



ORIGINAL ARTICLE

Immunological activities are modulated by enteral administration of an elemental diet in mice

Juscilene S. Menezes^{a,*}, Mariléia C. Andrade^b, Beatriz Senra^b,
Virilânia S. Rodrigues^b, Nelson M. Vaz^b, Ana Maria C. Faria^b

^aDepartamento de Imunologia, Instituto de Ciências Biomédicas, Universidade de São Paulo—USP, São Paulo, SP 05508-900, Brazil

^bDepartamento de Bioquímica e Imunologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais—UFMG, Belo Horizonte, MG 31270-901, Brazil

Received 3 September 2005; accepted 11 January 2006

KEYWORDS

Elemental diet;
GALT;
Immunoregulation;
Mucosa;
Protein;
Inflammatory bowel
diseases

Summary

Background & Aims: Elemental diets (EDs) have been used successfully in treatment of some intestinal inflammatory diseases; however, the mechanism that mediates their effects is still unclear. In this study we evaluated the immunological effect of enteral administration of an ED in mice.

Methods: C57BL/6 mice were fed an ED (El-Diet) from weaning up to adulthood and immunological parameters were analyzed.

Results: El-Diet-fed mice presented an underdeveloped gut-associated-lymphoid tissue with lower numbers of TCR $\alpha\beta$ +IELs and lamina propria cells and low levels of secretory IgA when compared to chow-fed mice. They showed a systemic decrease in the production of IgG and IgA as well as a skewing towards a Th2 profile of cytokine production upon in vitro stimulation with an increase in IL-4 and a reduction in IFN- γ and IL-6 secretion.

Conclusion: Our study demonstrated the role of EDs in modulating immunological activities in mice and proposes a rationale for their successful use in treatment of some intestinal inflammatory diseases.

© 2006 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.

*Corresponding author. Current address: Torrey Pines Institute for Molecular Studies (TPIMS), 3550 General Atomics Ct, San Diego, CA 92121, USA. Tel.: +1 858 455 3897; fax: +1 858 455 3715.

E-mail address: jmenezes@tpims.org (J.S. Menezes).

Introduction

The mucosa of the small intestine is estimated to be 300 m² in humans and it is constantly exposed to antigenic contacts. Approximately 30 kg of food

proteins reach the human intestine during a year and 130–190 g of these proteins is absorbed daily in the gut.¹ In addition, evidence of the number of bacteria colonizing the human intestinal mucosa is given by the presence of approximately 10^{12} microorganisms/g of stool.² It is also known that intestine has the most abundant lymphoid tissue in the body. There are 10^{12} lymphoid cells per meter of human small intestine and this number exceeds by several fold the number found in all other lymphoid organs together.³

The antigenic stimulation in the gut surface may trigger immunological phenomena: oral tolerance, local immunization or systemic immunization.⁴ Although it is clear that antigenic exposure in the gut leads to local and systemic immunological consequences, the exact relevance of this exposure is poorly understood. We have recently studied the role of food proteins in the maturation of the immune system in post-weaned mice.⁵ Adult C57BL/6 mice reared on a balanced protein-free diet (Aa-fed mice) had an underdeveloped gut-associated lymphoid tissue (GALT) with low levels of IgA resembling the features of suckling mice. They also showed low levels of serum IgG and IgA, reduced lymphoid organs and a predominant Th2 profile with a high concentration of IL-10 and IL-4 and a low level of IFN- γ .

Elemental diets (EDs) are composed of elemental protein source in the form of amino acids and other nutrients such as carbohydrates as simple sugar or glucose polymer, very small amount of fat, minerals and vitamins. Primarily, EDs have been designed and used to provide nutritional support during conditions such as: post-operative management and pre-operative preparation, maldigestion and malabsorption states, accelerated metabolic states and hepatic failure.⁶ However, EDs have been used successfully in treatment of inflammatory bowel diseases.^{7–10} Several clinical reports have shown that EDs are as effective as steroid treatment for remission from Crohn's disease.^{8,11,12} Although there are several explanations for this effect, such as alterations in gut flora, provision of trophic amino acids and modulatory effects of fatty acids, it is still unclear how they mediate their effect.¹³

Our recent data and other previous studies have shown that natural sources of antigenic stimulation such as food proteins and microbiota have an important impact on the activity of the immune system.^{5,14,15} It is conceivable that the reported beneficial effect of EDs by reducing antigenic stimulation in the treatment of intestinal inflammatory diseases is related to their ability to modulate the immune system. To test this hypothesis, C57BL/6 mice were fed an ED from weaning to

adulthood and had several immunological parameters analyzed. In our study, ED-fed mice showed great similarity to other models of mice reared under low antigenic stimulatory conditions: germ/antigen-free animals, mice fed a protein-free diet and neonate/pre-weaned mice. Our data revealed an immunological mechanism for the reported modulatory effects of EDs and provides a rationale for their use in the treatment of intestinal inflammatory diseases.

Methods

Animals

C57BL/6 mice were bred and reared under conventional conditions in our facilities. Our study was approved by the Ethical Committee for Animal Research (CETEA/UFMG).

Diets

Mice at 3 weeks of age were introduced to ED (El-Diet, Support Produtos Nutricionais Ltda, São Paulo, Brazil) or regular commercial chow (Nutrilabor, Guabi, SP, Brazil) from the weaning period (21 days) to 2.5 months of age (10 weeks). Additional amounts of methionine (0.8%), choline (0.2%) and cellulose (3.8%) were mixed with the ED to adjust the nutritional requirements for mice. ED was administered in solid form as pellets and in liquid form in drinking bottles. Tap water was given ad libitum.

Cell preparations

Spleen and lymph nodes (inguinal, brachial, mesenteric and caecal) were removed, cell suspensions prepared using a tissue homogenizer and cells were gently centrifuged. Single-cell suspensions from bone marrow were prepared by injecting RPMI 1640 into femurs to flush out cells, followed by gentle pipeting and washing twice with medium.

Isolation of intraepithelial lymphocytes (IELs)

IEL were isolated as previously described.⁵ Briefly, the small intestine was removed and placed into a Petri dish containing cold $\text{Ca}^{2+}/\text{Mg}^{2+}$ -free HBSS solution with HEPES buffer (2% FCS). Peyer's patches and connective tissues were removed; the small intestine was opened longitudinally and washed twice to remove fecal contents. Small intestine was cut into 0.5 cm segments and

Download English Version:

<https://daneshyari.com/en/article/2683406>

Download Persian Version:

<https://daneshyari.com/article/2683406>

[Daneshyari.com](https://daneshyari.com)