

Butyric Acid: Putting Some Fiber Into Your Parenteral Nutrition Solution

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The concept of altered immune function of the intestine during the administration of parenteral nutrition (PN) has been demonstrated by a number of researchers over the past 2 decades.^{1,2} Deterioration of the gut-associated lymphoid tissue (GALT) can have profound consequences on local (gastrointestinal [GI]) and system (pulmonary) immune functions and the organism's ability to protect the host due to a breakdown in the GI tract's barrier function.^{3,4} Such a breakdown in this barrier function and decline of intestinal and pulmonary immunoglobulin A (IgA) production can lead to the host's susceptibility to a number of bacterial and viral infections.^{5,6} Mechanisms that mediate this PN-associated loss in immune functionality within the GI tract can result because of a shift in cytokine production with a loss of interleukin-7 (IL-7),^{7,8} IL-4, and IL-10^{1,3} and an increase in proinflammatory cytokines, including interferon- γ (IFN- γ)⁹ and tumor necrosis factor- α (TNF- α).^{10,11} Such a shift in cytokines may well mediate many of these adverse PN effects, and strategies to prevent these changes have been approached in a variety of ways.

Although small amounts of a complex diet can prevent PN-associated changes to GALT,^{11,13} this strategy may not always be clinically possible. Thus, strategies to modify current PN solutions with additional factors have been a focus of the Fukatsu laboratory and others. Other strategies that can prevent the GALT from changing with PN administration include use of arginine-supplemented PN,¹⁴ glutamine-supplemented PN,^{15,16} exogenous administration of GI hormones including bombesin¹⁷ or glucagon-like peptide-2,¹⁸⁻²⁰ or exogenous IL-7.²¹ Such approaches have benefits but also several obstacles, including cost, lack of approval from the U.S. Food and Drug Administration, and safety concerns.

In this issue of the *Journal and Parenteral and Enteral Nutrition (JPEN)*, Murakoshi et al²² studied the ability to alter the composition of the PN solution with the addition

of butyric acid and the subsequent alteration of the GALT, pulmonary production of IgA, and intestinal crypt/villus architecture. For more than a decade, the strategy of using short-chain fatty acids (SCFAs) with PN has been shown to have the potential to prevent several PN-associated adverse changes.^{23,24} SCFAs can increase epithelial cell transporter activity, including the glucose transporter 2, and elevate the production of proglucagon.²³ Further work in this area has shown that butyrate is the key SCFA that can mediate many of these changes, including the ability to augment intestinal adaptation after a major intestinal resection.²⁵ The mechanisms by which butyrate works have not been fully elucidated; however, a number of experiments have shown that the actions of butyrate are complex and multifactorial.²⁶ In fact, butyrate can augment epithelial cell proliferation, a point that is also suggested by the preservation of intestinal architecture by Murakoshi et al²² in this issue of *JPEN*. Butyrate has other potentially beneficial actions that can improve the overall composition of the luminal microbiota, sustain epithelial integrity, improve defense mechanisms, and even downregulate bacterial virulence.²⁶ As we now see in this publication, administration of butyrate with the PN solution can partially prevent the loss the local GALT system.

The Fukatsu et al study helps to pave a potential pathway for the development of future PN formulations supplemented with butyrate. Clearly, the challenges will be to better understand the mechanisms by which butyrate mediates its intestinal action and to ensure a high level of safety with its administration.

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