Proceedings of the Nutrition Society (2008), **67 (OCE)**, E163 doi:10.1017/S0029665108007957

Joint meeting of the Société Française de Nutrition and The Nutrition Society, 6–7 December 2007

Large intestinal resection induces changes in human colon: study of H+/oligopeptide cotransporter 1 (PepT1), Na+/H+ exchangers 3 and 2 (NHE 3 and NHE 2) and intestinal microbiota

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Short-bowel syndrome (SBS) is usually observed after an intestinal resection that retains a remnant of small bowel of <2 m. Clinically, SBS is described as diarrhoea, and malnutrition. In patients with SBS with the colon in continuity with the small bowel an increase in nutrient absorption has been observed, reflecting compensatory adaptation(1). The aim of the present study was investigate molecular colonic changes in patients with SBS with a jejuno-colonic anastomosis.

Mucosal biopsy samples were obtained from the proximal, mid-transverse and distal colon of ten patients with SBS and from ten control subjects. Three variables were studied in the colon: (a) a marker of proliferation, Ki67, was detected by immuno-histochemistry; (b) PepT1, NHE3 and NHE2 mRNA were quantified by real-time quantitative PCR; (c) the bacterial profile was determined by temporal temperature-gradient gel electrophoresis of 16r DNA from faecal samples. Student's *t* test and unpaired *t* test (Mann-Whitney test) were used to compare patients with SBS and controls. Data are expressed as mean and SD or median and range.

In the ten patients with SBS the median remnant small bowel length and percentage residual colon were respectively 35 (range 0–80) cm and 60 (range 40–100). The total number of epithelial cells per crypt in patients with SBS compared with the controls was 69 (SD 4) *v.* 54 (SD 1; $P=0.0026$). The percentage epithelial Ki67-positive cells was not significantly different, suggesting a morphological adaptation without hyperproliferation activity. In the controls a gradient of NHE 3 mRNA was observed, with a higher abundance in the proximal>mid-transverse>distal colon. The amount of NHE 3 and NHE 2 appeared to be similar for both groups. Few of the patients with SBS (three of ten) showed a high expression of PepT1 mRNA in comparison with the controls. In patients with SBS the biodiversity of the dominant bacterial flora was drastically reduced. Four group-specific probes targeting 16S rRNA were used. In patients with SBS the Lactobacillus group increased, whereas the *Clostridium leptum* group was reduced.

In a series of adult patients with SBS with a jejuno-colonic anastomosis the present study showed that in the residual colon when compared with adult controls: (a) the total number of epithelial cells per crypt was higher in patients with SBS ($P<0.003$) without an increase in proliferation, suggesting a morphological adaptation; (b) there was overexpression of PepT1 mRNA in the proximal site for the patients with SBS; (C) there was a microbiota adaptation with an increase in the Lactobacillus group, whereas the *Clostridium leptum* group was reduced. Furthermore, the present study has established the regional colonic distribution and the respective abundance of NHE 2, NHE 3 and PepT1 mRNA in a control population.

1. Crenn P, Morin MC, Joly F, Penven S, Thuillier F & Messing B (2004) *Gut* **53**, 1279–1286.