EDITORIALS

Lactulose or Lactose in Hepatic Encephalopathy?

Lactulose (1-4-α-galactoside-fructose) is a synthetic disaccharide which is not absorbed, as there is no disaccharidase enzyme to split a combination of galactose and fructose. The unabsorbed lactulose reaches the large intestine where the bacterial enzymes produce lactic acid and lower the colonic pH to 5 (normal pH 7). This lowering of pH decreases ammonia production as well as absorption from the colon and perhaps facilitates excretion of ammonia from blood into the gut, resulting in reduction of blood ammonia. Other substances such as sorbitol or magnesium sulphate cause diarrhoea, but do not reduce blood ammonia, as they do not lower colonic pH.

In the treatment of chronic hepatic encephalopathy, lactulose is administered in a dosage of about 80-140 ml/day in four divided doses to ensure 2-3 semi-solid stools daily. In acute hepatic encephalopathy, the initial dose is 80 ml lactulose every hour till a liquid stool is passed and thereafter every 6 hours as in chronic encephalopathy. Alternatively, lactulose enemas may be given for an instantaneous drop in colonic pH. Lactulose, though of proven benefit in the treatment of hepatic encephalopathy, has certain disadvantages: (i) it is expensive (Rs. 40 for 300 ml) and is not easily available in India, (ii) its taste is not acceptable to most patients, (iii) administration of four doses per day is inconvenient for ambulatory patients and (iv) although administration of neomycin and lactulose has been shown to have an additive effect, it is not an ideal combination as neomycin markedly decreases aerobic bacteria in the colon which are necessary for splitting up of lactulose.

Lactose is a naturally occurring disaccharide present only in milk (45 g/litre in cow's milk and 70 g/litre in human milk). Enzyme lactase present in brush border of small intestine breaks down lactose into glucose and galactose. In the presence of lactase deficiency, lactose is not split in the small intestine and causes osmotic diarrhoea and lowering of stool pH due to formation of lactic acid in colon. In healthy Caucasians subjects from Europe, North America, Australia, the incidence of lactase deficiency is 10-15% but it is 70-75% in population from India, Africa, American Negroes and Australian aboriginals; these differences are due to hereditary factors. Lactase when orally administered in a dosage higher than the capacity of intestinal lactase to split it, causes liquid stools in 2-3 hours. Those with low lactase levels require a smaller dose (30 g or more), while those with normal lactase levels require a higher dose (60 g or more). In the treatment of chronic hepatic encephalopathy, use of lactose was advocated in patients with lactase deficiency. In acute hepatic encephalopathy, lactose enemas (1 litre 20% t.i.d) were recently shown to be useful by instantaneously lowering colonic pH to 5 or less.

In chronic hepatic encephalopathy, 40 g lactose in 350 ml of water may be administered orally. If diarrhoea does not occur, the dose of lactose is increased by 10 g daily till a controlled diarrhoea results (2-3 liquid stools in 3 hrs). In acute hepatic encephalopathy, 400 ml of 20% lactose enema is given 8 hourly. Lactose is preferred to lactulose by us in the management of hepatic encephalopathy for following reasons: (i) lactose is freely available, (ii) the sweet taste of lactose is better accepted than that of lactulose, (iii) lactose is cheap (1 kg costs Rs. 50), (iv) a single oral dose is given immediately on getting up in the morning so that controlled diarrhoea stops within the next 3 hours; if required, a second dose may be given in evening, (v) neomycin can be administered later during the day after diarrhoea ceases. Since neomycin damages the small intestinal mucosa and decreases lactase levels, a combination of lactose and neomycin may prove to be superior to a combination of lactulose and neomycin.

To summarise, either lactulose or lactose can (i) lower colonic pH, (ii) decrease ammonia production as well as ammonia absorption by avoiding colonic stagnation, (iii) provide a substrate to colonic bacteria and thus reduce the metabolism of exogenous proteins.

References

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