NOTE *Internal Medicine*

The Effect of Orally Administered Cisapride on Intestinal Motility in Conscious Horses

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ABSTRACT. Seven Thoroughbred horses were laparotomized and Force Transducers were fixed on the proximal jejunal and cecal serosa. After observation of the digestive tract motility in consciousness, cisapride (0 , 0.5, 0.75 or 1 mg/kg) was orally administered. In horses treated with 0.75 mg/kg or 1.0 mg/kg cisapride, the migrating contraction (MC) of the jejunum was significantly increased in frequency.—
KEY WORDS: cisapride, equine, intestinal motility.

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A high incidence of digestive disorders has been reported in horses with abnormal function of the digestive tract [2], and the regulation of the tract motility was of importance in the treatment. Cisapride [14] is a benzamide produced by Janssen Co., Ltd., Belgium, and it is known to induce acetylcholine release by the intermediation of a serotonin receptor in the intestinal nerve plexuses, resulting in a migrating contraction (MC) of the digestive tract with a regulated mobility [3, 12, 14].

In horses cisapride has been mostly given orally [2] for treatment of flatulence or constipation colic as well as prevention of postoperative ileus [4, 8, 16]. The dose dependency remains unclear in response to the intestinal motility after oral administration, although reactions to the drug have been after intramuscular and intravenous administration [5, 16] except for a single report [13].

This study was undertaken to observe the dose dependency effect of orally given cisapride on the motility of the jejunum and cecum in conscious horses.

Seven adult male Thoroughbred horses weighing 457.5 ± 9.2 kg, were fed twice a day and freely given water. After laparotomy Force Transducers (F-121S; Star Medical, Japan) were fixed on the serosal surfaces of the proximal jejunum (50 cm distant from the duodenum-colon fold) and of the cecum (50 cm distant from the apex) to measure MC of the digestive tract. The animals were tranquilized by a sedative, xylazine(1 mg/kg), followed by a rapid intravenous injection of a mixture of 10% guaiacol glycerine-ether and thiopental sodium (2 g). They were laid on their back and fixed on the operation table. Anesthesia was maintained by aspiration of isoflurane and oxygen. According to a routine method [10], laparotomy was carried out at the median ventral wall to expose the digestive tract, and the Force Transducers were fixed on the serosal surface using 4–0 nylon string. A coaxial cable was passed through the thoracic subcutis, extracted from the withers and fixed on the body surface.

The contraction motility was recorded starting immediately after waking from anesthesia. The coaxial cables from the Force Transducers were connected to a resistance box (FB-01; Star Medical, Japan) and continuous recording was made by a thermal array-recorder (PTA-1200; Nihon Kohden Kogyo, Japan) using a strain-pressure amplifier (AP- 100F; Nihon Kohden Kogyo, Japan). The intervals between two successive MCs were measured and their values were represented by their means ± standard deviations.

Cisapride was given within 5 to 10 min after a physiologic strong contraction (MC) appearing at the proximal jejunum at 2 weeks postoperation, when the animals had recovered from the effects of laparotomy [10]. The drug was administered at doses of 0.5, 0.75 and 1 mg/kg in 500 m*l* distilled water and the control animals received the same volume of distilled water. For investigation of the dose dependency, the frequencies of MC appearing at the proximal jejunum at 10 hr before and after administration, were measured. Mean values and standard deviations were calculated, and the significance of difference was examined by Wilcoxon test.

Figure 1 shows recording traces of jejunum and cecum motility in a cisapride-treated horse. The mean duration of MC in the jejunum before drug administration was 7.9 ± 1.7 min (N=7), and the mean interval between MCs was 130.1 ± 26.0 min (N=7). In the cecum, no MC was observed.

After administration of cisapride (1 mg/kg), the interval between MCs was shortened in a dose-dependent manner, with little or no change in their duration and amplitude. With the administration of 0 mg/kg, no significant increase in MC frequency was observed from 4.6 ± 1.0 times/10 hr to 5.0 ± 1.0 times/10 hr. With the administration of 0.5 mg/kg, the frequency of MC was increased from 5.1 ± 1.0 times/10 hr to 6.6 ± 0.8 times/10 hr, although there was no significant difference between the two mean values (Fig. 2). With administration of a higher dose of 0.75 or 1.0 mg/kg, a significant increase ($P<0.05$) in the MC frequency was observed: from 4.3 ± 0.8 times/10 hr to 7.1 ± 0.9 times/10 hr with the former dose, and from 4.3 ± 0.9 times/10 hr to 7.4 ± 0.5 times/10 hr with the latter dose (Fig. 2). Any dose of the drug produced little or no effect on the basal contractile activity on which the MCs were superimposed (see Fig. 1). In the cecum , administration of cisapride (0.5 to 1.0 mg/kg) did not induce MCs, nor did it alter the basal contractile activity (Fig. 1).

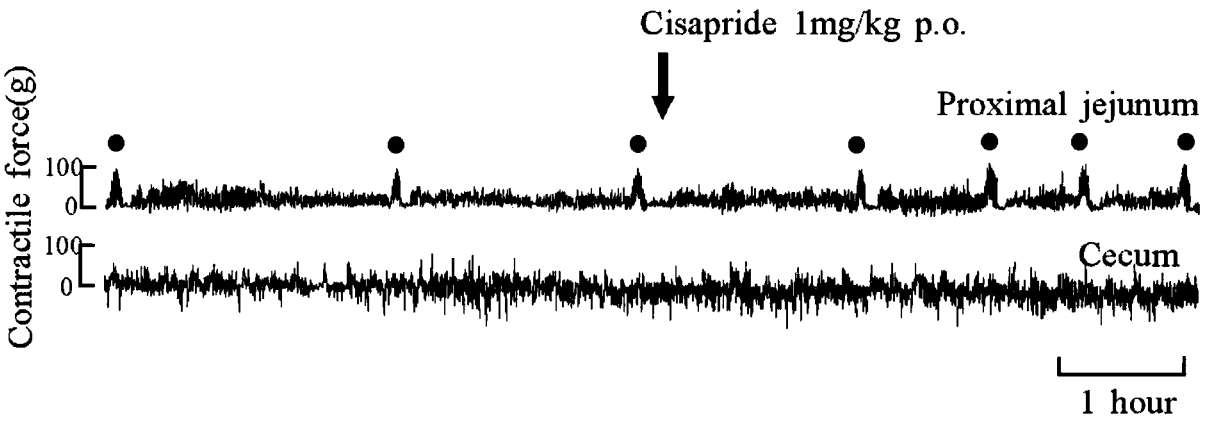

Fig. 1. Digestive tract motility after cisapride(1 mg/kg, p.o.) treatment. The frequencies of MC at the proximal jejunum were decreased after treatment. ●: Phase III, migrating contraction (MC).

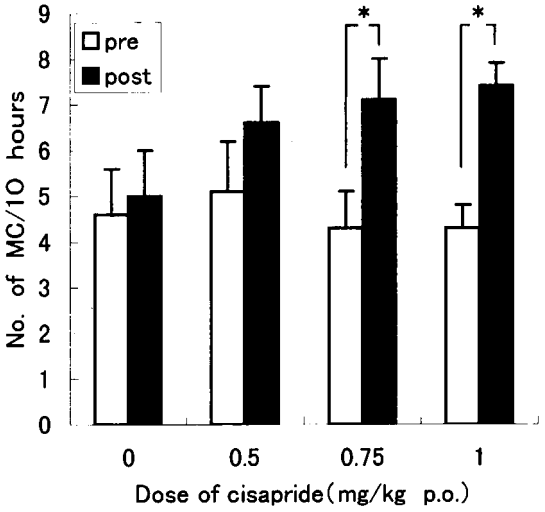

Fig. 2. Dose dependency of the frequencies of phase III (MC) at the proximal jejunum in cisapride-treated horses. The frequencies of MC were significantly increased after administration of cisapride (0.75 mg/kg or 1.0 mg/kg). pre: 10 hr before treating, post: 10 hr after treating. *: $P<0.05$.

In horses, the incidence of digestive disorders is high due to constipation, flatulence and postoperative ileus [1] in association with dysfunction of intestinal motility, such as lowered functions and loss of MC [7]. Strong contractions, that is MC, periodically occur in the mammalian small intestine, seemingly inhibiting the house-keeper and bacterial overgrowth [11, 15]. The equine MC is considered to be of importance for homeostasis of the intestines [1], for fast sending of the intestinal content into the lower cecum and colon to induce effective fermentation [10]. Consequently, the induction of MC might be effective for the harmonious regulation of motility in digestive disorders with lowered and abnormal motility.

There have been few reports on the effect of orally administered cisapride, which is known to induce MC [1, 13], probably because of the long-time required for recording of the intestinal contractions as well as the specific techniques needed.

The frequency of MC significantly increased after administration of more than 0.75 mg/kg cisapride. Milne [8] reported that on oral dose of 0.8 mg/kg cisapride was clinically effective for chronic gas sickness in horses, as observed in the present study. Steinebach and Cole [13] reported that clinical signs were improved in horses with constipation colic after nine oral dosings of cisapride (0.1 mg/kg) at 8 hr-intervals. King and Gerring [6] observed an increased electric potential at the left dorsal and small colons in a pony after intravenous treatment with 0.1 mg/kg cisapride, indicating that the drug might have an effect on the regulation of mobilities not only of the small intestine but also of the colon. On the other hand, no effect of cisapride has been reported on the equine cecum [6, 8], as observed in the present study. Such difference in effectiveness of cisapride between the intestinal parts might be ascribed to the difference in the distribution of serotonin (5-HT) receptors, that is, the targets of cisapride [9].

The present study revealed that the frequency of MC increased after oral administration of 0.75 mg/kg or 1.0 mg/kg cisapride in horses, inducing the harmonious regulation of the intestinal movement. Cisapride might be effective on digestive tract disorders involving lowered motility and abnormal functions.

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