Effects of erythromycin on pressure in pyloric antrum and plasma motilin and somatostain content in dogs

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INTRUDUCTION

Erythromicin (EM) is a potent agonist of motilin (MTL) receptors[1]. EM may enhance the gastroenteric motion by binding with MTL receptors[2]. However, effects of EM pyloric antrum and its mechanism are not clear. The purpose of this study was to investigate the relation between EM, plasma MTL and somatostatin in regulation of pyloric sphincter muscle function in dogs.

MATERIALS AND METHODS

A randomized study was performed using male or female dogs weighing between 11kg-19kg. Before operation, dogs was prohibited form eating food for 24h.

Animals were anaesthetised with i.v. injection of pentobarbital (2.5%, 1mg/kg). The upper medial incision of abdomen was performed. The anterior wall of gastric antrum was cut about 0.5cm, the tube of the gastric pressure meter (WYY-1 type, Sapceflight Medicine Engineer Research Institute) was inserted and fixed. The pressure graph was recorded by the pressure transducer.

Erythromycin lactate was dissolved in 5% glucose liquid, and transfused i.v. (5mg/kg per hour). Isoptin (1mg/kg) was injected i.v. at an interval of 60min. At 90min i.v. atropine sulfoacid (0.1mg/kg) was given. During 120min of pre- and post-infusion, pressure measure was done for 2min and 1ml blood sample was collected from dog femoral vein every 15min. Nine blood samples (1ml each) were collected from each dog. 3ml EDTA-Na2 and 200KIu aprotinin was added into the samples. Blood samples were immediately centrafuged at 3 500r/min for 15min at 4℃. The plasma was stored at -70℃. MTL and SS was assayed by radioimmune method. (MTL and SS radioimmune reagment box, East-Asia Immune Technique Research Institute). The concentration of MTL and SS in blood was counted with a FJ-2003-50G counter.

Statistical analysis

Statistical analysis was carried out using the Statistical analysis System. When a significant analysis of variance was found, Student's *t* test between two samples was performed.

RESULTS

The changes of plyoric pressure and the concentration of MTL and SS in plasma before and after i.v. transfusion (Table 1).

Our results showed that the dog pyloric antrum basic pressure, total pressure and wave amplitude significantly increased after administration of EM. The interval time of high pressure wave amplitude was reduced and the frequency increased. After i.v. injection of antagonists isoptin and atropine, the plyoric pressure was inhibited repidly. The level of MTL in plasma of dogs and the change of the plyoric pressue induced by EM was related significantly, and were also infuenced by atropine and soptin. The concentration of SS in plasma of dogs was increased after EM administration and not inhibited by atropine and isoptin.

DISCUSSION

EM is one of most common antibiotics. To investigate the gastroenteric side effects of EM, Pilot and Itol, *et al*[3], have found that the i.v. infusion of EM might mimick the migrating synthetical electric current of muscles (or contraction) during dog digestion induced by MTL. The effect of EM was similar with MTL in vivo or vitro, EM competitively inhibited the compination of receptors and MTL, therefore EM is considered one of the agonists on MTL receptors. Sarna, *et al*[4] have found that i.v. EM 1mg • kg^{-1}/h-3mg • kg^{-1}/h

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(far below the dose of antibiotics) might induce migrating synthetical electric current of III phase muscles, beginning at stomach and migrating downward, which was related to MTL release. The main physiological action of MTL is to enhance the gastroenteric motion and increase the gastric and plyoric pressure. By i.v. EM 5mg • kg^{-1}/h, the plyoric pressure increased immediately, suggesting that EM could increase the pressure in plyoric antrum and it was highly sensitive; and the effect of EM was related with MTL. We believe that EM might be used to treat the gastroduodenal reflux diseases in future.

It has been found that the effect of EM on dog stomach, duodenal and gall doct might be inhibited by atropine[5], indicating that EM act on preconjunctional receptors of cholinergic. Some studies have suggested that EM and MTL have a similar gastroenteral action and race specificity. EM could induce the contration of rabbit gastric smooth musles, and was not inhibited by atropine, but blocked by antagoists of calcium passway Nifedipine. This indicated EM effect was related with calcium passway. Our result is similar with other investigators'.

There have been a lot of investigations on the effect of gastroenteric hormone. Increase in plyoric pressure was increased by human or dog duodenal infusion of HCl or florence oil, suggesting that gastroenteric hormone could regulate pyloric motion. We observed for the first time the plasma SS changes, and found that the plasma SS level was not blocked by isoptin and atropine after i.v. EM, and the plasma SS was higher in late stage. This phenomenon may be related to be autoregulation in vivo in order to maintain the balance among gastroenteral hormones like MTL and normal plyoric pressure.

In summary, the study suggested EM may increase the pressure in plyoric antrum. The effect may be related to the plasma motilin and somatostatin level.

Table 1 Pyloric pressure and plasma MTL and SS content before and after infusion of erythromycin in dogs. (n = 10, $\bar{x}\pm s$)

Parameters	Before drug administration	Erythromycin	Verapamil	Atropine
Total pressure (kPa)	20.1±2.2	34.5±3.1[a]	10.3±0.4[a]	8.2±0.2[a]
Basic pressure (kPa)	4.1±2.5	6.9±0.9[a]	4.4±0.8	5.2±0.2
Wave amplitude pressure (kPa)	16.0±14.4	27.6±9.6[a]	5.9±0.4[a]	3.0±0.1[b]
Wave frequency (time/min)	9.8±4.5	5.4±0.5[a]	2.9±0.4[a]	2.0±1.0[b]
Wave interval (s)	3.0±1.1	6.7±0.6[a]	3.8±0.4	3.1±0.1
Plasma MTL (ng/L)	426.9±53.4	553.9±87.2[a]	447.9±67.6	378.3±8.2[a]
Plasma SS (ng/L)	64.6±13.7	75.2±4.7[a]	85.6±2.9[b]	105.6±0.2[b]

[a]P<0.05, [b]P<0.01 *vs* before used medicine.

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