



## Nutritional support in a patient with Cytomegalovirus (CMV) enterocolitis in the acquired immunodeficiency syndrome (AIDS)

Jóyce da Rosa Bisotto<sup>1</sup>, Albert Pinto Coelho Gorini<sup>1</sup>, Luana Dias Claudino<sup>1</sup>, João Vitor Dal Ponte Zatt<sup>1</sup>, Daniel Trahtman de Boer<sup>1</sup>, Gustavo Matas Kern<sup>1</sup>, Yasser Abrahão Abdalla<sup>1</sup>, Vanessa Cardoso Fontana<sup>1</sup>, Leticia Misturini Lutz<sup>1</sup>, Jaqueline Costa Coelho<sup>2</sup>

<sup>1</sup> Academic of Medicine at the University Lutheran of Brazil.

<sup>2</sup> Nutrologist Physician at the Nutrology Service of Hospital Ernesto Dornelles.

Corresponding Author: Albert Pinto Coelho Gorini.

Academic of Medicine at the University Lutheran of Brazil.

E-mail: albertgorini@gmail.com

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### Abstract

**Introduction:** Several diseases of the gastrointestinal tract should be taken into account in patients with the human immunodeficiency virus (HIV) since diarrhea negatively affects the patient's quality of life. Given this condition, Cytomegalovirus (CMV) enterocolitis may present with fever, weight loss, intermittent diarrhea, and hematochezia. **Objective:** This study aimed to report the effect of enteral supplementation with L-glutamine and oligomeric enteral nutritional therapy (ENT) formula in patients with cytomegalovirus, and with refractory diarrhea associated with wasting HIV syndrome. **Methods:** The information contained in this report was obtained through a review of the medical record and a review of the literature. **Results:** This is the report of S. S. A, a female, 27 years old, who was admitted to Hospital Ernesto Dornelles, in Porto Alegre, from 11/15/2020 to 12/30/2020, diagnosed with HIV for a month, without undergoing treatment. The patient was hospitalized due to worsening abdominal pain starting 2 days ago, with diarrhea and mental confusion. On physical examination, she presented pain in the lower abdominal region. From anthropometry, the measured weight of 67kg, the self-reported height of 1.67m, and BMI of 24kg/m<sup>2</sup>. On 11/17, she presented PCR-CMV positive for CMV and underwent laparotomy for pneumoperitoneum with endarterectomy due to perforation of the distal ileum. In use of ganciclovir for CMV. On December 2, the upper digestive endoscopy with biopsy showed an esophagus with the Z-line located close to the diaphragmatic clamping, with esophageal mucosa with extensive, friable, serpiginous ulcers, being a valuable diagnosis in CMV enterocolitis.

From 12/04 to 12/08, she used exclusive enteral L-glutamine 20g/day. On 12/09, she started an oligomeric formula via the low-flow enteral route with progression to the caloric and protein targets. On 12/30, the patient had improved diarrhea, with a depressible and painless abdomen, and had been discharged. **Final Considerations:** In the present report, it was obtained a beneficial effect with the nutritional intervention using L-glutamine and enteral oligomeric formula in the treatment of diarrhea. Thus, the improvement in the condition in just 5 days can be explained by the rhythm of the enterocyte cell cycle, which occurs in an average period of 3 days, and it is possible that the 4 day period of nutritional intervention is sufficient to increase endogenous levels of L-glutamine.

**Keywords:** L-glutamine. Enterocolitis. Cytomegalovirus.

### Introduction

Several diseases of the gastrointestinal tract should be taken into account in patients with the human immunodeficiency virus (HIV) since diarrhea negatively affects the patient's quality of life. Given this condition, Cytomegalovirus (CMV) enterocolitis may present with fever, weight loss, intermittent diarrhea, and hematochezia [1-3]. In this aspect, it becomes important to understand the effects of and components of the diet, specifically prebiotics and probiotics, on the intestinal barrier function. Stressors often reduce barrier function, and these effects can be reversed by supplements like zinc or glutamine, which are among the barrier-enhancing substances. Other dietary factors

in the diet that improve the barrier are vitamins A and D, tryptophan, cysteine, and fiber; in contrast, ethanol, fructose, and dietary emulsifiers increase permeability [4].

Also, recent studies of human cytomegalovirus (HCMV) infection have shown that the virus significantly alters cellular metabolism, especially glucose and glutamine utilization. Glucose is not broken down by the tricarboxylic acid (TCA) cycle in infected cells; rather, it is used biosynthetically for the synthesis of fatty acids for membranes needed during infection. Also, HCMV may integrate its mechanisms to manipulate cell signaling and stress responses to induce new adipocyte-like differentiation in order to alter metabolism so that glucose can be used synthetically, i.e. for fatty acids and lipids. This process diverts glucose from the TCA cycle and requires the induction of enzymes that can convert glutamine to  $\alpha$ -ketoglutarate to maintain the TCA cycle (anaplerosis). We discuss data proposing that the anaplerotic utilization of glutamine may be mediated, in part, by the activation of c-Myc, and the induction of adipocyte-like differentiation may result from the activation of the endoplasmic reticulum resident kinase PKR-like kinase ER. These changes in metabolism during HCMV infection are comparable to those seen in many tumor cells [5].

Therefore, the present study presented a case report to provide evidence found by other authors, this study aimed to report the effect of enteral supplementation with L-glutamine and oligomeric enteral nutritional therapy (ENT) formula in patients with cytomegalovirus, and with refractory diarrhea associated with wasting HIV syndrome.

## Methods

### Case Report

The present study was elaborated according to the rules of CARE case report. Available in: <https://www.care-statement.org/>.

### Ethical Aspects

This study was analyzed and approved by the Research Ethics Committee (CEP) and obtaining the patient's consent through the Informed Consent Form (TCLE) according to CNS/CONEP Resolution 466/12.

### Patient Information and Clinical Findings, Timeline, Diagnostic Assessment, Therapeutic Intervention and Follow-up

This is the report of S. S. A, a female, 27 years old, who was admitted to Hospital Ernesto Dornelles, in

Porto Alegre, from 11/15/2020 to 12/30/2020, diagnosed with HIV for a month, without undergoing treatment. The patient was hospitalized due to worsening abdominal pain starting 2 days ago, with diarrhea and mental confusion. On physical examination, she presented pain in the lower abdominal region. From anthropometry, the measured weight of 67kg, the self-reported height of 1.67m, and BMI of 24kg/m<sup>2</sup>. On 11/17, she presented PCR-CMV positive for CMV and underwent laparotomy for pneumoperitoneum with endarterectomy due to perforation of the distal ileum. In use of ganciclovir for CMV. On December 2, the upper digestive endoscopy with biopsy showed an esophagus with the Z-line located close to the diaphragmatic clamping, with esophageal mucosa with extensive, friable, serpiginous ulcers, being a valuable diagnosis in CMV enterocolitis. From 12/04 to 12/08, she used exclusive enteral L-glutamine 20g/day. On 12/09, she started an oligomeric formula via the low-flow enteral route with progression to the caloric and protein targets. On 12/30, the patient had improved diarrhea, with a depressible and painless abdomen, and had been discharged.

## Discussion

As presented by the present case report, glutamine is the main energy source of the enterocyte, and diarrhea and weight loss are frequent in HIV-infected patients. In this sense, a randomized, double-blind, placebo-controlled study using isonitrogenous doses of alanyl-glutamine (24 g/day) and placebo (glycine, 25 g/day) for 10 days. Before and after this nutritional supplementation, urinary excretion of lactulose and mannitol was determined by high-performance liquid chromatography, analyzing the effect of alanyl-glutamine supplementation on intestinal permeability and absorption in these patients. Forty-six patients with HIV/AIDS were included, 36 of whom were male, aged  $37.28 \pm 3$  (mean  $\pm$  standard error) years. Twenty-two and 24 subjects were treated with alanyl-glutamine and glycine, respectively. In nine patients among all in the study protocol who reported diarrhea in the 14 days prior to study entry, urinary excretion of mannitol was significantly lower than patients who did not report this symptom [median (range): 10.51 (3, 01-19.75) vs. 15.37 (3.93-46.73);  $p=0.0281$ ] and the lactulose/mannitol ratio was significantly higher [median (range): 0.04 (0.00-2.89) vs. 0.02 (0.00-0.19);  $P = 0.0317$ ]. There was also a significant increase in urinary excretion of mannitol in the alanyl-glutamine-treated group [median (range): 14.38 (8.25-23.98) before vs 21.24 (6.27-32.99) after the treatment;  $n=14$ ,

P=0.0382]. Therefore, nutritional supplementation with alanyl-glutamine was associated with an improvement in intestinal absorption [6].

Yet another randomized, double-blind, placebo-controlled, 8-week study to evaluate the efficacy and safety of oral glutamine therapy in patients who developed irritable bowel syndrome with increased intestinal permeability after an enteric infection. Eligible adults were randomized to glutamine (5 g/t.i.d.) or placebo for 8 weeks. Fifty-four subjects on glutamine and 52 on placebo completed the 8-week study. The primary endpoint occurred in 43 (79.6%) in the glutamine group and 3 (5.8%) in the placebo group (a 14-fold difference). Glutamine also reduced all secondary endpoint means: IBS-SS score at 8 weeks (301 vs 181,  $p < 0.0001$ ), daily stool frequency (5.4 vs  $2.9 \pm 1.0$ ,  $p < 0.0001$ ), Bristol Stool Scale (6.5 vs 3.9,  $p < 0.0001$ ) and intestinal permeability (0.11 vs 0.05;  $p < 0.0001$ ). 'Intestinal hyperpermeability' (increased urinary lactulose/mannitol ratios) was normalized in glutamine, but not in the control group. Adverse events and study drug discontinuation rates were low and similar in both groups. No serious adverse events were observed. Therefore, oral glutamine dietary supplements have safely reduced all major irritable bowel symptoms [7].

Also, the effects of glutamine and alanyl-glutamine therapy on diarrhea and antiretroviral drug levels in AIDS patients were analyzed in a randomized, double-blind, placebo-controlled study in northeastern Brazil. Gastrointestinal symptom scores improved with receiving high doses of alanyl-glutamine ( $p < 0.05$ ) or glutamine ( $p < 0.01$ ). Antiretroviral drug levels increased in patients who received alanyl-glutamine ( $p = 0.02$ ) or glutamine ( $p = 0.03$ ) by 113% ( $p = 0.02$ ) and 14% ( $p = 0.01$ ), respectively. Therefore, the dose-related efficacy of alanyl-glutamine and glutamine in treating diarrhea and increasing levels of antiretroviral drugs has shown that these supplements can help improve therapy for AIDS patients who have diarrhea and/or weight loss [8].

## Final considerations

In the present report, it was obtained a beneficial effect with the nutritional intervention using L-glutamine and enteral oligomeric formula in the treatment of diarrhea. Thus, the improvement in the condition in just 5 days can be explained by the rhythm of the enterocyte cell cycle, which occurs in an average period of 3 days, and it is possible that the 4 day period of nutritional intervention is sufficient to increase endogenous levels of L-glutamine.

## Acknowledgement

Nil.

## Ethics approval

This study was analyzed and approved by the Research Ethics Committee (CEP) and obtaining the patient's consent through the Informed Consent Form (TCLE) according to CNS/CONEP Resolution 466/12.

## Informed consent

Those responsible for the patient signed the consent form.

## Funding

Not applicable.

## Data sharing statement

No additional data are available.

## Conflict of interest

The authors declare no conflict of interest.

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