Effect of cigarette smoking on human gastric secretory responses

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SUMMARY The effect of smoking three cigarettes over a one-hour period on the pentagastrin-stimulated submaximal plateau of acid and pepsin secretion was observed in 12 healthy human volunteers comprising men and women and smokers and non-smokers. No significant overall change in secretion was observed. In one subject, however, acid secretion was significantly inhibited (p < 0.01) and in one individual significant late stimulation (p < 0.01) of both acid and pepsin was observed.

It is widely held that cigarette smoking is harmful for patients with peptic ulcer disease. There is clinical evidence (Jamieson, Illingworth, and Scott, 1946; Doll, Jones, and Pygott, 1958) of an association between heavy cigarette smoking and peptic ulceration. Studies on the effect of smoking on human gastric secretion, however, have been inconclusive. Steigmann, Dolehide, and Kaminski (1954) showed a greater acid response to smoking in ulcer patients than in normal subjects. But Cooper and Knight (1956), in a study of duodenal ulcer patients found no significant difference in acid or pepsin secretion between those who smoked and those who refrained.

The purpose of this study was to determine the effect of smoking cigarettes on the pentagastrin-stimulated submaximal plateau of acid secretion in normal human subjects and thus provide a basis on which the secretory effect of cigarette smoking in peptic ulcer patients could be properly studied.

Methods

Subjects
Twelve healthy human volunteers with no gastrointestinal symptoms were studied. The age range was 21-56 years (mean 35 years). Six were regular smokers (mean age 44 years) and six were non-smokers (mean age 26 years); in both of these groups half were men (mean age 35 years) and half were women (mean age 36 years).

The subjects were fasted and smoking prohibited for at least eight hours before each test. No more than one test was performed each day on any one subject and no more than two tests during any one week. A radiopaque double-lumen nasogastric tube was passed and positioned fluoroscopically to lie in the most dependent portion of the stomach.

Procedure
The stomach was emptied and a 15-minute basal collection obtained before any experiment commenced. Gastric secretion was collected continuously throughout each experiment using low pressure suction and measured at intervals of 15 minutes.

A continuous intravenous infusion of 0.15 M sodium chloride (46 ml per hour) was given throughout each test by means of a Harvard infusion pump. Pentagastrin was added to the infusion in appropriate concentrations and replenishing of the infusing syringe arranged by means of a three-way stopcock.

Determinations
The volume of gastric juice in each 15-minute collection was measured. The concentration of acid was determined by titrating against 0.01 N sodium hydroxide using an automatic titrimer (Fisher Scientific Instruments). Outputs were calculated as m-equiv per 15-minute period. The concentration of pepsin was measured by a modification (Glass, Pugh, and Wolf, 1951) of the Anson-Mirsky method (Anson and Mirsky, 1932) using a spectrophotometer (Perkin-Elmer Model 124) and the result expressed as micrograms of tyrosine liberated from the haemoglobin substrate.

Experimental Design
First the maximum acid output in response to 6 μg/kg pentagastrin (Multicentre Study, 1969) was determined in each individual. A dose-response
study for pentagastrin was then obtained for each subject by administering 0.0005 μg/kg/min, 0.001 μg/kg/min, and 0.002 μg/kg/min intravenously during successive periods of one hour. From these data it was possible to calculate for each subject the dose of pentagastrin which, when given by continuous intravenous infusion, stimulated an acid secretion equal to approximately 50% of the maximum response. This selected dose was employed in every subsequent test in that individual to study the effect of smoking.

Next, eight control plateaux of acid secretion were obtained in six subjects in response to the selected dose of pentagastrin and maintained for two hours. A plateau was considered to have been achieved when three consecutive acid outputs over a 15-minute period varied by less than 15%. Such a plateau was achieved in most of these and subsequent tests within 90 minutes and in all by 120 minutes. Six studies in five subjects were abandoned because of failure to achieve an acceptable plateau within two hours.

Five smoking experiments were then performed in each volunteer. In these, as soon as the pentagastrin-stimulated plateau was achieved, the subject smoked three cigarettes (always of the same filter-tipped brand) over a period of one hour. In six tests nausea occurred in five subjects, and these tests were rejected. This left 54 tests for statistical analysis in all of which the volunteers were comfortable and relaxed.

The acid outputs of the 15-minute collections were expressed as percentages, taking the mean of the three plateau collections as 100%. The statistical significance of the difference between each 15-minute output after smoking and the mean control plateau response was calculated by Student's t test for paired values.

**Results**

**EFFECT OF SMOKING ON ACID SECRETION**

The results of 54 tests in 12 subjects are shown in Figure 1. The overall effect of smoking three cigarettes on the pentagastrin-stimulated submaximal acid plateau was negligible. However, when individual responses were examined, it was found that in one subject (A.E.) there was 30% inhibition of acid secretion (Fig. 2). This was statistically significant (p < 0.01) within 30 to 45
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Fig. 3. The output of acid in response to smoking in one human subject. Each point represents the mean of five studies. The mean plateau output of acid was 4.18 m-equiv/15 min (46% of the maximum response). The stimulation of acid was statistically significant (p < 0.01).

Fig. 4. Effect of smoking on pepsin output in normal subjects Each point represents the mean of 54 tests in 12 subjects. The value taken as 100% is the output during the plateau of acid secretion for the 30-minute period immediately before smoking. Control data are the mean of eight tests in six of the subjects.

Fig. 5. The output of pepsin in response to smoking in one human subject. Each point represents the mean of five tests. The mean output of pepsin before smoking was 1,323 units per half hour and was taken as 100%. The stimulation of pepsin was statistically significant (p < 0.01).
minutes and persisted for most of the remainder of the test. In one subject (K.H.) significant stimulation (p < 0.01) of acid output was observed, which occurred after the smoking hour, was maintained for the remainder of the test, and was of the order of 30% (Fig. 3).

**EFFECT OF SMOKING ON PEPsin SECRETION**

The data collected from 54 tests in 12 subjects are shown in Figure 4. In the analysis of these data the 30-minute pepsin outputs were expressed as percentages of the plateau level, which was taken as the mean of the last 30 minutes immediately before smoking. They were compared by Student’s t test for paired values in the same manner as the acid outputs. Again the overall effect of smoking was negligible. Although slight stimulation was detected in most experiments, this was statistically significant (p < 0.01) only in the subject (K.H.) who exhibited significant stimulation of acid secretion (Fig. 5). In this subject pepsin output reached 180% of the control level. It is interesting that the subject in whom acid secretion was inhibited produced no comparable pepsin response.

**Discussion**

This study has shown that smoking three cigarettes over a period of one hour has a negligible overall effect on human gastric secretion. It has also shown that some individuals experience a significant secretory response.

Gray (1929) studied 50 patients with duodenal ulcer and found an increase in acid secretion if they smoked on a fasting stomach or two hours after a test breakfast. Schnedorf and Ivy (1939) found a reduction in acid secretion in normal smokers in response to three or four cigarettes but no alteration in patients with peptic ulcer. In a study of hospital controls and peptic ulcer patients Steigmann et al. (1954) found a definite increase in gastric acidity from smoking one cigarette in a high percentage of cases. By contrast, Cooper and Knight (1956) in a study of 147 patients with duodenal ulcer found no change in the volume, pH, free acid or pepsin output of gastric juice in response to smoking two to three cigarettes.

The major criticisms of these studies were that the day-to-day variations in individual subjects were uncontrolled: the effect of smoking was studied in the basal state and the subjects did not serve as their own controls. Our study has overcome all of these criticisms by studying the effect of smoking on the pentagastrin-stimulated submaximal plateau of acid secretion. These tests were repeated on five occasions in each of 12 subjects comprising men and women, smokers and non-smokers, and the results subjected to a highly critical statistical analysis.

From these results it appears unlikely that smoking might exert a harmful effect on the normal human stomach, unless the habit has a significant effect on some gastric function such as mucus production or motility, other than acid and pepsin secretion. However, this conclusion cannot be extended to the ulcer patient. Indeed the available evidence suggests that the peptic ulcer patient usually experiences stimulation of gastric secretion in response to smoking. Clearly these patients must now be studied utilizing the method which we have employed in normal human subjects.

The variable response to smoking in normal individuals appears to suggest that nicotine may be the factor responsible. Nicotine acts on the parasympathetic and sympathetic ganglia by first stimulating and then blocking transmission of nerve impulses. The response to this drug in any one individual could depend on the dominance of one or the other part of the autonomic system. A possible parasympathetic dominance in duodenal ulcer patients could explain the observed stimulation of acid secretion in response to cigarette smoking.

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**References**


