting IA in resected bowel.

# **Materials and Methods**

A systematic search of MEDLINE/PubMed was performed and updated to December 2022. The following terms were used:

"colostrum AND short bowel syndrome," "colostrum AND intestinal adaptation," and "colostrum AND intestine AND surgery." Abstracts were screened using predefined inclusion and exclusion criteria. Inclusion criteria included studies in English, involving humans or animals undergoing bowel surgery with postoperative colostrum administration. The exclusion criteria were non-English language, use of colostrum in non-surgical patients, and surgeries unrelated to the intestine. Only original articles were included.

Full texts of selected articles were reviewed by two independent authors. References of included articles were screened to identify additional relevant papers not indexed in PubMed. This review was conducted according to the latest PRISMA guidelines (Figure 1).<sup>16</sup>

# Results

The initial search retrieved 734 articles. Two additional studies were identified through references, for a total of 736 abstracts screened. Forty-six papers were excluded based on language. Another 680 were excluded because they involved non-surgical patients or surgeries unrelated to the bowel. The selection process

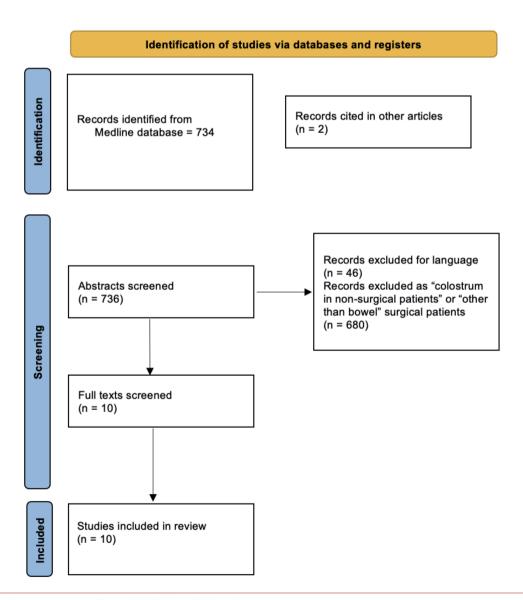


Figure 1. Selection process according to PRISMA guidelines. 16



is shown in Figure 1. Ten studies met all criteria: 5 on animal models (piglets), 4 on humans, and 1 involving both species.<sup>19</sup>

#### **Animal studies**

All animal studies were randomized controlled trials. A total of 167 piglets were included, although one paper did not report the exact number.<sup>20</sup> Two studies used only female piglets; others did not specify sex. Age at surgery ranged from 4 hours to 4 weeks. All animals underwent small bowel resection, ranging from 50% to 75%, with colon preservation (Table 1).

Some studies initially included larger populations to compare resected versus transected bowel groups. However, results from transected groups were excluded, as they did not meet the inclusion criteria.

In all six studies, postoperative colostrum supplementation was compared to standard formula feeding. Study durations ranged from 7 days to 8 weeks. Of five studies examining body weight, one found a significant increase in the colostrum

group, one showed no difference, and three found no statistical difference.

Stool characteristics were analyzed in two studies. One found no difference in stool weight; the other reported improved texture in the colostrum group.

Blood parameters were evaluated in two papers. Pereira-Fantini et al. observed increased serum IGF-1 and IGF-BP3 in the colostrum group. One study reported elevated plasma GLP-2 following colostrum supplementation.

None of the studies showed a reduction in PN or EN needs, indicating no benefit in achieving enteral autonomy.

Two studies reported increased bowel length in colostrum-fed piglets at sacrifice. Bowel weight remained unchanged in two studies.

Histological findings were mixed. Aunsholt et al. found reduced villus length in both jejunum and ileum, while Nagy et al. reported increased ileal villus height. Three studies reported increased crypt depth; one found a decrease in jejunal crypt length, suggesting no IA response.<sup>21</sup>

**Table 1.** Summary of randomized controlled trials on colostrum use after bowel resection in piglets. All studies compared colostrum to standard formula. Outcomes included growth, blood markers, bowel morphology, and histology. No clear benefit on enteral autonomy was observed.

	Heemskerk 2022	Nagy 2004	Paris 2004	Pereira-Fantini 2008	Aunsholt 2014*	Aunsholt 2017
Type of study	Randomized controlled	Randomized controlled	Randomized controlled	Randomized controlled	Randomized controlled	Preniclinical, randomized controlled
Population (n)	24	35	45	NR	33**	30
Age at surgery	7 days old	4 weeks	3 weeks	4 weeks	n 19=4 hours of life; n 14=56 hours of life	2 days of life
N° of patients	24	21	31	NR	33	30
Extent of resection	75% resection: 50 cm jenum and ileum <i>in situ</i>	75% resection from 50 cm from the treitz to 250 cm proximal to the ICV	75% resection from 50 cm from the treitz to 250 cm proximal to the ICV		,	50% distal small intestine, 2 cm proximal to ICV+ileostomy
Type of Colostr post-operative nutrition Control	um Infant formula+ Bovine colostrum Infant formula+ casey, whey proteins and carbohydrate	PIF+ bovine CPC  PIF or  Pig chow	PIF+ bovine CPC  Pig Chow or Infant fomula or PIF or PIF+fiber at 163 gr/172 MJ enery	PIF+ bovine CPC PIF	Bovine colostrum N/A	PN+Bovine colustrum PN or PN+ formula
Study duration	4 weeks	8 weeks	8 weeks	8 weeks	7 days	7 days
Body weight	No SSD	No SSD	Increased	NR	Comparable	No SSD
Stool weight	NR	NR	NR	NR	NR	No SSD
Stool frequency	NR	NR	NR	NR	NR	NR
Stool texture	NR	Increased	NR	NR	NR	NR
Serum IGF-1	NR	NR	NR	Increased	NR	NR
Serum IGF-BP3	NR	NR	NR	Increased	NR	NR
Plasma GLP-2	NR	NR	Increased	NR	NR	NR
Reducing EN/PN	No	No	No	No	NR	NR
Bowel length	No SSD	NR	Increased	Increased	No SSD	No SSD
Bowel weight	No SSD	NR	NR	NR	No SSD	NR
Villus Jejunum length Ileum	No SSD No SSD	Increased Increased	NR NR	NR NR	Decreased Decreased	Increased Decreased
Crypt Jejunum depth Ileum	Decreased No SSD	Increased Increased	NR NR		Increased in terms piglets Increased in terms piglets	Increased Increased
Mitotic index	No SSD	NR	NR	NR	Increased in preterms	NR

<sup>\*</sup>Results refer to comparison between preterm and term piglets with colostrum supplementation; \*\*colostrum supplementation was given before resection in preterm piglets; NR, Not Reported; N/A, not applicable; PIF, Polymeric infant formula; CPC, colostrum protein concentrate; ICV, ileocecal valve; PN, parenteral nutrition; EN, enteral nutrition; No SSD, No statically significant difference.





#### **Human studies**

Four studies involving 56 patients were included (Table 2). Two were randomized, double-blind, controlled trials; one was single-blind. Patients received either colostrum or artificial milk as nutritional support (enteral or parenteral). One study included both pediatric and adult patients.<sup>22</sup> Patients varied in SBS etiology and were not grouped by cause. All required nutritional support (EN or PN).

One study reported improved body weight with colostrum; another found no difference.<sup>23</sup> No significant differences were observed in stool weight in four out of five studies; only one reported a reduction in the colostrum group. Stool frequency varied across studies, reported as increased, reduced, or unchanged. Stool consistency improved in three out of five studies; one study noted worsening.

Two studies measured serum IGF-1 and IGF-BP3; only one reported increases. One study showed reduced nutritional support needs; another did not confirm this. Due to ethical reasons, no intestinal biopsies were performed.

# **Discussion**

SBS has serious consequences for long-term health and quality of life. Prolonged PN is associated with significant risks, especially Central Line-Associated Bloodstream Infections (CLABSI), a major cause of morbidity and mortality.<sup>24,25</sup> Promoting intestinal adapta-

tion is essential to reducing PN dependence and reversing IF. EN is a key driver of IA.  $^{26}$ 

Human Milk (HM) is considered the gold standard for infant feeding, especially in IF.<sup>27,28</sup> It contains bioactive substances such as immunoglobulins, prebiotics, and growth factors like GH and EGF, which enhance IA.<sup>29,30</sup> These benefits have not been matched by formula-based products.<sup>31</sup>

Colostrum is a complex fluid that supports nutrition, immunity, and organ development. It contains antimicrobial agents, immunostimulatory peptides, and growth factors.<sup>32</sup> Its use in post-surgical settings has shown some benefit. For example, Eslamian *et al.* conducted a randomized, double-blind, placebo-controlled trial in ICU patients undergoing major surgery and found improvements in gut function with bovine colostrum.<sup>34</sup>

Data on colostrum use in pediatric SBS are limited. The piglet model closely mirrors human SBS and has been widely used.<sup>35</sup> Included studies examined clinical and histological outcomes. Some used transected controls, but these were excluded, as they do not reflect clinical SBS.<sup>36,37</sup>

One piglet study showed weight gain and elevated GLP-2 in the colostrum group,<sup>37</sup> possibly indicating IA. However, this did not correlate with other IA markers. Another study found no difference between term and preterm piglets fed with colostrum.<sup>23</sup> In humans, Brink et al. reported weight gain in a single patient on colostrum,<sup>38</sup> but this was not replicated in other studies.

Only one study found fewer evacuations and firmer stools with colostrum, though this did not translate into improved nutrient

Table 2. Summary of human studies comparing colostrum to standard milk in SBS patients. Mixed results on stool parameters and nutritional support; no biopsies performed.

	Brink 1977*	Rangercroft 1978	Aunsholt 2012	Lund 2012	Aunsholt 2017	
Type of study	Case report	Clinical trial	Randomized, double blind, Randomized, double blind, Randomized single blind			
			crossover	crossover	clinical trial	
Population (n)	1	24	9	12**	10	
Age at surgery	6 days of life	NR	3 years and 3 months (1-14 y)	55.7±10.7 years	NR	
Primary diagnosis	NEC	NR	Intestinal atresia (n=2); gastroschisis (n=3); NEC (n=3 midgut volvolus (n=1)	Chron disease (n=10); ); Ileus (n=2)	NR	
Nutritional support prior to surgery	PN+EN	NR	PN (n=9); EN (n=6)	PF (n=4); PN (n=5); OA (n=3)	PN	
N° of patients	24	21	31	NR	33	
Extent of resection	NR	NR NI	R, but preserved colonic contin	uity NR	NR	
Type of Colostrum post-operative nutrition	Frozen human colostrum	Fresh human colostrun	n 20% replacement of BFR with bovine colostrum	Bovine colostrum supplement	50% of EN replaced with colostrum	
Control	N/A	Humanized cow's milk	Milk mix	Iso-energetic and Iso-proteinaceous control	Breast milk or standard formula	
Study duration	NR	NR	12 weeks	4 weeks	8 weeks	
Body weight	Increased	NR	NR	No SSD	Comparable	
Stool weight	Reduced	No SSD	No SSD	No SSD	No SSD	
Stool frequency	Increased	No SSD	Reduced	NR	NR	
Stool texture	Reduced	Reduced	Increased	Reduced	NR	
Serum IFG-1	NR	NR	No SSD	NR	Increased	
Serum IGF-BP3	NR	NR	No SSD	NR	Increased	
Plasma GLP-2	NR	NR	NR	No SSD	NR	
Enzymatic activity	NR	NR	No SSD	No SSD	NR	
Reducing EN/PN	Yes	No	NR	NR	NR	

<sup>\*</sup>Results were compared to the period prior to colostrum supplementation; \*\*8 patients completed the study; NR, Not reported; N/A, not applicable; PIF, Polymeric infant formula; CPC, colostrum protein concentrate; BFR, basal fluid requirement; PF, parenteral fluid; PN, parenteral nutrition; EN, enteral nutrition; No SSD, No statically significant difference.





absorption. Serum IGF-1 and IGF-BP3 increased in some studies, but without matching histological evidence. Crypt depth increased in most animal studies, suggesting some IA benefit.<sup>39</sup>

Overall, no conclusive evidence supports colostrum as superior to standard formula in SBS. Only one study (on one patient) reported reduced need for PN.<sup>18</sup> Short study durations may not capture subtle mucosal changes. However, increased bowel length in two piglet studies<sup>20,37</sup> may indicate a potential benefit in mucosal development.

Colostrum cannot yet be recommended as part of our SBS nutritional protocol. The literature remains insufficient. Due to SBS rarity (24.5 cases per 100,000 live births), 40 larger studies are difficult. We need standardized and sensitive outcome measures to evaluate IA more accurately.

### **Conclusions**

The clinical role of colostrum in SBS remains uncertain. Current trials are limited, with small, heterogeneous populations. However, colostrum appears well tolerated, with no major adverse effects reported.

Its richness in bioactive components and safety profile make it an interesting subject for future research. For now, the evidence does not support routine use of colostrum in SBS rehabilitation. More robust studies with clear markers of intestinal adaptation are needed before its role can be defined.

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