

Early dinner reduces nocturnal gastric acidity

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SUMMARY This study examines whether eating food at different times has differential effects on intragastric pH. Experiments were done in 23 healthy volunteers (12 men). Intragastric acidity was monitored by ambulatory 22 hour pH-metry. Composition of meals was standardised: breakfast and lunch at 7 am and 12 noon respectively, and dinner at 6 or 9 pm, in random order. The time of going to bed and getting up was also standardised. With early dinner nocturnal pH was higher, than with late dinner (pH median: 1.67 and 1.39, $p < 0.001$). During the remaining time periods, pH values were similar. Thus early dinner may be helpful in conditions where low intragastric acidity is desirable.

In the past, there have been numerous attempts to raise intragastric pH by dietary means.¹⁻⁵ Many of these attempts have failed because food buffers are, at the same time, strong stimulants of gastric secretion.^{6,7} The intake of a protein meal may, by its buffer effect, raise gastric acidity, but this increase is followed by the fall of the pH as a result of stimulation of acid secretion (submitted data).⁸

In the present study we have examined whether different times of intake of meals of identical composition have differential effects on intragastric pH. We have previously observed that, after dinner, intragastric pH first falls to low values and then rises after midnight.⁹⁻¹³ We tested the hypothesis that the early administration of dinner would augment this effect. In order to examine this question we used intragastric pH-metry.¹⁰

Methods

SUBJECTS

The experiments were performed in 23 healthy volunteers (12 men, 11 women, mean age 24, range 19 to 32). Four subjects were smokers. During the study day smoking was not allowed. None of the volunteers had a history of gastrointestinal diseases

or was taking any medication. Informed consent was given. The trial was approved by the local Ethics Committee.

STUDY DESIGN

The volunteers underwent two 22 hour tests at least one week apart. Dinner was given at either 6 pm or 9 pm in random order. Thirteen subjects took dinner first at 6 pm and 10 first at 9 pm, respectively.

TIME COURSE OF A pH-METRY

On the study day, the volunteers started to fast at 12 am and were admitted to the laboratory at 4 pm. They spent the next 15 hours in the hospital but were fully ambulatory. An electrode was introduced through an anaesthetised nostril (lidocaine gel) and positioned in the gastric corpus under fluoroscopic control. The electrode cable was fixed to the skin of the cheek and connected to a data logger which was carried in a bag. Measurements began at 5 pm.

Meals were standardised. Composition and energy contents are given in the Table. Dinner was eaten in the laboratory. The subjects went to bed at 11 pm and rose at 6.45 am. Breakfast was at 7 am. At 8 am, the subjects left the hospital and followed their usual daily activities. Lunch was at 12 am. No food was allowed between the three meals. Alcoholic beverages and smoking were forbidden during the test. Tap water was allowed *ad libitum*. The subjects noted in a diary card the time and quantity of intake

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Table Composition of meals, time of intake and energy contents of standard meals

Dinner 6 pm or 9 pm 2436 kJoule	100 g bread+20 g butter 40 g cheese 30 g ham
Breakfast 7 am 2752 kJoule	100 g bread+20 g butter 1 egg 180 g yoghurt
Lunch 12 am 2548 kJoule	100 g bread+20 g butter 40 g cheese 30 g ham 100 ml soup
Total energy content	7736 kJoule

of tap water and events such as pain or nausea. They also recorded their daily activities. At 4 pm the volunteers returned to the hospital and the pH-electrode was removed after radiological control of its position.

pH-MONITORING AND RECORDING

pH-monitoring was performed according to the recommendations of a recent meeting about technical aspects of intraluminal pH-metry.¹⁴ A miniaturised bipolar glass electrode with a combined reference electrode (model 440-M4, Dr Ingold AG, Urdorf, Switzerland) was used. The diameter of the electrode was 4 mm. It was mounted on a polyvinyl tube with an outer diameter of 3 mm. The reference electrode was situated 3 cm proximally to the glass electrode.

At the beginning of the test, the glass electrode was connected to a microprocessor equipped transportable data logger with a memory capacity of 64K byte which was used as recorder (LZ105, Kaufhold, Berlin, West Germany).

After calibration at room temperature using commercial buffer solutions with a pH of 7.40 and 1.10 (Radiometer type S1356 and S1386, Copenhagen, Denmark), the glass electrode was introduced into the stomach of the volunteer. During the 22 hour measurement, intragastric acidity was recorded continuously with a frequency of 0.5 Herz (39 600 values recorded for 22 hours) and stored as mV. At the end of the test, a calibration with the same buffers was performed again.

EVALUATION OF DATA

The data logger stored mV values. After the end of the experiment, the logger was connected to a computer (Euromak, Kaufhold, Berlin, West Germany) and the data were transferred to a floppy disk. The two calibrations allowed the program to determine drift and slope of the electrode; when the 22 hour drift was lower than 0.3 pH units, it was corrected assuming linear drift. A drift greater than

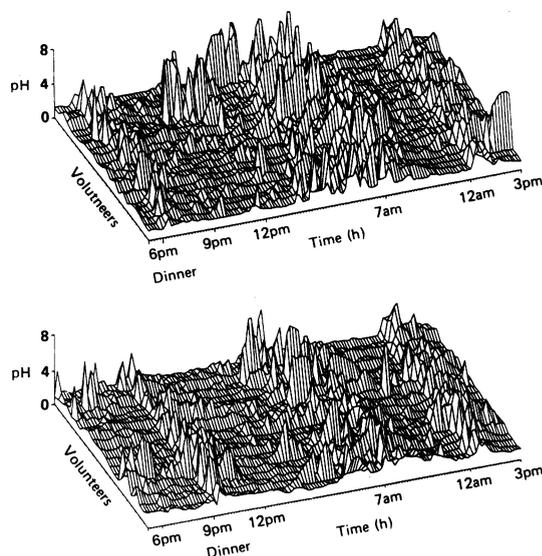


Fig. 1 Individual pH curves of 23 volunteers. Upper panel: dinner at 6 pm, lower panel: dinner at 9 pm.

0.3 pH unit was never observed. The program converted each stored mV value into a pH value. As calibrations were made at room temperature, the program performed temperature corrections when converting mV values to pH values.

PRESENTATION OF DATA AND STATISTICS

From individual raw pH values pH curves were calculated as follows: in each individual pH-metry the median pH values of 300 subsequent pH values (corresponding to a 10 minute interval) were calculated. pH curves using these medians were presented in two different and complementary ways: (a) means of the 23 curves was calculated and displayed as a function of time (b) 46 individual pH curves in a tridimensional design.

For statistical analysis, medians were calculated from 5 pm to 6 pm, from 6 pm to 9 pm, from 9 pm to 12 pm, from 12 pm to 3 am, from 3 am to 7 am, from 12 pm to 7 am, and from 7 am to 12 am. Differences were evaluated using the non-parametric Wilcoxon's matched pair test. Medians were chosen for statistical analysis because pH values are not normally distributed. Thus medians are appropriate measures of the centre.

Results

All volunteers tolerated the procedure well, none reported side effects such as pain and nausea, and all slept without interruption between 12 pm and 6 am.

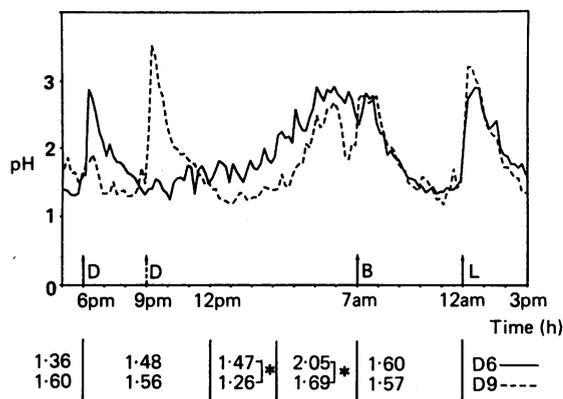


Fig. 2 Mean pH curves of 23 volunteers. Solid curve: dinner at 6 pm (D6), dotted curve: dinner at 9 pm (D9). D=dinner; B=breakfast; L=lunch. Median pH values within predefined time segments are given below the curves. *= $p < 0.02$.

Individual pH curves are shown in Figure 1. In each case, the typical food related circadian rhythm of pH was observed (Fig. 1).

Mean pH curves are shown in Figure 2. Median pH values in predefined time segments are given below the curves. Both in time period from 5 pm to 6 pm and from 6 pm to midnight median pH values were similar when dinner was taken at 6 pm or 9 pm. pH returned to acid values (1.43 after dinner at 6 pm, 1.26 after dinner at 9 pm, $p > 0.1$) for about three hours after the meal. After midnight, however, pH was higher after dinner at 6 pm than after dinner at 9 pm. In the time period from 7 am to 12 am median pH values were again similar (Fig. 2).

Inter-individual variability of pH was high, but intra-individual variability was low. Subjects who had high nocturnal acidity in one test also had high acidity in the other test and *vice versa* (Fig. 3).

Discussion

The pH profiles obtained in the present study are similar to those observed in our previous studies.⁹⁻¹¹ Thus, dinner leads to a short lasting increase of the pH values; pH then drops during three to four hours and rises during the remainder of the night. When the subjects get up from bed in the morning, pH drops even before breakfast. A precipitous drop is observed after breakfast, independent of the time of dinner. Lunch raises the pH from the late morning low. Thus, meals appear to be the main determinants of circadian pH changes. This is corroborated by the observation of others that intragastric pH changes little in subjects who either fast or get continuous,

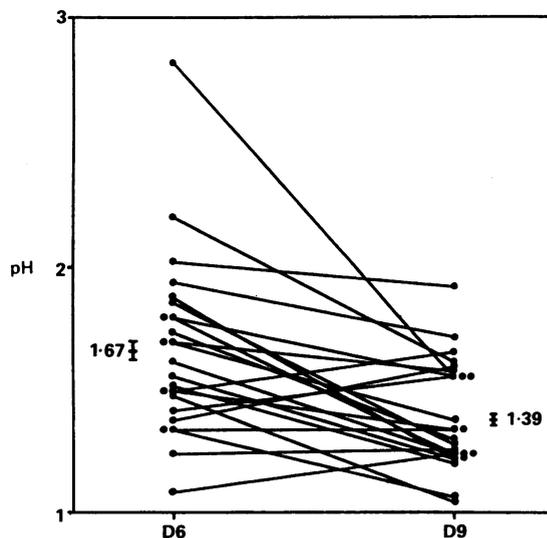


Fig. 3 Median pH values for the time period from midnight to 7 am after D6 (dinner at 6 pm) and after D9 (dinner at 9 pm). Means (\pm SD) are significantly different from each other ($p < 0.001$).

enteral or parenteral nutrition.¹⁵⁻¹⁷ Along the same line, there is no circadian rhythm of gastrin in fasting subjects; serum gastrin concentrations are closely related to the intake of the meals. There are high concentrations after each meal and low concentrations during the night.¹⁸⁻²¹

The data of the present study confirm the hypothesis that an early dinner prolongs the phase of long nocturnal high intragastric pH. Thus, with early dinner pH is higher during the second part of the night than with late dinner. The two graphs shown in Figure 1 illustrate this fact: after early dinner, high pH values occur earlier and are higher during the night than after late dinner. No statistically significant differences were observed in the evening and after breakfast when early and late dinner were compared (Fig. 2).

The data also show a good intra-individual reproducibility of the data; subjects who have a high nocturnal pH with dinner at 9 pm have an even lower acidity with dinner at 6 pm and *vice versa* (Fig. 3).

The mechanism by which an early meal raises nocturnal intragastric pH remains to be elucidated. We propose the following hypothesis. There is a typical time sequence of the effect of a meal on gastric functions. Maximal acid output occurs one hour after the meal. Thereafter acidity decreases in parallel to gastric emptying. Serum gastrin concentration, acid output and pH values are closely related.²² Four hours after a meal the stomach is almost empty but

acid output is still three times higher than basal.²³ It is estimated that meal stimulation of acid secretion ceases approximately seven hours after eating.²⁴ This is confirmed by our observation that approximately four to eight hours after a meal intragastric pH starts to rise from low values.^{25,26} The higher nocturnal pH values after an early dinner could simply signify that postprandial stimulation of gastric secretion ceases just in time as not to interfere with the nocturnal rise of pH, while a late dinner would produce such an interference and prevent the nocturnal rise. In addition, gastric emptying after late dinner might be slower than after early dinner;²⁷ this could contribute to the more prolonged meal stimulated acid secretion during the night.

It is uncertain whether the nocturnal rise of intragastric pH simply reflects lack of stimulation of acid secretion or whether in addition sleep plays a role. It is likely that sleep affects gastric acidity but the type of this effect is controversial.^{9,13,28-31} In this context it is of importance that intragastric pH-metry does not interfere with sleep.

In addition, a low diameter intragastric probe does not affect gastric secretion, gastric emptying and duodenogastric reflux.³² Previous studies examining the effect of meals on gastric acidity^{33,37} were invasive; their interpretation is therefore difficult.

As early dinner raises intragastric pH during the night and as nocturnal pH is a main determinant of ulcer healing,^{38,39} it is suggested that the time of dinner should be examined in controlled clinical trials involving patients with duodenal and gastric ulcer. When the aim of treatment is to obtain a high intragastric pH, the patients might profit from taking early dinner.

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