Commentary

Assessing food intolerance: don't lose control

In 1970, Cuatrecasas *et al* showed that healthy individuals could have an isolated deficiency of intestinal lactase.[1] Shortly thereafter, it was shown that a large fraction of the world's adult population became lactase deficient[2] owing to a genetically programmed reduction in lactase activity,[3] a state now known as lactase non-persistence.

Initial studies[4] showed that many lactase non-persistent subjects had easily identifiable symptoms after ingestion of a challenge dose of 50 g lactose (the equivalent of one quart of milk). When early, unblinded studies[5 6] suggested that physiological quantities of milk (one cup or less) could induce appreciable symptoms, lactose intolerance became a favoured explanation for a variety of what otherwise would have been considered to be functional abdominal symptoms. The widespread dissemination of this information in lay publications has led a sizable fraction of the population of the United States to believe that lactose, in trivial quantities, is the cause of a wide array of abdominal symptoms.

One of the prevailing ideas concerning lactose malabsorbers was that continued ingestion of this disaccharide leads to improved tolerance. Since intestinal lactase activity is not increased by ingestion of lactose, this improved tolerance has been attributed to adaptation of the colonic flora to the continued availability of lactose. Presumably, this adaptation results in altered bacterial metabolism of lactose, which reduces the osmotic load and gas production. The former reduces diarrhoea and the latter the bloating, abdominal discomfort and flatulence associated with lactose malabsorption. Support for this concept has been provided by objective data[7] showing (*a*) an increase in faecal β-galactosidase activity, the rate limiting enzyme in lactose metabolism; (*b*) a decrease in faecal pH suggesting more effective fermentation; and (*c*) a decrease in breath H_2 excretion, suggesting an alteration of the fermentation pathway. While these objective measurements provide a rationale for why intolerance symptoms might be improved by continued lactose ingestion, symptoms are a subjective phenomenon. Improvement in tolerance can only be established by showing that lactose induced symptoms are reduced in a double blind, placebo controlled challenge study.

Briet and coworkers, in this issue (see page 632), demonstrate the critical need for appropriate controls in the evaluation of diet induced abdominal symptoms. These authors challenged a group of lactose intolerant subjects with a 50 g dose of lactose before and after a 13 day period during which the subjects received 34 g lactose daily. As expected, subjects reported a notable reduction in symptoms, and significant alterations were observed in faecal pH and β-galactosidase activity and breath H_2 excretion. The crucial feature of the experimental design of Briet *et al*'s study was the inclusion of a control group consisting of a parallel group of lactase non-persistent subjects who received 34 g sucrose for 13 days. These subjects demonstrated none of the objective findings of the lactose adapted group; in fact, there was a significant reduction in

faecal β-galactosidase activity in the group receiving sucrose. Nevertheless, a comparable reduction in symptoms to the lactose challenge was observed in the sucrose treated subjects. Consequently, it seems that the symptomatic improvement associated with chronic exposure to lactose had nothing to do with the bacterial adaptation reactions but rather was psychogenic in origin. Interestingly, faecal weight was not significantly altered following lactose or sucrose adaptation but, in both groups, the number of stools passed fell from roughly four to two in the 12 hour period following lactose challenge. Thus, what one might think to be a physiological process relatively immune to psychogenic factors, the urge to defecate, also seemed to be susceptible to the placebo effect.

Briet *et al*'s observations further emphasise the dissociation between objective measurements and symptoms in lactose intolerance and the need for double blind, placebo controlled studies in symptom assessment. For example, it is relatively easy for physicians to demonstrate lactase non-persistence or lactose malabsorption via measurements of lactase activity or breath H_2 excretion, respectively. However, intolerance to a given dose of lactose only can be established via the demonstration that the subject has a significant increase in symptoms in a well-controlled challenge study. Such studies have shown that even subjects who believe themselves to be extremely lactose intolerant have minimal symptoms when exposed to one to two cups of milk (12.5 to 25 g lactose) with meals each day.[8 9] The belief that physiological doses of lactose induce appreciable symptoms seems to be a misapprehension resulting from the extrapolation from studies in which 50 g doses of lactose were administered without food.[4]

Observations concerning the psychogenic aspects of symptoms of lactose intolerance seem to be applicable to the entire field of food intolerance. For example, in a survey of 7500 households in the United Kingdom, Young *et al*[10] found that 19.4% of subjects complained of various types of food intolerance. However, based on the results of objective testing of 93 selected individuals, the authors concluded that the prevalence of true food intolerance was only about 1.8% of the population. A similar discrepancy between claims of food intolerance and objective demonstration of symptoms has been observed in several other studies.[11]

Medical students are taught that it is very important to listen carefully to patients' beliefs concerning the origin of their symptoms. Such a practice may yield useful information for many disease states; however, for the vast majority of patients complaining of food intolerance, such information is likely to be misleading.

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