Glutamine: A Life Saving Nutrient, But Why?

Paul Wischmeyer M.D.

Editor-in-Chief: Journal of Parenteral and Enteral Nutrition
Co-Chair- 2009 Society of Critical Care Medicine Congress
Director of Nutrition Support Service
Vice-Chair for Clinical and Translational Research
Associate Professor of Anesthesiology
University of Colorado Health Sciences Center
“I am going to cure this disease and take better care of the people that have it then the doctors who cared for me!”
The Ideal Therapeutic

- Clinically Effective
- Widely applicable
- Little or no adverse effects
- Inexpensive
- Physiologically Justifiable
- Easy to administer
- Can be used as pre-treatment to prevent disease and complications

- Only one class of agents can make these claims:

**Nutritional Therapeutics**
What Should Make You Change Your Practice?

- Therapy Makes Mechanistic Sense
- Majority of Studies Support Use of Therapy (on clinically relevant endpoints)
- Meta-Analysis Supports Use
- No Evidence of Harm/Low Cost
- Makes Sense in the Developmental History of Mankind…?
Why This Does Not Happen Often?

- Lack of Scientific Mechanism
- Single studies split on outcome benefit or...
- Show benefit on clinically irrelevant endpoints
- Meta-Analysis does not support use
- Evidence of Harm/Risk is present
- High Cost
So I Will Show You That Glutamine...

- Has multiple strong mechanistic benefits
- Most all single studies show benefit on meaningful outcomes
- Meta-Analysis does support use or consideration of use
- No Evidence of Harm/Low Cost ...and...
Why You Should Use a New Therapy in Your ICU?

- Therapy Makes Mechanistic Sense
- Majority of Studies Support Use of Therapy (on clinically relevant endpoints)
- Meta-Analysis Supports Use
- No Evidence of Harm/Low Cost
- Makes Sense in the Developmental History of Mankind...?
Does GLN make Mechanistic Sense??
What is Glutamine?

Isn’t it just a metabolic fuel?
Chronic Pouchitis After Ileal Pouch-Anal Anastomosis: Responses to Butyrate and Glutamine Suppositories in a Pilot Study

Paul Wischmeyer, B.S.,* John H. Pemberton, M.D., and Sidney F. Phillips, M.D.

Nonspecific, idiopathic inflammation of ileal pouch mucosa ("pouchitis") after ileal pouch-anal anastomosis is a common complication of this surgical approach. The epithelium of the pouch is ileal, but variable degrees of colonic metaplasia are natural sequelae of construction of such a pouch. One hypothesis is that pouchitis is caused by a deficiency of epithelial nutrition. Thus, a lack of butyric acid (the principal metabolic fuel of colonocytes) or of glutamine (the main fuel of enterocytes) may develop. In this study, our aims were to determine the concentration of total short-chain fatty acids in random stool samples obtained from patients with an ileal pouch-anal anastomosis with and without pouchitis and to test the therapeutic effects of butyrate and glutamine suppositories on pouchitis. During the study, all conventional therapy for pouchitis was discontinued. For 21 days, 9 patients participated in a butyrate trial, and 10 patients were treated with glutamine. Total concentrations of fecal short-chain fatty acids were significantly less in patients with pouchitis than in those without pouchitis. During treatment, 6 of the 10 patients who received glutamine had no recurrence of symptoms, but only 3 of the 9 patients who received butyrate responded similarly. Hence, further studies of glutamine in the treatment of pouchitis seem warranted.
Effect of Glutamine and Butyric Acid in Severe Pouchitis

- Glutamine
- Butyric Acid

Patients in Remission

Treatment

Glutamine
Butyric Acid
“Let knowledge grow from more to more, and so be human life enriched”

—The University of Chicago motto
How does glutamine prevent inflammation of the ileal pouch?

i.e. - where and how is the glutamine acting?
Hypothesis:

Glutamine is directly cytoprotective to the intestinal epithelial cell.
GLN Protects Intestinal Cells Against Injury

Lethal heat injury (49 deg C x 90 min)

NH₂CL injury (2 mM NH₂CL x 60 min)
Glutamine is a powerful effector of heat shock protein expression in Drosophila Kc cells.

Sanders MM, Kon C.
Department of Pharmacology, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, Piscataway 08854.
We have investigated the effects of extracellular anions on the regulation of expression of the heat shock response in Drosophila Kc cells incubated in defined balanced salt solutions. Widely varying chloride concentrations had no effect on normal or heat shock protein (hsp) expression. Increasing glutamate concentrations from zero to 15 mM increased hsp expression more than 100-fold while affecting expression of non-heat-shock proteins minimally. Glutamine was 20-100-fold more potent than glutamate in supporting hsp expression, while other amino acids were less effective or supported no detectable hsp synthesis in heat shock. Inhibition of glutamine synthetase with methionine-sulfoximine resulted in very low hsp expression with glutamate and normal high level expression with glutamine, confirming the importance of glutamine. The absence of glucose and treatment with 2-deoxyglucose did not change the requirement for adequate glutamine for hsp expression. Cells heat shocked under conditions which gave very low hsp expression resumed growth when returned to normal medium as well as cells which expressed normal levels of hsp.
Measurements of free amino acid levels in cells heat shocked in the presence and absence of glutamine showed a correlation between glutamine levels and amount of hsp expression. We conclude that a physiological process regulated by glutamine or a glutamine metabolite is important for normal hsp expression in heat shock conditions in Drosophila.