RESEARCH STUDIES

Intestinal Permeability, Food Antibodies, and the Effects of Specific, Glutamine-Rich Food Complexes

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Background

Glutamine is a conditionally essential amino acid that is an important fuel source for the small intestine. The mucosal lining of the intestine consists of rapidly proliferating cells that use large amounts of glutamine for energy. It is known that tumor progression and the depression of natural killer cell activity is associated with glutamine depletion (For further information, refer to the *Health Focus* section of this issue: **Intestinal Function, Permeability, Specific Food Antigen Response, and Validation for Treatment With Whole Foods**). Given glutamine's widespread use and importance in the intestine, it is a suspected potential therapeutic agent for some intestinal disorders, including the increased permeability and food allergy hypersensitivities observed in this study.

Objective

The objective of this study was to supply a whole food complex rich in glutamine to patients suffering from abnormal intestinal permeability and food allergy hypersensitivities in order to test its efficacy in repairing these conditions and restoring health.

Design

Inclusion of subjects in the trial was dependent on positive tests for both intestinal permeability and food antibody assessment (FAA) using test kits from Great Smokies Diagnostic Laboratory (Asheville, NC). Fifteen adult participants with abnormal intestinal permeability were selected to receive a glutamine-rich proprietary whole food supplement (Standard Process Inc., Palmyra, WI) for 60 days. Two participants were disqualified for improperly following protocol guidelines for testing. Following initial testing, a subset of the participants (n=8) eliminated for the duration of the study those foods for which they tested positive for IgG. All participants were retested for intestinal permeability and FAA at the end of the 60-day trial period.

Results

IP testing of participants revealed the following:

Ten of the 13 subjects who completed the study tested positive for excessive lactulose recovery in urine (≥0.60% lactulose recovery) during the initial testing, indicating an increase in intestinal permeability to large molecules (paracellular permeability).

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There is a strong likelihood that other macromolecules, toxins, and antigens were also crossing the intestinal barrier into the lymphatic and circulatory systems—the so-called "leaky gut" syndrome. Increased permeability increases the load on the body's detoxification systems, may stimulate immune activity, and has been associated with food allergy, inflammatory bowel disease, arthritis, and other inflammatory conditions (Iwata et al., 2001; Arnott et al., 2000; Dainese et al., 1999; Vaile et al., 1999; Chou et al., 1998; Majamaa and Isolauri, 1997; Sartor, 1997).

Nine of the 10 subjects with excessive lactulose recovery also showed elevated mannitol recovery indicating excessive permeability of intestinal epithelial cells to small molecules (transcellular permeability). This is indicative of the passage of small antigens across the mucosal barrier triggering an immune response.

Four of the 13 subjects completing the study had abnormally reduced mannitol recovery indicating a decrease in transcellular permeability of intestinal epithelial cells to small molecules. This suggests chronic malabsorption of critical dietary nutrients. Low mannitol recovery has been associated with gluten enteropathy, malabsorption, and failure to thrive in children, typically as a result of damage to the intestinal microvilli (Aguilera et al., 2000; Ahmed and Fuchs, 1997; Cox et al., 1999; Hamilton et al., 1987). It is important to note that one subject showed both excessive lactulose recovery and severely decreased mannitol recovery simultaneously. This illustrates that excessive paracellular permeability can occur even in subjects with chronic malabsorption issues and probably indicates both damaged microvilli and a reduction of intercellular tight junctions.

There was a significant recovery from excessive intestinal permeability in all but three of the 13 subjects who completed the study (Figure 1). The three subjects who did not improve all had indications of malabsorption (low mannitol recovery) and also did not restrict IgG reactive foods (see below). The greatest recovery was in subjects with the highest initial lactulose recovery values. The average lactulose recovery for the entire sample decreased from 0.70% at the start of the trial to 0.45% (P=0.04) after 60 days during which subjects consumed a glutamine-rich whole food supplement. When the subjects (n=3) displaying decreased mannitol and lactulose recovery (malabsorption) were excluded from the analysis, the improvement in the remaining subjects was even more dramatic, from 0.85% down to 0.47% lactulose recovery (P=0.005; Figure 2).

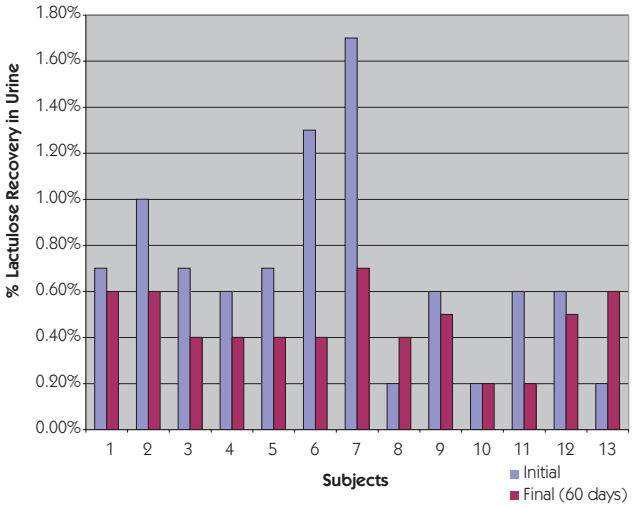

Figure 1 Initial and final lactulose recovery values in study subjects consuming a glutamine-rich whole food complex for 60 days (n=13).

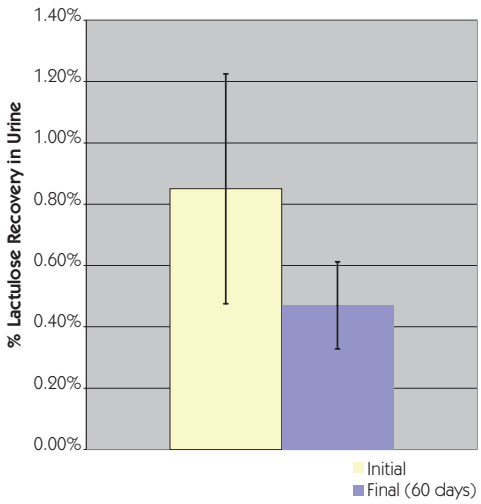

Figure 2 The average final lactulose recovery value decreased significantly in study participants whose initial values were abnormally high (n=10; P=0.005). Participants with malabsorption were excluded from this analysis (n=3), although their inclusion did not change significance.

There was a trend toward recovery in the four subjects showing malabsorption of mannitol (P=0.11). The lack of significance is probably due to the small sample and future studies with larger sample sizes may elucidate the significance of this.

There also was a trend toward reduction of the total IgE load (unrelated to the specific foods tested) in these subjects, although it did not achieve statistical significance (P=0.07). This suggests an overall reduced allergic hypersensitivity in study subjects following treatment. Future studies can determine the extent to which this trend, if real, is correlated with repair of excessive intestinal permeability, as other studies have

suggested (Dupont and Heyman, 2000; Ohtsuka et al., 1999; Knutson et al., 1996). It is reasonable to suspect that a permeable intestine increases exposure to environmental allergens (Imamura et al., 1996; Wyczolkowska et al., 1988). Poorly digestible lectins and related factors in some foods are known to influence intestinal permeability as well as the absorption of dietary antigens (Watzl et al., 2001; Greer and Pusztai, 1985).

Subjects were tested for IgG responses to 88 different foods (Table 1). Eight of the 13 study participants were required to restrict a limited list of foods that they responded to in their Specific Food Antibody Test #1. These participants showed significant improvement in intestinal permeability (P=0.05) on average, as indicated by lactulose recovery values, while the subjects who did not restrict foods showed no significant improvement in permeability (P=0.60; Figure 3A and 3B).

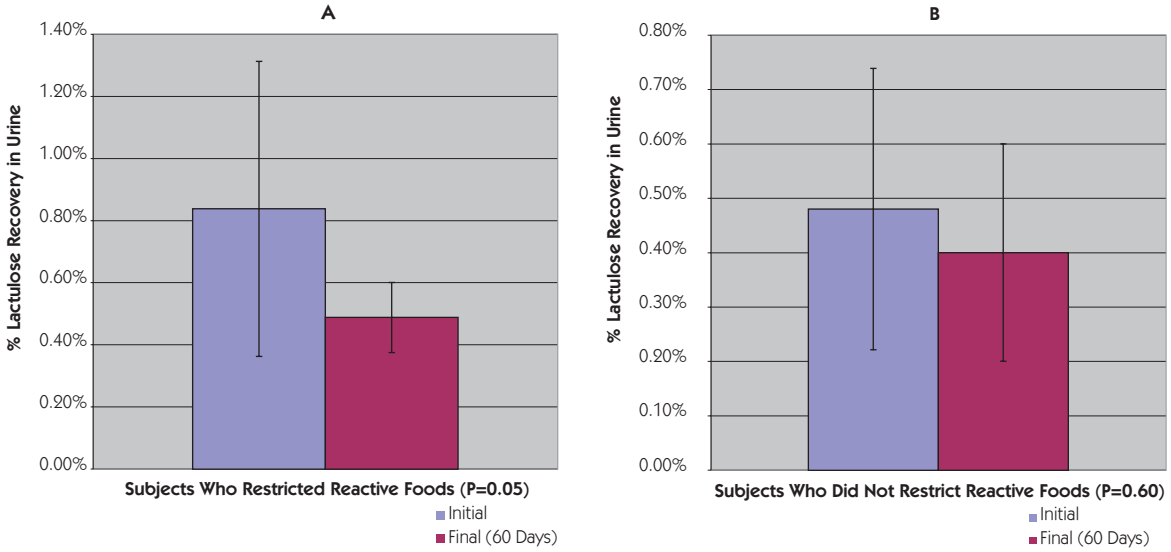

Figure 3 Study participants (n=8) who restricted foods for which they tested positive for IgG showed significant improvement in lactulose recovery values (A; P=0.05) following treatment, while participants who did not restrict foods (n=5) showed no significant improvement (B; P=0.60).

Interestingly, supplemental hair analysis for heavy metals in some study subjects indicated a possible correlation between intestinal malabsorption and metal toxicity, a curious finding that should be pursued in future studies. These individuals tested extraordinarily high in their IgE responses, a finding that is supported in literature on heavy metal toxicity and intestinal permeability (Strenzke et al., 2001; Watzl et al., 1999).

Final Thoughts

Due to patient quality of life concerns, it was not possible in this study to include a subset of control subjects with abnormal intestinal permeability that did not receive the glutamine-rich whole food supplement during the study period. This is the nature of applied clinical nutrition. As a result, it is impossible to preclude other possible factors responsible for the improved condition of these patients at the end of the study. However, the improvement in intestinal permeability that was observed was quite dramatic and, everything else held constant, the outcome strongly suggests a therapeutic benefit of glutamine-rich whole food complexes in the treatment of abnormal intestinal permeability.

Table 1 Study participants were tested for IgG and IgE antibodies against 88 common foods.

Dairy	Fruits	Nuts & Grains	Miscellaneous	Vegetables
Casein	Apple	Almond	Yeast	Alfalfa
Cheddar Cheese	Apricot	Buckwheat	Cane sugar	Asparagus
Cottage Cheese	Avocado	Corn	Chocolate	Beet
Cow's Milk	Banana	Corn Gluten	Coffee	Broccoli
Goat's Milk	Blueberry	Gluten	Honey	Cabbage
Lactalbumin	Cranberry	Kidney Bean		Carrot
Yogurt	Grapefruit	Lentil	**Poultry/Meats**	Celery
	Grape	Lima Bean	Beef	Cucumber
Fish/Shellfish	Lemon	Oats	Chicken	Garlic
Clam	Orange	Peanut	Egg White	Green Pepper
Cod	Papaya	Pecan	Egg Yolk	Lettuce
Crab	Peach	Pinto Bean	Lamb	Mushroom
Lobster	Pear	Rice	Pork	Olive
Oyster	Pineapple	Rye	Turkey	Onion
Red Snapper	Plum	Sesame		Pea
Salmon	Raspberry	Soy		Potato, Sweet
Sardine	Strawberry	Sunflower Seed		Potato, White
Shrimp		Walnut		Spinach
Sole		Wheat		String Bean
Trout				Tomato
Tuna				Zucchini

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