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## New paradigm of oral rehydration in patients affected by irritable bowel syndrome with chronic diarrhea

Marco Chiarelli, Matilde De Simone, Gerardo Cioffi, Ugo Cioffi

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### Abstract

Irritable bowel syndrome with diarrhea is a very frequent clinical condition characterized by disabling intestinal symptoms. This disease presents with daily abdominal pain for at least 3 months related to defecation and associated with a change in the frequency of bowel movements and the shape of the stool. International surveys about this disease report a global prevalence of about 1.5%. A new amino acid based electrolyte solution has recently been commercialized for oral rehydration in diarrhea. It is composed of water, electrolytes, and five selected amino acids that function as sodium co-transporters without containing glucose. In recent years, some studies explored the effectiveness of the amino acid based electrolyte beverage in oncologic patients with gastrointestinal mucositis, reporting good results. Recently, a prospective study to evaluate the clinical impact of the amino acid based medical beverage was conducted in patients with diarrhea predominant irritable bowel syndrome. The research was based on a real-life methodology minimizing the disruption of the routine care. One hundred patients suffering from irritable bowel syndrome with diarrhea drank a solution based on selected amino acids twice a day for 2 wk. Each enrolled patient completed the study and showed a significant response rate with regard to stool consistency and pain reduction. Based on this data, we can hypothesize that the amino acid based oral rehydration solution could be a valid tool in the treatment of patients affected by irritable bowel syndrome with diarrhea. It is certainly necessary to plan high-quality clinical trials comparing glucose based oral solutions and amino acid based solutions in patients with persisting diarrhea. Probably in the near future all oral rehydration solutions will contain amino acids.

**Key Words:** Diarrhea; Irritable bowel syndrome; Diarrhea-predominant irritable bowel syndrome; Medical food; Amino acid beverage formulation

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**Core Tip:** Amino acid based solution has shown promising results in improving symptoms of chemotherapy related diarrhea. Irritable bowel syndrome with diarrhea is a very frequent gastrointestinal disorder. A recent study has been conducted to evaluate the clinical impact of the amino acid based medical beverage on the symptoms of diarrhea predominant irritable bowel syndrome with a real-life methodology. The amino acid based medical beverage seems to be well tolerated and improve gastrointestinal symptoms. The results of this study are very promising and the amino acid based solution will likely become part of the standard treatment for chronic recurrent diarrhea in the near future.

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## INTRODUCTION

Irritable bowel syndrome with diarrhea is a very frequent clinical condition characterized by disabling symptoms. In 2021, the Rome Foundation Global Study defined the Rome IV criteria for irritable bowel syndrome with predominant diarrhea[1]. This disease is characterized by daily abdominal pain for at least 3 months related to defecation and associated with a change in the frequency of bowel movements and the shape of the stool (soft or liquid stool)[2,3]. This condition is very frequent: A meta-analysis highlighted a pooled-prevalence of 1.4% of irritable bowel syndrome with diarrhea in 1.4% of the population[4]. Moreover, this syndrome is globally distributed: An international survey involving 26 countries reported a global prevalence of 1.2%[5].

The standard oral rehydration solution recommended by the World Health Organization is a simple solution employed for the prevention and treatment of infectious diarrhea in children worldwide[6]. This oral solution is based on a glucose-coupled sodium transport mechanism with absorption of molecules across the luminal membrane: This elementary oral solution can significantly reduce the mortality for diarrhea in the pediatric population[6]. A new amino acid based electrolyte solution has recently been commercialized. It is composed of water, electrolytes, and five selected amino acids that function as sodium co-transporters without containing glucose.

Diarrhea due to gastrointestinal mucositis can be a relevant problem in patients treated with chemotherapy or radiation therapy. In recent years, five studies that evaluated the effectiveness of the amino acid based electrolyte beverage in oncologic patients has been published[7-11]. A retrospective analysis on 118 patients suffering gastrointestinal toxicity related to chemotherapy or radiation therapy showed a reduction of gastrointestinal symptoms (diarrhea and nausea) and dehydration improvement in patients who took the amino acid based beverage for more than 7 d[7]. A pilot study on a small group of patients with chemotherapy related diarrhea reported a reduction in the frequency of the stool and an improvement in the consistency of the bowel evacuations[8]. Encouraging results have also been reported in patients with chronic diarrhea caused by immune therapy or related to neuroendocrine tumors[9,10]. A clinical trial conducted on patients affected by hematological malignancies and treated with high dose Melphalan and autologous stem cell transplant reported a reduction in high-grade diarrhea, although a small number of patients enrolled was able to maintain compliance with taking the oral solution twice daily, due to a high incidence of nausea post-stem cell transplant[11]. Although these are preliminary data, they demonstrate how the amino acid based electrolyte solution can be an effective support in different clinical settings characterized by chronic diarrhea.

Niles and colleagues conducted a very well-designed study to evaluate the clinical impact of the amino acid based medical beverage on the symptoms of diarrhea-predominant irritable bowel syndrome[12]. The real-life approach to this work is confirmed by the administration of the study through a clinical research platform with data collection by a mobile-phone application. This methodology allows to enroll a large number of patients and provide results that adhere to the real life of the patients.

One hundred patients affected by this syndrome took the selected amino acid based beverage twice daily for 2 wk in normal activities. Each patient enrolled completed the trial: This is the main aspect of the study. The tolerability of the drink demonstrates how the amino acid based electrolyte solution is well-tolerated in patients with irritable bowel syndrome with diarrhea. The clinical aspects of the investigation, in fact, highlighted a relevant frequency of stool consistency responders (40%) and pain and discomfort responders (53% and 55%, respectively). Based on the data of the study, we can hypothesize that the amino acid based oral rehydration solution could be a valid tool in the treatment of patients affected by irritable bowel syndrome with diarrhea.

This new amino acid based oral solution contains five amino acids (valine, aspartic acid, serine, threonine, and tyrosine) which appear to perform three functions on the intestinal epithelium: Acting as sodium co-transporters facilitating the protein sodium-glucose co-transporter 1, it decreases the para-cellular permeability, improves the efficacy of

tight-junctions, and increases the proliferation of intestinal villi[13]. These complementary functions could be the key of success in contrasting the loss of water and electrolyte in diarrhea-related syndromes.

## CONCLUSION

It is certainly necessary to plan high-quality clinical trials comparing glucose based oral solutions and amino acid based solutions in patients with persisting diarrhea. Water and electrolyte supplementation remains a cornerstone in the treatment of patients affected by diarrhea, but probably in the near future all oral rehydration solutions will contain amino acids.

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