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Nutrient Control of Gastrointestinal Transit-a Bench-to-Bedside Story

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This lecture will be focused on the physiology of how nutrients control the movement of a meal through the gut. The goal of the seminar is to illustrate the bench-to bedside impact of translational research that link basic science to clinical medicine.

The following areas will be covered:
1. Control of upper gut transit by nutrient-triggered inhibitory feedback,
2. Examples of exploiting feedback control in nutritional support.
3. Clinical conditions associated with impaired transit control
4. Clinical consequences of uncontrolled transit
6. A novel, nutrient-based approach to the problem of accelerated transit.

The movement of food through the small intestine is tightly controlled via the triggering of nutrient-triggered inhibitory feedback. Load-dependent slowing of gastric emptying is achieved through a metering mechanism based on the length of nutrient spread (1).

Post-ulcer surgery is the classic example of accelerated gastric emptying. In that setting, dumping symptoms are the consequences of exaggerated feedback response (2) secondary to uncontrolled transit of the meal through the small intestine (3).

Fat-intolerant patients have similar complaints of postprandial symptoms of bloating, nausea and diarrhea. We found that fat intolerant patients had accelerated gastric emptying to suggest that their symptoms resulted from excessive nutrient-triggered feedback (4).

Once food is emptied, controlled transit through the small intestine becomes the next point of regulation. There are 2 transit control mechanisms in the small intestine: the jejunal brake (5) which is located in the proximal end of the small intestine and the more potent, ileal brake (6,7,8) which is located in the distal end. Both of these controls are important since fat absorption normally involves the proximal as well as the distal small intestine (9).

Impairment or loss of these transit controls have serious consequences including the dumping syndrome and malnutrition, both resulting from accelerated intestinal transit. With accelerated transit, digestion may be so impaired that the triggers for activating the transit controls are not available.

Based on the therapeutic goal jump-starting the transit control response before a meal is presented to the small intestine, a novel, nutrient-based therapy based on a premeal containing

fatty acids is effective in slowing intestinal transit in a dose-dependent fashion by activating nutrient-triggered inhibitory feedback (10).

Since the time of residence in the small intestine (speed of intestinal transit) is also an important determinant of the bioavailability of oral medications, inflammatory bowel disease (IBD) patients with chronic diarrhea and accelerated transit may have poor absorption of oral drugs. By slowing intestinal transit, a premeal containing fatty acids is effective in improving bioavailability of oral medications (11). This strategy to increase the time available for dissolution and absorption of oral drugs is also effective in normal subjects without accelerated transit (12).

These results are quite encouraging since IBD and other diseases may be easier to treat than we think if only we pay closer attention to the problem of accelerated transit, perform gut transit testing to confirm this abnormality and work to bring transit under control.

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