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Alpha-ketoglutarate reduces duodenal myoelectric disturbances induced by *E. coli* enterotoxin in pigs[1]

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ABSTRACT

Pigs with bipolar electrodes implanted on the antrum and duodenum were exposed to heat-labile enterotoxin from *E. coli* (LT) infused intraduodenally. The exposure was repeated after three days of supplementing feed with α-ketoglutarate (AKG). 0.5 μg/kg of LT induced prolonged changes in the migrating myoelectric complex (MMC) without inducing clinical signs of enterotoxaemia. AKG had no effect on the basic MMC pattern, but prevented LT-induced changes. The possible mechanism of AKG and LT-induced alteration may involve gamma-aminobutyric acid (GABA) synthesis and activation of GABAergic neurotransmission in the gut.

KEY WORDS: migrating myoelectric complex, enterotoxin, α-ketoglutarate

INTRODUCTION

Gastrointestinal tract motility is crucial for its functions. Heat-labile enterotoxin (LT) produced by enterotoxigenic *E. coli* is a major virulent factor responsible for infectious diarrhoea in young animals and children. Enterotoxaemia-induced ileus can lead to death due to endotoxaemia and septicaemia. It has been shown that various bacterial toxins influence the migrating myoelectric complex (MMC) in pigs, rats and calves. After administration of endotoxins, MMC cycles are shortened and more frequent. In pigs, elevated MMC migration velocity and cycling frequency are maintained one day after endotoxin administration during feeding and return to basal values 4 days later (Bruins et al., 2003).

Glutamine has a beneficial effect on gut morphology (Potsic et al., 2002). However it is debated whether glutamine has beneficial effects on the gut during disease. Since glutamine is unstable in solutions, α-ketoglutarate (AKG) can be used as a glutamine

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precursor. No studies have been performed on the influence of AKG on motility or MMC during enterotoxaemia. Therefore, the present study was designed to evaluate the effect of heat-labile enterotoxin on MMC in weaned pigs, followed by investigating the effect of AKG on parameters of MMC in animals exposed to enterotoxin.

MATERIAL AND METHODS

Castrated male pigs (10.5-13 kg BW) had surgically implanted bipolar silver electrodes on serosal membrane of the stomach antrum and duodenum, as described by Gacsalyi et al. (2000). The electrodes were connected to a telemetric transmitter permitting constant measurement of GI tract electrical activity. The animals were also fitted with a duodenal cannula.

Ten pigs were subjected to intraduodenal infusion of *E. coli* LT (Sigma, USA) in doses 0.1 and 0.5 μg/kg BW. LT was injected in a 2 ml bolus at the end of phase I of MMC between 2 and 3 p.m. Each dose was tested on the same pig with a one- or two-day interval. A further 8 pigs were used for studying the effect of AKG. The MMC in each animal was recorded under control conditions, after infusion of LT at 0.5 μg/kg BW, after 1-3 days of feeding AKT at 10 mmol/kg BW, and after LT infusion at 0.5 μg/kg BW given on the 5th day after starting AKT supplementation.

RESULTS

The pigs were in good condition and stable during the entire experiment. LT had no effect on the duration or signal power of electromyographic events in the antrum. In the duodenum after LT infusion, the duration of the MMC cycle increased at night (postprandially). The increase was due to elongation of phase II (Figure 1). The velocity of phase III migration in the duodenum was significantly increased following LT administration (Figure 2).

Feed supplementation with AKT had no effect on basic electrical activity in the antrum. The velocity of phase III in the duodenum was unchanged after 3 days of AKG supplementation. Administration of LT on the 5th day of AKT supplementation did not affect the velocity of phase III (Figure 3)

DISCUSSION

In the present study we have shown that low doses of LT induce disturbances in gut motility without evoking other clinical signs. Therefore, exposure to bacterial toxins even without inducing disease may cause alterations in gut function that are followed by a decrease in feed utilization. Feed supplementation with AKG has no effect on basic motility, but prevents changes

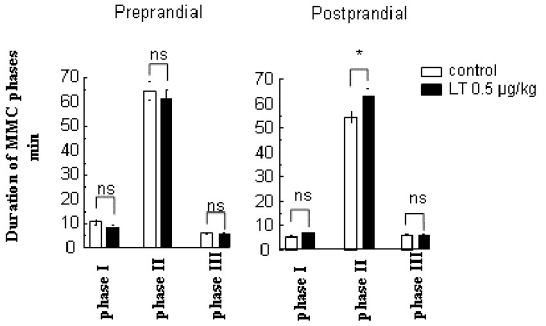

Figure 1. Duration of duodenal MMC phases in control (white columns) and after intraduodenal administration of *E. coli* heat-labile enterotoxin (LT) 0.5 µg/kg BW (black columns) recorded in 10 pigs. Data expressed as mean ± SE. * different from respective control; P<0.05 (paired t-test)

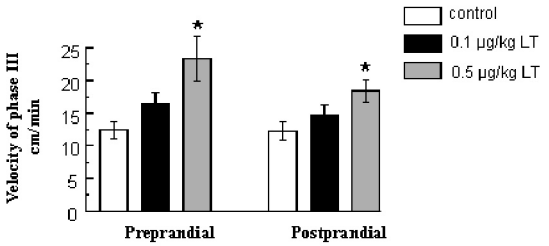

Figure 2. Velocity of phase III (cm/min) in the duodenum of weaned pigs in control (white columns), after intraduodenal administration of LT 0.1 µg/kg (black columns), and LT 0.5 µg/kg (grey columns). Data expressed as mean±SE (n=8) * different from respective control; P<0.05 (ANOVA, Dunett post hoc test)

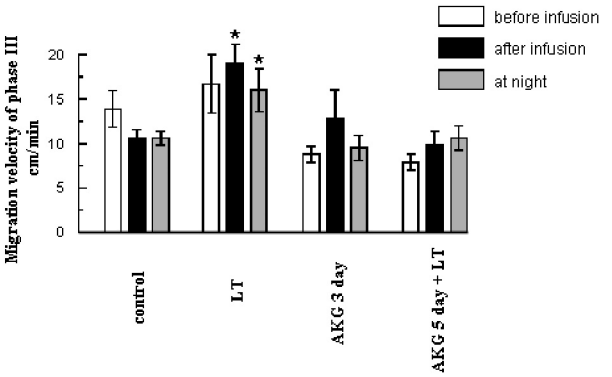

Figure 3. Migration velocity of phase III before (white columns), after infusion (black columns), and at night (grey columns) in control conditions, after administration of *E. coli* heat-labile enterotoxin (LT) 0.5 µg/kg BW infusion, after the 3rd day of α-ketoglutarate (AKG) supplementation, and after LT infusion on the 5th day of AKG supplementation. Data expressed as mean±SE (n=8). * different from respective control; P<0.05 (paired t-test)

induced by LT. It has been assumed that enhanced gamma-aminobutyric acid formation (GABA) in the intestinal mucosa by ornithine α-ketoglutarate treatment might be of physiologic importance in the regulatory processes of cell growth and differentiation (Raul, 1995). The presence of GABA-positive neurons in the submucosal and myenteric plexus has been shown in pigs (Timmermans and Scheuermann, 1998). Spontaneous relaxations of the rat gastroduodenum include responses that involve a GABAergic nitric oxide-related pathway, which is targeted by VIP (Krantis et al., 1998).

CONCLUSIONS

Feed supplementation with α-ketoglutarate may have a beneficial effect on subclinical forms of enterotoxaemia, decreasing diarrhoea and improving feed utilization that leads to better health.

REFERENCES

Bruins M.J., Luiking Y.C., Soeters P.B., Akkermans L.M., Deutz N.E., 2003. Effect of prolonged hyperdynamic endotoxemia on jejunal motility in fasted and enterally fed pigs. Ann. Surg. 237, 44-51

Gacsalyi U., Zabielski R., Pierzynowski S.G., 2000. Telemetry facilitates long-term recording of gastrointestinal myoelectrical activity in pigs. Exp. Physiol. 85, 239-241

Krantis A., Mattar K., Glasgow I., 1998. Rat gastroduodenal motility in vivo: interaction of GABA and VIP in control of spontaneous relaxations. Amer. J. Physiol. 275, G897-G903

Potsic B., Holliday N., Lewis P., Samuelson D., DeMarco V., Neu J., 2002. Glutamine supplementation and deprivation: effect on artificially reared rat small intestinal morphology. Pediat. Res. 52, 430-436

Raul F., Gosse F., Galluser M., Hasselmann M., Seiler N., 1995. Functional and metabolic changes in intestinal mucosa of rats after enteral administration of ornithine alpha-ketoglutarate salt. J. Parent. Enter. Nutr. 19, 145-150

Timmermans M.W., Scheuermann D.W., 1998. Distributional pattern and targets of GABA-containing neurons in the porcine small and large intestine. Eur. J. Morphol. 36, 133-142

STRESZCZENIE

Alfa-ketoglutaran zmniejsza zaburzenia mioelektryczne wywołane przez entrotoksynę *E. coli* u świń

Świnie z zainplantowanymi elektrodami bipolarnymi na antrum i dwunastnicy były eksponowane na ciepłowrażliwą enterotoksynę *E. coli* (LT), która była podawana dodwunastniczo. Ekspozycję powtarzano po trzydniowym wzbogaceniu paszy w α-ketoglutran (AKG). 0,5 µg/kg LT doprowadzało do długotrwałych zmian w migrującym kompleksie mioelektrycznym (MMC) bez wywołania objawów klinicznych enterotoksemii. AKG nie miał wpływu na podstawowy zapis MMC, ale zapobiegał zmianom wywołanym przez LT. Przypuszczalny mechanizm działania AKG na zmiany w MMC wywołane LT polega na syntezie kwasu gama-amino masłowego (GABA) i aktywacji GABA-ergicznej neurotransmisji w jelicie.