

# Assessment and outcome of pediatric intestinal pseudo-obstruction: A tertiary-care-center experience from Turkey

Yeliz Çağan Appak<sup>1\*</sup>, Maşallah Baran<sup>2\*</sup>, Mustafa Onur Öztan<sup>3</sup>, Miray Karakoyun<sup>1</sup>, Soysal Turhan<sup>4</sup>, Cem Tuğmen<sup>5</sup>, Sema Aydoğdu<sup>6</sup>, Cezmi Karaca<sup>6</sup>, Gökhan Köylüoğlu<sup>3</sup>

<sup>1</sup>Department of Pediatric Gastroenterology, Hepatology and Nutrition, SBU Tepecik Training and Research Hospital, İzmir, Turkey

<sup>2</sup>Department of Pediatric Gastroenterology, Hepatology and Nutrition, İzmir Katip Çelebi University & SBU Tepecik Training and Research Hospital, İzmir, Turkey

<sup>3</sup>Department of Pediatric Surgery, İzmir Katip Çelebi University & SBU Tepecik Training and Research Hospital, İzmir, Turkey

<sup>4</sup>Department of Cardiovascular Surgery, SBU Tepecik Training and Research Hospital, İzmir, Turkey

<sup>5</sup>Department of Organ Transplantation and General Surgery, SBU Tepecik Training and Research Hospital, İzmir, Turkey

<sup>6</sup>Department of Pediatric Gastroenterology, Hepatology and Nutrition, Ege University School of Medicine, İzmir, Turkey

**Cite this article as:** Çağan Appak Y, Baran M, Öztan MO, et al. Assessment and outcome of pediatric intestinal pseudo-obstruction: A tertiary-care-center experience from Turkey. *Turk J Gastroenterol* 2019; DOI: 10.5152/tjg.2019.18287.

## ABSTRACT

**Background/Aims:** Pediatric intestinal pseudo-obstruction (PIPO) is a severe disorder of gut motility. In this rare and difficult-to-manage disease, complex treatment method, such as intestinal transplantation, is sometimes needed. This study evaluated the management and follow-up results of patients with PIPO who received treatment at our center.

**Materials and Methods:** The cases of 13 patients with PIPO were reviewed retrospectively. Demographic data, clinical features, etiologies, pharmacological and surgical treatments, nutritional support, anthropometric findings, small bowel transplantation (SBT), and survival rates were assessed.

**Results:** Two of the patients were diagnosed at 1 and 5 years of age, while other patients were diagnosed during neonatal period. The etiological cause could not be identified for 5 patients. Pharmacological treatment response was observed in 38.4% of patients. Post-pyloric feeding was applied in 4 patients, but no response was observed. Gastrostomy decreased the clinical symptoms in 3 patients during the abdominal distension period. Total oral nutrition was achieved in 38.4% of the total-parenteral-nutrition (TPN)-dependent patients. It was observed that anthropometric findings improved in patients with total oral nutrition. Liver cirrhosis developed in 1 patient. Venous thrombosis developed in 4 patients. The SBT was performed on 3 patients. One of these patients has been followed up for the last 4 years.

**Conclusion:** Pediatric intestinal pseudo-obstruction is a rare disease that can present with a wide range of clinical symptoms. While some patients require intestinal transplantation, supportive care may be sufficient in others. For this reason, patients with PIPO should be managed individually.

**Keywords:** Intestinal pseudo-obstruction, child, intestinal transplantation, nutrition, treatment

## INTRODUCTION

Chronic intestinal pseudo-obstruction (CIPO) is a clinical condition characterized by the severe impairment of gastrointestinal peristalsis with partial or complete intestinal obstruction symptoms, the lesion that occludes the intestinal lumen is absent (1,2). Any segment of the gastrointestinal system can be involved (1-3). Clinical symptoms vary from patient to patient, based on the localization and the extent of the involved segment. The number of studies, especially the ones concerning children about this rare disease, is limited in the literature. It

has been suggested that the CIPO that occurs in infants and children may be a different condition from the one that occurs in adults. According to the latest European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommendation, this condition should be referred to as pediatric intestinal pseudo-obstruction (PIPO) (4). Literature about this disease is also limited in our country, and it mostly comprises case presentations and case series (5-7). A nationwide survey in Japan identified 62 patients with PIPO from 47 centers with a prevalence of 3.7 in 1 million people (8). Available

\*These authors contributed equally to the study

Corresponding Author: Maşallah Baran; mbaran2509@gmail.com

Received: April 11, 2018 Accepted: April 11, 2018 Available online date: January 11, 2018

© Copyright 2018 by The Turkish Society of Gastroenterology · Available online at www.turkjgastroenterol.org

DOI: 10.5152/tjg.2019.18287

data suggest that PIPO is rare and likely to have an incidence of <1 in 40,000, possibly even <1 in 100,000 (4).

Limited knowledge about PIPO, the difficulty in diagnosing the disease, and the ineffectiveness of pharmacological treatment lead to a low quality of life of these patients, along with high morbidity and mortality rates (9,10). Nevertheless, nutritional, pharmacological, and surgical treatments, as well as the recent developments in intestinal transplantation, have improved patient care (1,3,9). This study evaluates the management, pharmacological and surgical treatments, clinical features, nutritional support, anthropometric findings, survival rates, and the results of the small bowel transplantation (SBT) in the patients with PIPO who were followed up in our center.

### **MATERIALS AND METHODS**

In this study, we evaluated 13 patients with PIPO, retrospectively. Patients (7/13) who were diagnosed with PIPO at our pediatric gastroenterology clinic and patients (6/13) who were referred for intestinal transplantation between February 2012 and February 2018 were included in the study. The PIPO diagnosis was made according to the ESPGHAN evidence and the consensus-based recommendations criteria (4). According to these criteria, PIPO is defined as a disorder characterized by the chronic inability of the gastrointestinal tract to propel its contents via mimicking mechanical obstruction, in the absence of a lesion that might occlude the gut. Chronic is defined as the persistence of symptoms that lasts for 2 months, starting from birth or at least 6 months after. The diagnosis of PIPO requires at least 2 out of 4 of the following: an objective measurement of the small intestinal neuromuscular involvement (manometry, histopathology, transit); recurrent and/or persistently dilated loops of small intestine with air-fluid levels; genetic and/or metabolic abnormalities definitively associated with PIPO; and the inability to maintain adequate nutrition and/or growth with oral feeding (needing a special enteral nutrition and/or parenteral nutrition support) (4). Patients who were not considered to be suffering from PIPO and who did not meet these criteria were excluded from the study. We evaluated the patients' demographic data, applied treatments, responses to treatment, complications during the follow-up, nutritional status, and surgical procedure results, including the results of the SBT. Additionally, patient's z scores for their weight-for-age and height-for-age were evaluated up on admission and after follow-up. As for the treatment protocol, erythromycin was applied orally in a dose of 3–5 mg/kg/day orally, and octreotide in a dose of 1 mcg/kg/hour intravenously. The

other medications such as neostigmine, pyridostigmine, cisapride, trimebutine maleate, metoclopramide, domperidone, and laxatives were given according to the standard pediatric doses. Responses to the pharmacological treatments were assessed via the regression of symptoms, such as increasing intestinal peristalsis, reduced abdominal distension, and increased nutritional tolerance. An ethics committee approval was received from the ethical committee of the SBU Tepecik Training and Research Hospital (17.08.2017/20).

### **Statistical analysis**

The data were assessed using descriptive statistics for numbers, percentages, distributions, means, and standard deviations. The data were evaluated with the Statistical Package for Social Sciences version 20.0 (IBM Corp.; Armonk, NY, USA).

### **RESULTS**

Only 1 patient with PIPO had a preterm delivery history. The clinical symptoms of 2 patients manifested at 1 and 5 years of age; all the other patients were identified as symptomatic during the neonatal period. The median age of the patients with PIPO at the time of the symptom onset was 2 days (minimum 1 day-maximum 96 months). The mean age of the patients up on admission was  $35.3 \pm 35.9$  months (minimum 4 days-maximum 9 years old), and the average follow-up period was  $26.4 \pm 18.6$  months. Vomiting was the most common cause of admission for all the patients. Abdominal distention was present in 92.3% of the patients, and chronic constipation occurred in 23%. Three patients had megacystis microcolon intestinal hypoperistalsis (MMIH), 2 had intestinal neuronal dysplasia (IND), 2 had Waardenburg syndrome (WS), and 1 had enteric anendocrinosis (EA), while the etiological cause could not be found for 5 patients. The symptoms for 3 of the patients diagnosed with MMIH manifested during the prenatal period, and these patients were followed after birth.

Six patients had an ostomy operation in the early infancy period due to ileus, and 4 of these patients benefited from the operation. The ratio of reiterated surgery in all patients was 4/13 (30.7%). Five patients (38.4%) responded to pharmacological treatments applied during the pseudo-obstruction attacks, and 3 of those patients reached the targeted level of nutritional tolerance. The other 8 patients did not respond to the given pharmacological treatments. The most frequently used pharmacological treatments were somatostatin derivation (octreotide), cholinergic agents, and erythromycin. The

**Table 1.** All the collected data of patients with PIPO and follow-up results

Patient	Clinical onset age/ Gender	Admission age to our clinic	Intestinal biopsy results	Diagnosis	Operation	Pharmacological treatment/ response(+/-)	Nutrition	last age survival/SBT
1.	<1 mo/M	14 mo	Large ganglion cells	-	Ileostomy, Gastrostomy	Erythromycin/-, Neostigmine/+ Pyridostigmine/+ (only during the pseudo-obstruction attack periods)	Oral-enteral (polymeric formula) and mixed nutrition, intermittent TPN	3.5 y/ alive/ -
2.	<1 mo/F	22 mo	Ganglion cells positive	MMIH	Colecotomy, Jejunum- ileum resection, Gastrostomy Vesicostomy	Octreotide/-, Erythromycin/-	TPN-dependent	3y/alive/ waiting for multivisceral Tx
3.	<1 mo/M	18 mo	-	MMIH	Jejunostomy, Vesicostomy	Erythromycin /-, Neostigmine/- Pyridostigmine/-	TPN-dependent	2 y/ lost to follow up/ -
4.	<1 mo/F	5 y	Ganglion cells positive	-	Gastrostomy	Erythromycin /-, Octreotide/- Pyridostigmine/- Domperidone/- Nicotine/-	TPN-dependent	6.5 y/ alive/ waiting for SBT
5.	<1 mo/M	3 y	Aganglionic colon, ganglion cells positive jejunum	WS type 4	Jejunostomy, Resection- bypass, Colecotomy	Erythromycin/-, Octreotide/-	TPN-dependent, TPN-free after Tx (polymeric formula and mixed nutrition)	7.5 y/ alive/SBT at 5,5 y
6.	<1 mo/M	4. day	Hypoganglionism in jejunum	WS type 4	Ileostomy, Jejunostomy	Erythromycin /-, Cisapride/- Domperidone/-, Octreotide/- *Probiotic(-3 month), Erythromycin /- Cisapride/-, Domperidone/+ (6 months) Octreotide/+ (4 weeks)	TPN-dependent, TPN free after Tx	21 mo ex /SBT at 9 mo
7.	<1 mo/F	5 y	-	-	-	-	TPN-dependent first 8 months, hydrolysed formula, transition to TPN-free (polymeric and mixed nutrition)	8 y/ alive/-
8.	<1 mo/F	1,5 mo	Microcolon, ganglion cells positive colon and ileum	-	Bridektomi, ileostomy	Erythromycin /+ (3 month), Trimebutine maleate/+ (4 weeks), Octreotide/+	TPN-dependent first 10 months, hydrolysed formula transition to TPN-free	5 y/ alive/-
9.	12 mo/M	3 y	-	-	Gastrostomy, Jejunostomy	Pyridostigmine/-	TPN support first 2 years, transition to oral and enteral nutrition (polymeric formula)	6y/ alive/-
10.	<1 mo/F	5 mo	-	MMIH	Ileostomy, Jejunostomy Gastrostomy, Vesicostomy	Metoclopramide/-	TPN-dependent follow up/-	6 mo/lost to
11.	<1 mo/F	2 mo	No enteroendocrine cell	EA	-	Octreotide/- nutrition (polymeric)	Partial TPN+enteral formula)	8 mo/ ex/-
12.	<1 mo/M	7 y	Degenerative ganglion cells	IND tip B	Partial colectomy, Colostomy, Bridektomi	Laxative/+(only during the pseudo-obstruction attack periods)	Trimebutine maleate/+ (6 months)	TPN-free 9 y/ alive/ -
13.	5 y/F	9 y	Large ganglion cells	IND	Cecostomy, Partial colectomy, ileostomy	Octreotide/+ (4 weeks)	TPN-free	11 y/ alive/-

F: Female; M: Male; MMIH: Megacystis-microcolon-intestinal hypoperistalsis; WS: Waardenburg Syndrome; EA: Enteric anendocrinosis; IND: Intestinal neuronal dysplasia; SBT: Small bowel transplantation, Tx: Transplantation; TPN: Total parenteral nutrition; \*Including Lactobacillus reuteri (5 drops/day)

**Table 2.** Anthropometric data of the patients up on admission and after the follow-up

Patients	Admission		Follow-up duration (month)	Finally	
	Weight for age z scores	Height for age z scores		Weight for age z scores	Height for age z scores
1.	-2.04	-1.77	28	-3.50	-3.78
2.	-2.90	-3,17	14	-3.80	-3.90
3.	-2.70	-2,90	6	-4.09	-3.74
4.	-4,06	-4.68	19	-2.62	-4.11
5.	-5,47	-4.06	57	-0.74	-0.92
6.	-3.01	-2.80	21	-3,19	-2,73
7.	-2.36	-1.77	38	-2.06	-1.56
8.	-0.16	-0.52	63	-1.11	1.01
9.	-2.25	0.65	40	-5.78	-3.88
10.	-5.83	-4.3	1	-6.26	-5.01
11.	0.31	1.04	6	-1.34	-0.48
12.	0.19	0.06	26	0.21	-0.05
13.	-0.73	0.10	24	-0.69	-0.95

applied pharmacological treatments and the patients' responses are presented in Table 1.

Four of the patients were dependent on total parenteral nutrition (TPN). Post-pyloric nutrition was used in 4 patients who did not tolerate oral and nasogastric nutrition. In these patients, after the polymeric formula was not tolerated, an extensively hydrolyzed formula was initiated, but the desired enteral nutrition could not be attained. Gastrostomy was applied to 3 of these patients at our clinic. Enteral nutrition of 2 patients was supported intermittently by gastrostomy infusion, and 1 of these patients required intermittent TPN. One patient was partially dependent on TPN. Three other patients were TPN dependent at the beginning of the treatment, but they were able to switch to oral nutrition gradually. Two patients who were TPN dependent before the SBT surgery have restored total oral nutrition after the transplantation. The 2 patients with IND could maintain oral feeding, except during the pseudo-obstruction attack periods. The nutritional monitoring of the patients is presented in Table 1.

Isolated SBT was performed in 3 patients. The SBT caused severe sepsis episodes in 2 patients and vascular thrombosis in 1 patient. A 2-year-old SBT patient developed graft dysfunction due to insufficient vascular flow intraoperatively; the same patient is 3 years old now and waiting for a multivisceral transplantation due to liver failure. The 9-month-old SBT patient died of sepsis and

Epstein-Barr virus-related post-transplant lymphoproliferative disease 1 year after the operation. The patient who had SBT at 5 years of age has been followed for 4 years without any problems. One TPN-dependent patient is currently waiting for SBT in our clinic.

A review of the other organ dysfunctions in these patients revealed that, other than intestinal system problems, the most frequent health concerns were related to renal issues (38%). Three patients had vesicoureteral reflux, and 2 patients had unilateral renal atrophy. Four patients, 3 of whom had MMIH, had megacystis. Venous thrombosis was detected in the follow-up of 4 patients who were TPN dependent. For 1 of these patients, thrombosis existed in all the main vascular accesses; therefore, SBT could not be performed. Persistent gastrointestinal system bleeding caused by vascular ectasia was observed in 1 patient with IND. Liver failure was observed in the 1 TPN-dependent patient who was 27 months old. All the collected patient data including the age of clinical onset, admission age to our clinic, diagnosis, intestinal biopsy results, treatments, results of SBT, and follow-up are presented in Table 1. Additionally, anthropometric findings of the patients at the admission and after the follow-up are presented in Table 2.

**DISCUSSION**

In 38.4% of our patients with PIPO, after the parenteral nutritional support and pharmacologic and surgical treatment, a progressive total oral nutrition was achieved

gradually. When we evaluated the study sample, 61.5% of patients had an indication for intestinal transplantation, and 3 of these patients underwent SBT. In particular, it has been determined that the patients with MMIH did not benefit from pharmacological and non-transplant surgical treatments and the treatment responses were inadequate. It has been found that the anthropometric findings recover in TPN-dependent patients who can be transferred to total oral nutrition. The majority of our patients seem to need surgical procedures and undergo surgery. However, in patients with PIPO, it is essential to minimize the number of surgical interventions to avoid potential complications (4). Depending on the etiology, some cases can be easily diagnosed during the early stages. Prenatal symptoms can be detected in about 20% of PIPO cases, with megacystis being the most frequently reported indication (11). In our patients, the detection rate of fetal megacystis is 23%. As in some of our patients, some cases are difficult to diagnose and cannot be diagnosed until much later, after the patient has received unnecessary treatments and surgeries (2).

The digestive system problems of patients with PIPO restrict normal oral feeding, and the patients cannot receive the calories they require. It has been reported that 60%-80% of PIPO cases diagnosed in the first year of life required parenteral feeding (12). Some patients are TPN dependent and cannot tolerate oral intake (13). For such patients, nasogastric or nasoduodenal feeding should be provided to deliver sufficient calories before the permanent feeding tube administration (14,15). We have applied post-pyloric feeding in 4 of the patients with PIPO, but successful enteral feeding could not be accomplished. Oral feeding is the primary independent factor associated with positive prognosis. Therefore, patients receiving parenteral feeding should ingest as much oral food as they can tolerate (14,15). Some patients with PIPO can tolerate enteral feeding with gastrostomy or jejunostomy (16). Two of our patients received intermittent enteral feeding by gastrostomy infusion, in addition to oral feeding. Procedures like gastrostomy and enterostomy are also essential treatments because they reduce complaints such as abdominal distension and vomiting. When surgery is indicated, a gastrostomy tube can be inserted during the same procedure (4). Ostomies may be utilized to perform motility investigations (manometries) by serving as the insertion sites for the manometry catheters (4). We have observed that 3 of our patients with PIPO benefited from gastrostomy; abdominal distension and vomiting reduced.

Pharmacological treatment for patients with PIPO typically aims to avoid bacterial overgrowth, gain gastrointestinal motor function, and enable oral intake. It has been demonstrated that 11% of the adult patients are asymptomatic between the subacute obstructive episodes and do not require chronic pharmacological treatment (17). Erythromycin, octreotide, cholinesterase inhibitors, prokinetics, and probiotics are the most frequently used pharmacological agents (10,18). Pharmacological treatment response in our patients is 38.4%. Our patients have responded to erythromycin, octreotide, neostigmine, pyridostigmine, trimebutine maleate, domperidone, and laxative treatments. Overall, there is no recommended drug treatment to improve gastrointestinal motility in the majority of patients with PIPO (4). Eight of our patients who did not respond to pharmacological treatment were found to have MMIH, EA, and WS. The pharmacological treatment response in these patients is lower, and the need for SBT should be assessed.

Intestinal manometry can be helpful in defining the pathophysiological mechanisms that are involved in PIPO, such as neuropathic or myopathic causes. However, the diagnostic specificity's low, and in most patients, it does not affect the treatment. Antroduodenal manometry has been applied in PIPO to assess a patient's prognosis, response to treatment, and oral feeding tolerance (19). When a PIPO diagnosis is considered, a normal manometry is valuable as it can essentially exclude the possibility of PIPO (20). The ESPGHAN recommends that in children with suspected or confirmed PIPO, an esophageal, colonic, or anorectal manometry can be used to assess the extent of the disease (4). A manometric assessment of the entire gastrointestinal system is useful in planning the treatment and deciding the necessity of isolated or multivisceral transplantation, especially in severe PIPO cases (10). Due to technical incompetence, manometric assessment of our patients could not be undertaken at our clinic.

The most frequent cause of morbidity and mortality in patients with PIPO is related to the side effects of long-term TPN use (21). Although the prognosis for patients with PIPO varies, one-third of children die within the first year of life (22). In our follow-up, only 1 of the patients died within the first year. Intestinal transplantation is a life-saving option for patients who are experiencing TPN complications and intestinal failure. A study assessing 27 children with PIPO reported that 8 patients had intestinal transplantation, all the patients tolerated full enteral feeding, and 3 patients died during follow-up (23). Two

of the 3 patients who underwent successful SBTs in our center received full enteral feeding after SBT. It is seen that the z scores of the patients who have switched to total oral nutrition improved. Patients who were dependent on TPN and could not switch to sufficient enteral nutrition were found to have a significant increase in z scores of both the weight and height. It has been thought that complications and genetic causes in addition to enteral feeding problems may contribute to growth retardation in these patients.

TPN-dependent cases generally require central venous catheterization. In patients who receive long-term intravenous therapy, catheterizations with central venous access devices may lead to venous thrombosis and venous stenosis over time (24,25). Vascular thrombosis complications have been observed to be more frequent in femoral venous (FV) catheterization (24). Graft anastomosis was performed on the vena cava inferior (VCI) during SBT (26). We do not recommend the FV catheterization in the TPN-dependent patients who are candidates for transplantation due to the thrombosis and decreased flow in the VCI. In 1 of our patients who had a history of FV catheterization, graft dysfunction was observed during SBT due to the VCI flow inadequacy.

Pediatric intestinal pseudo-obstruction is a rare disease with dramatic clinical variations. At one end of the spectrum, there are TPN-dependent patients with several related complications who have high morbidity and mortality. At the other end, there are patients with mild symptoms, apart from their pseudo-obstruction attacks. Intestinal transplantation is the only solution for the severe PIPO cases, particularly the TPN-dependent patients. Some patients can only survive with enteral feeding methods and ongoing pharmacological treatment. Each patient's treatment approach and follow-up care should be considered independently.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the Ethics Committee of SBU Tepecik Training and Research Hospital (17.08.2017/20).

**Informed Consent:** Written informed consent was obtained from parents and patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Acknowledgments:** We appreciate the following colleagues for referring their patients to our center for intestinal transplantation: Prof. Dr. Tanju Özkan (Uludağ University), Prof.

Dr. Reha Artan (Akdeniz University), Prof. Dr. Aydan Kansu (Ankara University), Prof. Dr. Deniz Ertem (Marmara University), and Assoc. Prof. Dr. Selim Gökçe (Bezmialem Vakıf University).

**Author Contributions:** Concept - Y.C.A., M.B.; Design - Y.C.A, M.B ; Supervision - M.B., C.T., S.A., C.K., G.K.; Resource - Y.C.A., M.B., M.K., C.T., S.A., C.K., G.K.; Materials - Y.C.A., M.K., O.O., S.T.; Data Collection and/or Processing - Y.C.A., M.K., O.O., S.T.; Analysis and/or Interpretation - Y.C.A., M.B.; Literature Search - Y.C.A., M.B., O.O., S.T., C.T.; Writing - Y.C.A., M.B.; Critical Reviews - S.A., C.K., G.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

## REFERENCES

1. De Giorgio R, Cogliandro RF, Barbara G, Corinaldesi R, Stanghellini V. Chronic intestinal pseudo-obstruction: clinical features, diagnosis, and therapy. *Gastroenterol Clin North Am* 2011; 40: 787-807. [CrossRef]
2. Gabbard SL, Lacy BE. Chronic intestinal pseudo-obstruction. *Nutr Clin Pract* 2013; 28: 307-16. [CrossRef]
3. Yeung AK, Di Lorenzo C. Primary gastrointestinal motility disorders in childhood. *Minerva Pediatr* 2012; 64: 567-84.
4. Thapar N, Saliakellis E, Benninga MA, et al. Paediatric Intestinal Pseudo-Obstruction: Evidence and Consensus-Based Recommendations from an ESPGHAN-Led Expert Group. *J Pediatr Gastroenterol Nutr* 2018 Mar 22 [Epub ahead of print]. [CrossRef]
5. Dalgiç B, Sari S, Doğan I, Unal S. Chronic intestinal pseudoobstruction: report of four pediatric patients. *Turk J Gastroenterol* 2005; 16: 93-7.
6. Arslan M, Bayraktar Y, Oksuzoglu G, et al. Four cases with chronic intestinal pseudo-obstruction due to hollow visceral myopathy. *Hepatogastroenterology* 1999; 46: 349-52.
7. Oztas E, Ozin Y, Onder F, Onal IK, Oguz D, Kocafe C. Chronic intestinal pseudo-obstruction and neurological manifestations in early adulthood: considering MNGIE syndrome in differential diagnosis. *J Gastrointest Liver Dis* 2010; 19: 195-7.
8. Muto M, Matsufuji H, Tomomasa T, et al. Pediatric chronic intestinal pseudo-obstruction is a rare, serious, and intractable disease: a report of a nationwide survey in Japan. *J Pediatr Surg* 2014; 49: 1799-803. [CrossRef]
9. Stanghellini V, Cogliandro RF, de Giorgio R, Barbara G, Salvioli B, Corinaldesi R. Chronic intestinal pseudo-obstruction: manifestations, natural history and management. *Neurogastroenterol Motil* 2007; 19: 440-52. [CrossRef]
10. Di Nardo G, Di Lorenzo C, Lauro A, et al. Chronic intestinal pseudo-obstruction in children and adults: diagnosis and therapeutic options. *Neurogastroenterol Motil* 2017 Jan 29 [Epub ahead of print]. [CrossRef]
11. Faure C, Goulet O, Ategbo S, et al. Chronic intestinal pseudoobstruction syndrome: clinical analysis, outcome, and prognosis in 105 children. *French-Speaking Group of Pediatric Gastroenterology. Dig Dis Sci* 1999; 44: 953-9. [CrossRef]

12. Mousa H, Hyman PE, Cocjin J, Flores AF, Di Lorenzo C. Long-term outcome of congenital chronic intestinal pseudo-obstruction. *Dig Dis Sci* 2001; 47: 2298-305. [\[CrossRef\]](#)
13. Cucchiara S, Borrelli O. Nutritional challenge in pseudoobstruction: the bridge between motility and nutrition. *J Pediatr Gastroenterol Nutr* 2009; 48: S83-5. [\[CrossRef\]](#)
14. Pironi L, Arends J, Bozzetti F, et al. Home Artificial Nutrition & Chronic Intestinal Failure Special Interest Group of ESPEN. ESPEN guidelines on chronic intestinal failure in adults. *Clin Nutr* 2016; 35: 247-307. [\[CrossRef\]](#)
15. Joly F, Amiot A, Messing B. Nutritional support in the severely compromised motility patient: when and how? *Gastroenterol Clin North Am* 2011; 40: 845-51. [\[CrossRef\]](#)
16. Di Lorenzo C, Flores AF, Buie T, Hyman PE. Intestinal motility and jejunal feedings in children with chronic intestinal pseudo-obstruction. *Gastroenterology* 1995;108: 1379-85. [\[CrossRef\]](#)
17. Mann SD, Debinski HS, Kamm MA. Clinical characteristics of chronic idiopathic intestinal pseudo-obstruction in adults. *Gut* 1997; 41: 675-81. [\[CrossRef\]](#)
18. Hashizume N, Yagi M, Ushijima K, et al. Pharmacotherapy for pediatric chronic intestinal pseudo-obstruction: Nationwide survey in Japan. *Pediatrics International* 2017; 59: 467-72. [\[CrossRef\]](#)
19. Fell JME, Smith VV, Milla PJ. Infantile chronic idiopathic intestinal pseudo-obstruction: the role of small intestinal manometry as a diagnostic tool and prognostic indicator. *Gut* 1996; 39: 306-11. [\[CrossRef\]](#)
20. Cucchiara S, Borrelli O, Salvia G, et al. A normal gastrointestinal motility exclude chronic intestinal pseudo-obstruction in children. *Dig Dis Sci* 2000; 45: 258-64. [\[CrossRef\]](#)
21. Di Lorenzo C, Hyman PE. Gastrointestinal motility in neonatal and pediatric practice. *Gastroenterol Clin North Am* 1996; 25: 203-24. [\[CrossRef\]](#)
22. Vargas JH, Sachas P, Ament ME. Chronic intestinal pseudo-obstruction syndrome in pediatrics: results of a national survey by members of the North American Society of Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr* 1989; 7: 323-32. [\[CrossRef\]](#)
23. Sigurdsson L, Reyes J, Kocoshis SA, et al. Intestinal transplantation in children with chronic intestinal pseudo-obstruction. *Gut* 1999; 45: 570-4. [\[CrossRef\]](#)
24. Hamilton HC, Foxcroft DR. Central venous access sites for the prevention of venous thrombosis, stenosis and infection in patients requiring long-term intravenous therapy. *Cochrane Database Syst Rev* 2007; 3: CD004084. [\[CrossRef\]](#)
25. Rodrigues AF, van Mourik ID, Sharif K, et al. Management of end-stage central venous access in children referred for possible small bowel transplantation. *J Pediatr Gastroenterol Nutr* 2006; 42: 427-33. [\[CrossRef\]](#)
26. Benedetti E, Panaro F, Holterman M, Abcarian H. Surgical approaches and intestinal transplantation. *Best Pract Res Clin Gastroenterol* 2003; 17: 1017-40. [\[CrossRef\]](#)