

Pediatric Intestinal Failure, 10 years of experience from a specialized unit

Insuficiencia Intestinal Pediátrica, 10 años de experiencia en una Unidad de Cuidados Especializados

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What do we know about the subject matter of this study?

Intestinal failure is a rare clinical condition of unknown frequency due to the heterogeneity of the definitions used. Long-term parenteral nutrition and intestinal rehabilitation are the first-line treatment, achieving enteral autonomy in over 50% of specialized units.

What does this study contribute to what is already known?

To provide an update in the knowledge of pediatric intestinal failure and new information at the national level from a specialized unit with 10 years of experience in terms of frequency, causes, treatments performed, and achievement of enteral autonomy as the final objective.

Abstract

Intestinal Failure (IF) includes the loss of functional intestinal mass and the requirement of long-term Parenteral Nutrition (PN) to achieve the development and growth in childhood. **Objective:** To evaluate the experience in a specialized unit for pediatric patients with IF, describing the clinical characteristics of those admitted from November 2009 to December 2019. **Patients and Method:** Retrospective and descriptive review from clinical records of 24 cases that matched the inclusion criteria. The following variables were recorded: gender, neonatal history, origin unit, patient age and anthropometric diagnosis at admission to the unit, cause of IF, hospital stay, anthropometric data and parenteral nutrition dependency at discharge. In those patients with a diagnosis of short bowel syndrome (SBS), the cause of intestinal resection and the characteristics of the intestinal remnant were identified: anatomical classification, remnant length (defining ultra-short as < 25 cm), presence of ileocecal valve, and characteristics of the colon. **Results:** The median age at admission was 7.8 months. Seventeen cases were preterm. Regarding IF etiology, 10 patients presented SBS, 6 patients with Intestinal Neuromuscular Disease (INMD), 7 children with SBS associated with INMD, and 1 case of intestinal lymphan-

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giectasia. Within the SBS etiologies found in this group, intestinal atresia (8 cases) and necrotizing enterocolitis (9 patients) were the main causes with a similar proportion. Eight patients had no ileocecal valve. According to anatomical classification, 1 case was Type I, 8 were Type II, and 8 were Type III. Related to bowel length, 3 were ultrashort, besides being Type II; in those with > 40 cm of bowel length, 7 were Type III. Overall average hospital stay was 456.4 days. Enteral autonomy was achieved in 16 patients and 8 cases required home parenteral nutrition. **Conclusions:** IF requires life support, PN and prolonged hospital stay. The principal etiology of IF is SBS caused by congenital intestinal atresia and necrotizing enterocolitis. Nevertheless, the high frequency of INMD could be attributed to the local protocol analysis. Most of our patients had poor prognosis factors, however, the management by a specialized team allowed the achievement of enteral autonomy in 66.7% of cases.

Introduction

Intestinal failure (IF) is a complex pathology of variable prognosis and high impact. Several definitions have been used to describe it, one of them considers the reduction of intestinal function below the minimum to achieve digestion and absorption of nutrients necessary to meet the requirements of growth and development for children and metabolic maintenance for adults¹. Currently, the European Society for Clinical Nutrition and Metabolism defines it as a decrease in the absorption of macronutrients, water, and electrolytes due to a loss of intestinal function and the need for long-term Parenteral Nutrition (PN)², understood as that which lasts for more than 60 days³.

There is no information on the incidence, due to its rare frequency and the heterogeneity of diagnostic definitions. For example, in 2004, Wales et al. estimated a prevalence of 24.5 cases/100,000 live births, defining IF as PN > 42 days post-bowel resection or remnant < 25% of that expected for gestational age, with a case-fatality rate of 37.5%⁴.

Its causes include a) anatomical alterations, in which there is a compromise of intestinal length due to congenital malformations or surgical resection, b) functional disorders, such as alterations of intestinal motility, and/or c) congenital enterocytes disorders. Currently, the most frequent cause in pediatric age is short bowel syndrome (SBS) secondary to necrotizing enterocolitis (NEC)⁵. Regardless of the cause of SBS, management is focused on achieving adequate nutrition for growth and development, minimizing the risk of complications or death.

In 1968, Dudrick et al.⁶ published their experience in animals and humans with total parenteral nutrition (TPN) demonstrating, for the first time, the possibility of maintaining growth and tissue metabolism for prolonged periods, observing little difference between enteral or parenteral administration of nutrients in terms of growth and development. Also, in 1967, Ric-

kham described his experience in 17 newborns with intestinal remnants smaller than 75 cm, who received PN achieving a survival rate of 41.2%⁷. Although the caloric contribution through this route was limited, in some cases, it provided the necessary time for the intestine to adapt and thus eventually reach enteral autonomy. Current studies have been able to demonstrate that PN is the treatment of choice for IF.

The potential for intestinal adaptation depends mainly on the length, type, and quality of the residual intestine⁸. To complete this process, strict monitoring by a specialized multidisciplinary team is necessary, which has improved the prognosis and decreased the complications associated with the use of PN^{9,10}.

Currently, intestinal or liver-intestinal transplantation is reserved for selected cases since, even when performed, a lethality rate of up to 40% has been described in the first years after the intervention¹¹.

In our country, some institutions see pediatric patients with IF, but there are no known studies describing the characteristics of these patients. In 2009, the *Hospital San Juan de Dios* (HSJD) in Santiago, created a Special Care Unit (SCU) belonging to the Pediatrics Service, due to the need to treat patients with IF through long-term PN, for their nutritional and intestinal rehabilitation. This work is carried out by a specialized clinical team composed of a treating physician specialized in clinical nutrition, nurses, and nurse technicians exclusively from the unit, nutritionists from the pediatric service, other specialists through referral (child surgeons, infectious disease specialists, gastroenterologists), comprehensive rehabilitation team (occupational therapist, kinesiologist, and speech therapist), and psychosocial team. The unit, of intermediate complexity, receives patients from the Neonatology and Pediatrics units of the same center or referred from other hospitals in the country with the authorization of the director of the facility.

The objective of this study was to describe the demographic, clinical, etiological, and anatomical characteristics of patients with a diagnosis of IF admitted

to the SCU from the beginning of its operation in November 2009 until December 2019. As this center completes ten years of experience, it is expected to contribute new information and knowledge of this pathology at the national level.

Patients and Method

Design

Retrospective study including data from patients admitted to the SCU of the *Hospital San Juan de Dios*. Children between 0 and 18 years of age with a diagnosis of IF, defined as a gastrointestinal pathology requiring parenteral nutritional support for a period longer than 60 days, were included.

The data were collected from November 2009 to December 2019, directly by the members of the research team, from the information available in the medical records, clinical summary, and histopathological reports. Out of 66 patients admitted, 24 of them (36.3%) met the inclusion criteria.

Variables analyzed

The following variables were collected: sex, neonatal history (gestational age, birth weight classification according to intrauterine growth curves)¹², age at admission to the SCU, unit of origin, anthropometric diagnosis at admission, cause of intestinal failure, time of stay in the SCU, age at discharge from the unit, anthropometric data at discharge, and dependence on parenteral nutrition at discharge.

In those patients with diagnosis of SBS, the cause of intestinal resection and the characteristics of the intestinal remnant were identified as: anatomical classification, remnant length (defining ultra-short as < 25 cm), presence of ileocecal valve, and characteristics of the colon.

The causes of intestinal insufficiency were divided into three main groups:

1. SBS: Patients with small bowel resection, classified according to the anatomical characteristics of the remnant¹³.
 - a. Type I: resection involving part of the jejunum, ileum, and colon, with a terminal jejunostomy.
 - b. Type II: ileal involvement, without preservation of the ileocecal valve (ICV), with jejuno-colic anastomosis.
 - c. Type III: jejunal resection with preservation of at least 10 cm of terminal ileum with ICV and colon, with jejunal-ileocolic anastomosis.
2. Congenital enterocyte disorder: diagnosis determined by biopsy and/or electron microscopy.
3. Primary visceral neuromyopathy (VN): diagnosed

by biopsy; neither intestinal manometric nor genetic study was available in our center.

Anthropometric evaluation

Weight-for-height (W/L), height-for-age (H/A), and weight-for-age (W/A) indicators were used in patients under 5 years of age and from 5 years of age body mass index for age (BMI/A) and H/A were considered, applying the WHO 2006 and 2007 references¹⁴. In addition, the H/A indicator less than - 2 SD was used as the most sensitive parameter for the diagnosis of malnutrition.

Statistical analysis

Data were processed in Microsoft® Excel® for Office 365 version 1808. Frequencies and measures of central tendency were calculated, those variables with normal distribution were presented as mean and standard deviation, and those with non-parametric distribution as median and interquartile range.

Ethical aspects

The study was approved by the Hospital's Ethics Committee with Informed Consent, given the conditions of the work.

Results

The overall median age at admission was 7.8 months and an average of 35.7 months (min 1-max 173 months). Twelve cases came from Neonatology and a smaller number were referred from other centers. Of the total number of children, 17 had a history of prematurity, of which 4 were extremely premature. In 19 patients, the anthropometric data at admission was collected, presenting a risk of malnutrition or undernutrition in 14 children (table 1). The insertion of a 1-lumen tunneled central venous access for PN was planned for all patients in the unit. During the stay, all patients received continuous enteral nutrition by enteral tube or enterostomy, with amino acid, oligomeric, or polymeric formulas according to evolution, and always trying to preserve the oral route through rehabilitation.

The causes of IF were a) SBS in 10 patients, b) VN+SBS in 7 cases, c) isolated VN in 6 cases, and d) other causes, identifying 1 patient with intestinal lymphangiectasia. There were no cases of congenital enterocyte disorder.

Among the 17 patients with SBS (with or without VN), we found 7 with intestinal atresia, 6 with NEC, 3 with NEC plus gastroschisis, and one with intestinal atresia and gastroschisis (table 2A). In relation to the anatomical classification of SBS and the length of the

remnant, 3 cases correspond to the ultra-short type, all being Type II. Of the group with remnant > 40 cm, most (n = 7) presented Type III classification (table 2B).

The overall average hospital stay was 456.4 days (min 47-max 1640 days), with 539.5 days in the group from the HSJD and 140.4 in patients from other centers. At discharge, anthropometric data were obtained from 16 patients, showing a risk of malnutrition or undernutrition in 4 (table 3). Also, enteral autonomy was achieved in 16 patients (66.7%) and 8 required home parenteral nutrition. Out of these, 7 had SBS and 1 had isolated VN. Of the 7 children with SBS, 6 corresponded to Type II anatomical classification.

Regarding the intestinal remnant, 5 had length < 40 cm and of these 3 were ultra-short. In addition, 2 cases had associated VN (table 4). No patient met the criteria for intestinal or intestinal-hepatic transplantation during the study period. All of them were fed with enteral and oral nutrition to varying degrees at discharge. No deaths were recorded during the study period.

Discussion

The diagnostic criteria for IF have been variable and heterogeneous. The need for PN is a clinical indicator of the inability to absorb macronutrients, water, and electrolytes, either due to anatomical or functional causes. For this reason, we included patients with a need for PN > 60 days, due to gastrointestinal pathology. The latter allowed us to exclude cases with a need for nutritional support due to cardiological, respiratory, or neurological causes, not associated with an inability to absorb. We consider the definition used in this work to be the most appropriate for this reality and according to the accumulated evidence.

The most common causes of IF are congenital or acquired in the neonatal period, so it is to be expected that most of the patients admitted to the unit come from Neonatology. However, in some cases, the diagnosis and referral to a specialized center was delayed, which is evidenced by the median age of admission of those patients coming from other health care centers vs. the patients from our hospital (1 year and 8 months vs 3 months, respectively). This shows the need to establish referral protocols from primary and secondary care centers to referral centers in order to favor early and specialized management of patients and their families.

On admission, most of the patients presented nutritional deficiency, which could be attributed to the low index of diagnostic suspicion of IF and the deficient management in its early stages.

SBS was the most frequent cause of IF, similar to

that described in other series. However, the high proportion of VN found stands out, which in other studies is close to 10%¹⁵. This could be attributed to the high index of suspicion and the implementation of a local protocol of histological analysis to all cases with clinical suspicion of VN and/or with a diagnosis of intestinal failure of unusual evolution.

When analyzing in detail the 17 cases of SBS, the congenital cause was frequent, followed by NEC, which may be attributable to advances in the neonatal management of it¹⁶.

A high proportion of our patients with SBS presented a severity profile, due to a remnant intestine < 40 cm, absence of ICV, and one case had an associated diagnosis of Hirschsprung's disease. Despite the above, it should be noted that currently, the anatomical classification of SBS complements the prognostic analysis,

Table 1. Characteristics of patients admitted to the Special Care Unit (N = 24)

Admission age	Median (months) (ICR p25-p75)
Overall	7.8 (4.0-42.7)
Coming other HSJD units	6 (3.5-29.2)
Referral from other Centers	20.7 (18.6-58.5)
Gender	n (%)
Female	12 (50)
Male	12 (50)
Origin	N (%)
Neonatology Unit	12 (50)
Intensive Care Unit	5 (20.8)
Nutrition Ambulatory Unit	1 (4.2)
Basic Care Unit	1 (4.2)
Other Centers	5 (20.8)
Classification according Birth Weight	n (%)
SGA	4 (16.7)
AGA	19 (79.2)
LGA	1 (4.2)
Gestational Age (Weeks)	n (%)
>37	7 (29.2)
32-36	8 (33.3)
28-31	5 (20.8)
<28	4 (16.7)
Nutritional Status	n (%)
Undernourished	12 (50)
Malnutrition Risk	2 (8.3)
Eutrophy	3 (12.5)
Overweight	1 (4.2)
Obesity	1 (4.2)
Not available	5 (20.8)

HSJD: San Juan de Dios Hospital; SGA: Small for gestational age
AGA: Appropriate for gestational age; LGA: Large for gestational age.

Table 2A. Characteristics of patients with SBS (with and without VN) (n = 17)

Anatomical classification	n (%)
Type I	1 (5.9)
Type II	8 (47.1)
Type III	8 (47.1)
SBS Etiology	n (%)
Intestinal Atresia	7 (41.2)
NEC	6 (35.3)
NEC+ Gastroschisis	3 (17.6)
Intestinal Atresia+ Gastroschisis	1 (5.9)
Remnant small intestinal length	n (%)
Ultra-short <25 cm	3 (17.6)
Short 25-40 cm	4 (23.5)
>40 cm	10 (58.8)
Ileocecal valve	n (%)
Present	9 (52.9)
Absent	8 (47.1)
Characteristics of the colon	n (%)
Normal	16 (94.2)
Hirschsprung	1 (5.9)

SBS: Short bowel syndrome; NEC: Necrotizing enterocolitis; VN: visceral neuromyopathy.

Table 2B. Intestinal remnant length and anatomical classification of patients with Short Bowel Syndrome (with and without VN) (n = 17)

Remnant small intestinal length	Type I (n = 1)	Type II (n = 8)	Type III (n = 8)
< 25 cm	0	3	0
25-40 cm	0	3	1
> 40 cm	1	2	7

Table 3. Characteristics at discharge Special care unit (n = 24)

Time of stay	Promedio en días (DS)
Overall	456.4 (421.5)
HSJD	539 (436.2)
Other Centers	140.4 (59.9)
Nutritional Status	n (%)
Undernourished	4 (16.7)
Risk of Malnutrition	0 (0)
Eutrophy	7 (29.1)
Overweight	4 (16.7)
Obesity	1 (4.2)
Not available	8 (33.3)

HSJD: San Juan de Dios Hospital.

with type I as the most unfavorable and type III as the one with the best outcomes¹⁷. Based on this classification, our patients presented a greater distribution of type II and III SBS, which would provide better results in the intestinal rehabilitation process.

In order to achieve the rehabilitation of the patients admitted to the unit, prolonged hospitalization times were required, reaching up to 1640 days in one patient. The difference in the length of stay of those who came from another center stands out, which could be explained by the referral and counter-referral process, which involves the diagnosis, initial management, and rehabilitation plan, completing it in their center of origin.

The hospitalization times described reveal the complexity of these cases, requiring intensive management, both medical and surgical, of their complications and prior nutritional recovery in order to begin the intestinal rehabilitation process. Furthermore, in some cases, it reflects the biosocial difficulties faced by this pathology and its treatment. Currently, there are pharmacological interventions, such as synthetic GLP-2 analogs, which could accelerate intestinal rehabilitation, reducing the length of stay and eventually achieving intestinal autonomy^{18,19}.

The efficacy of the management provided in SCU is reflected in 2 aspects: The first, and most important,

Table 4. Enteral Autonomy (n = 24)

	Yes	No
Nº de cases	16 (66.7%)	8 (33.3%)
Average Days Hospital Stay (DS)	304.7 (295)	759.8 (503)
According to etiology		
1. SBS	10	7
- Anatomical classification		
• Type I	0	1
• Type II	2	6
• Type III	8	0
- Remnant small intestinal length		
• < 25 cm	0	3
• 25-40 cm	2	2
• > 40 cm	8	2
- With VN	5	2
- Absent ICV	0	6
- Colon with Hirschsprung	0	1
2. Neuromyopathy	5	1
3. Linfoangiectasia Intestinal	1	0

SBS: Short bowel syndrome; ICV: ileocecal valve; VN: visceral neuromyopathy.

is the percentage of enteral autonomy at discharge and, secondly, the decrease in malnutrition at discharge. Regarding enteral autonomy, this was achieved in 66.7%, which is comparable with the reported by Jo SC. et al (56.9%), Petit LM. et al (54%), Colomb V. et al. (55%), and recently reported by Gattini et al (48%)^{15,20,22}. The group of patients who did not achieve autonomy presented unfavorable prognostic factors²⁰ such as anatomical classification type I and II, absence of ICV, intestinal remnant < 40 cm, and VN.

Although it was possible to group the patients according to the length of the intestinal remnant, one of the difficulties found was the lack of precision in the recording of the intestinal remnant in the surgical protocols.

A limitation in our study was the lack of integrity in the recording of anthropometric data. Based on this study, a form for admission and discharge to the SCU was implemented, which will allow systematizing the registry, essential for clinical follow-up and development of future research.

In conclusion, although this work includes a small number of patients, it is valuable since IF is a rare condition, of high medical-surgical complexity, and the satisfactory results were the product of specialized and multidisciplinary work, achieving enteral autonomy in 66.7% of the patients. Finally, the demographic and clinical data obtained bring us closer to the reality of this pathology in our country and allow us to design, provide, and plan network strategies for multicenter interventions, in line with medical advances, in order to favor the prognosis and quality of life of patients and their families.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors state that the information has been obtained anonymously from previous data, therefore, Research Ethics Committee, in its discretion, has exempted from obtaining an informed consent, which is recorded in the respective form.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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