Suppressive Effect of Anticholinergic, Oxyphenonium Bromide, on Reserpine-Stimulated Gastric Secretion.* (24511)

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Relatively small doses of reserpine have been shown to act as a stimulant to gastric hydrochloric acid production(1,2). This effect has been observed both after oral and parenteral administration of the drug(3,4). Although the site of action of reserpine is unknown, its effect on gastric secretion may be attributable to an alteration of sympathetic-parasympathetic balance, resulting in parasympathetic predominance(5). If the parasympathetic effect is a function of dosage, as has been suggested(5), it may possibly be altered by administration of anticholinergic drugs. Studies in dogs have shown that increased secretion of hydrochloric acid induced by reserpine can be eliminated by subcutaneous administration of the anticholinergic drug, oxyphenonium bromide(6). For this reason, oxyphenonium bromide was chosen as the anticholinergic agent for this study.

Methods. Eleven healthy young adults, 22 to 38 years old, were selected. The investigation was divided into 3 study periods during which the drugs were administered orally in 4 equally divided doses daily as follows: The first study period consisted of 16 experiments on 11 subjects who recived oxyphenonium bromide daily for 7 days following a control period. In 11 experiments they were given 20 mg and in 5, 40 mg daily. Since there was no statistically significant difference between the 2 groups ($P>.5$) they were considered as one and listed in the second column in Fig. 1 as "oxyphenonium bromide 20 mg." The second group consisted of 8 subjects who, after a control period, received 0.5 mg of reserpine daily for 7 days. Following 2 weeks of rest they received for 7 days a combination of 0.5 mg of reserpine and 20 mg of oxyphenonium bromide daily. In the third group 7 subjects received .32 mg of reserpine daily for one week, rested for 2 weeks, and were then given a combination of .32 mg of reserpine and 20 mg of oxyphenonium bromide daily for another 7 days. These groups served as their own controls, and each period of drug administration was followed by a 2-week recovery period. Gastric contents of fasting subjects were aspirated during 4 consecutive 15-minute intervals prior to and on the final day of each period of drug administration. Gastric analyses were performed 2 hours after administration of reserpine and oxyphenonium bromide. This 2-hour interval was chosen to take advantage of the peak activity of these 2 agents. The action of reserpine on gastric acid production is apparent 60 to 90 minutes after oral administration and persists for 4 or more hours(3). With oxyphenonium bromide, a depression of gastric secretion occurs within 30 minutes of oral administration, and maximum effect persists from 1 to 5 hours(6,7). The free hydrochloric acid concentration and volume were measured and hourly production of free hydrochloric acid was calculated for each period.

Results (Fig. 1). The first 2 columns of the figure reveal that when 20 mg of oxyphenonium was administered, hourly production of free hydrochloric acid diminished significantly below control values ($P<.05$).

The next 3 columns in the figure reveal that when 0.5 mg of reserpine was given, free hydrochloric acid production increased significantly ($P<.08$), but when 20 mg of oxyphenonium bromide was added, hydrochloric acid production dropped significantly ($P<.02$). This drop in hydrochloric acid was even below control levels ($P<.05$).

Similar results were recorded in the last 3 columns of the figure. Free hydrochloric acid production rose significantly above control values after .32 mg of reserpine ($P<.05$) and

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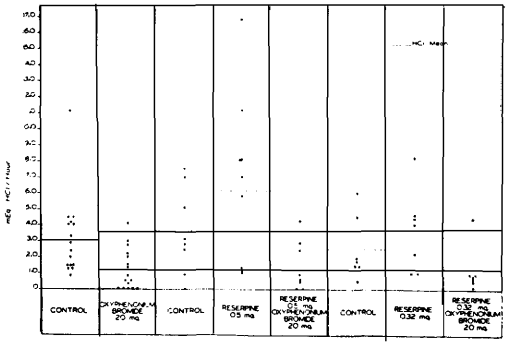

FIG. 1. Comparison of effects of orally administered reserpine and oxyphenonium bromide on human gastric secretion. • represent individual experiments.

dropped with a combination of .32 mg of reserpine and 20 mg of oxyphenonium ($P < .01$). Values obtained with this combination were found to be significantly lower than those of the controls ($P < .05$).

Discussion. Reserpine is believed to act centrally by altering the autonomic homeostatic mechanism(1). Its net effect can be explained on the basis of partial suppression of sympathetic activity at the hypothalamic level. The resultant parasympathetic predominance may explain the increased gastric secretion noted in reserpine-treated subjects. The observation that oxyphenonium bromide reduced gastric hydrochloric acid production in reserpine-treated subjects is in agreement with Plummer's study in dogs(1). The observation is further supported by a recent report from Krogsgaard, who was able to suppress reserpine-induced gastric hypersecretion by concomitant administration of oxyphenonium bromide in 2 of 5 patients who were given the drugs parenterally(8). Oxyphenonium bromide acts by blocking postganglionic cholinergic nerve transmission, and by blocking the impulses to the parietal cell may antagonize the effect of reserpine at the effector cell level(6).

No side effects were encountered with these agents, except for varying degrees of nasal stuffiness after larger dose of reserpine.

Summary. An anticholinergic drug, oxyphenonium bromide, (20 mg/day) was administered concomitantly with reserpine (.32 mg and .5 mg/day) to normal young adults. Addition of anticholinergic compound suppressed the rise in gastric free hydrochloric acid induced by administration of reserpine alone and reduced the gastric acidity below control levels in all instances.

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