Heat-labile enterotoxin enhances small intestinal colonization with F18ac+ verotoxigenic *E. coli* in newly weaned piglets.

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Enterotoxigenic *E. coli* (ETEC) play a major role in the post weaning diarrhoea complex. Upon weaning F4+ ETEC strains rapidly colonize the small intestinal mucosa of pigs and produce LT, STa and/or STb enterotoxins which enhance fluid secretion leading to diarrhoea, weight loss and mortality. F18 + verotoxigenic *E. coli* (VTEC) mainly cause oedema disease which peaks the second week post weaning. Here we have postulated that exposure to LT enterotoxin, even in subclinical concentrations, changes the intestinal mucosa in such a way that it allows an enhanced colonization with F18 VTEC. Using the small intestinal segment perfusion technique, 10 µg LT in a 20 cm long segment during 6 hours was the lowest dose tested that consistently induced fluid secretion (56 ± 70 g fluid/cm2 small intestinal mucosa). Whereas this dose removed some mucus from the mucosa (76 ± 7% mucus coverage), 30 µg had a much clearer effect (60 ± 7 % mucus coverage) in comparison with control segments (89% ± 5% mucus coverage). This was comparable with fluid loss and mucus clearance induced by inoculating the loops with 108 CFU F4ac+ ETECstrain GIS 26 (LT+, STa+ STb+) (356 ± 133 mg fluid/ cm2 and 68 ± 8 % mucus coverage). To analyse the effect of the enterotoxin *in vivo*, the eight meter long small intestinal tract of 4-week-old piglets was injected at 5 sites with a total dose of 1200, 500, 350 or 250 µg LT. Both highest dosages induced diarrhoea and mucus loss, whereas the effect of 350 µl LT was intermediate and no diarrhoea or mucus loss was observed after injection of 250 µg LT. Both latter dosages were injected intraluminal in 7 and 4 pigs, respectively, to see if the LT enterotoxin could enhance colonization of the 6 hours later intragastrically inoculated F18ab+ VTEC strain 107/86 (STx2e+) (1011 CFU in 10 ml PBS) in comparison with colonization in non-LT injected inoculated animals (n=7). The subclinical dose of LT (either 250 µg or 350 µg LT) prolonged the duration of VTEC excretion and significantly increased the VTEC colonization between 4 and 7 days after the inoculation.