GASTRIC ACID SECRETION IN BEAGLE DOGS USING INTRAMUSCULAR INJECTION OF STIMULANTS

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Accepted October 18, 1978

The most recent studies of gastric secretion in dogs have been performed by giving continuous i.v. infusion or bolus injection of stimulants to obtain quick and consistent secretory responses (1, 2). Mongrel dogs are almost invariably used for the experiments due to the facility of obtainment, and to handling of the foreleg veins. In contrast to mongrel dogs, Beagle dogs are rarely used for the study of gastric secretion, probably because their short, fat legs make for difficult and frequent utilization of veins, and also for economic reasons. In this communication we describe a new, standardized method for study of gastric secretion based on repeated i.m. administration of gastric stimulants to Beagle dogs.

Eight Beagle dogs (6 males and 2 females, 11-14 kg) prepared with Heidenhain pouches or gastric fistulae of the main stomach were used. The surgery was done about 6 months before start of the secretory tests. Studies were performed once or twice weekly on each dog. Histamine 2HCl (Wako), tetragastrin (San-A) and atropine sulfate (Merck) were prepared daily, in saline solution. Cimetidine (S.K.F.) was dissolved in 0.3 N HCl+saline solution and then neutralized with 0.3 N NaOH+saline solution. Prior to each test the animals were deprived of food but allowed free access to water for 20 hr. After obtaining two basal 15 min gastric collections, each stimulant was injected in varying doses into the vastus lateralis, every 15 min for 90 min, in a volume of 1 to 2 ml per dog. Gastric juice was collected from the Heidenhain pouch or gastric fistula by gravity drainage at 15 min intervals. Acidity was determined by titration with 0.1 N NaOH to pH 7.0 using an automatic titrator (Radiometer, Denmark). The results are expressed in mEq/15 min (output). Antisecretory agents given in a single dose were concomitantly injected with each stimulant into the same muscle using a separate syringe. Student's t-test was employed for determining the statistical significance.

Repeated i.m. injections were well tolerated by the animals. As shown in Fig. 1, the administration of histamine 2HCl or tetragastrin stimulated gastric acid secretion from both the gastric fistula and the Heidenhain pouch. The maximal response was obtained 45-75 min after the injection, i.e., 3-5 injections were required to induce a sustained plateau. The doses which induced the maximal acid output were 40 μg/kg/15 min or 2 μg/kg/15 min for histamine 2HCl or tetragastrin, respectively. It was shown that 10 μg/kg/15 min of tetragastrin weakly stimulated the acid secretion in dogs with gastric fistula as compared with administration of 2 μg/kg/15 min. Even in dogs with the Heidenhain pouch, 4 μg/kg/15 min
FIG. 1. Gastric acid output in response to 3 to 4 doses of histamine 2HCl or tetragastrin in dogs with gastric fistula (GF) and dogs with Heidenhain pouch (HP). Each gastric stimulant was given i.m. at 15 min intervals (arrows). Each point represents the mean±s.e. of 6 observations obtained in one or two experiments on each dog.

FIG. 2. Effects of a single i.m. administration of atropine sulfate or cimetidine on gastric acid secretion, induced by repeated i.m. injections of gastric stimulants to dogs with either the gastric fistula (GF, 4 dogs) or the Heidenhain pouch (HP, 4 dogs). Each point represents the mean±s.e. of 6 to 8 observations obtained in one or two experiments on each dog.
of tetragastrin showed an apparent weak stimulation of gastric acid as compared with 2 \( \mu g/\) kg/15 min. A single i.m. administration of atropine sulfate at 0.01 mg/kg significantly (\( P<0.05 \)) inhibited acid secretion stimulated by the maximal doses of histamine 2HCl or tetragastrin in dogs with the gastric fistula or the Heidenhain pouch (Fig. 2). Cimetidine also significantly (\( P<0.05 \)) inhibited the response to these stimulants in dogs with gastric fistula or Heidenhain pouch in a dose-related manner (Fig. 2). The inhibition by cimetidine was much greater in dogs with the Heidenhain pouch than in dogs with gastric fistula.

The present studies indicate that repeated injections of gastric stimulants into the muscle induce a stable acid secretion in conscious Beagle dogs. These results appear to be almost the same as those seen with a continuous intravenous infusion of the corresponding stimulants reported by other workers (2–5). For example, Grossman & Konturek (2) found that the doses of 160 \( \mu g/\) kg/hr for histamine 2HCl and 8 \( \mu g/\) kg/hr for pentagastrin were required to induce maximal responses in mongrel dogs with intravenous infusion. When the doses used in the present study were totaled per hour, the maximal acid output was produced in a dose of 160 \( \mu g/\) kg/hr for histamine 2HCl and 8 \( \mu g/\) kg/hr for tetragastrin. This similarity suggests that the i.m. administered stimulants are quickly absorbed, and accumulate in blood to enhance acid secretion. As expected, atropine sulfate 0.01 mg/kg markedly inhibited the tetragastrin stimulated acid secretion in all dogs with either the gastric fistula or the Heidenhain pouch. Hirschowitz and Sachs (5) have reported that atropine 0.08 mg/kg i.v. inhibited the acid secretion in response to histamine 1 mg/kg/hr in fistula prepared dogs. We confirmed herein these observations in Beagle dogs with the gastric fistula and the Heidenhain pouch. In contrast, Grossman & Konturek (2) reported that atropine sulfate, 0.1 mg/kg, had no influence on histamine stimulated acid secretion in mongrel dogs with both the gastric fistula and the Heidenhain pouch. Strain difference, different routes of administration of the stimulant and the inhibition might account for these discrepancies. We found that cimetidine inhibited the gastric acid secretion induced by two stimulants, in all dogs, dose-dependently. These findings are consistent with reports by other researchers (6) who used the infusion method in mongrel dogs. However, it was shown that atropine was a more profound inhibitor than cimetidine, at least against tetragastrin. In conclusion, the advantages of this model are, (a) the use of Beagle dogs is feasible for the study of gastric secretion, (b) the efficacy of antisecretory agents can be accurately evaluated.

REFERENCES

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