Letters

Intragastic acidity and serum gastrin after sufdotidine

Sir,—The recent paper by Smith and Pounder (Gut 1990; 31: 291–3) shows that the new competitive H₂ receptor antagonist sufdotidine, taken in doses of 600 mg b.d., induces virtually 24 hour gastric acidity. Thus its antisecretory effect closely resembles that of the proton pump inhibitor omeprazol.¹

The study, however, is not without relevant methodological problems.

(1) The gastric circadian acidity pattern is characterised by high frequency real pH fluctuations both in basal conditions and during drug induced events. These changes can be properly described with a scanning rate equal to or lower than one point per minute.²

The hourly sampling rate is inappropriate to represent what is happening to gastric acidity in time-dependent metabolic events and the usual acidity indexes calculated from these low frequency acquired pH profiles are almost invariably unreliable.³

(2) The trapezoidal rule is a fairly robust way of calculating integrals of functions that are not very smooth, provided that the increment is several times lower than the duration of the shortest fluctuation of the function to be integrated.⁴ Since the circadian pH profile shows many rapid pH fluctuations² the one hour step does not allow the use of this numerical integration method.

(3) The experimental data not included in their paper for 10:00 and 20:00 hours in duodenal ulcer patients. Their main clinical remission, cannot be replaced with datapoints obtained in normal subjects. More important, acidity measurements pertaining to healthy subjects are unlikely to correspond to those achieved with a very powerful H₂ receptor antagonist, such as sufdotidine. Moreover, since the integral of equally spaced series of data reflects the arithmetic mean, this replacement is simply useless.⁵

(4) The authors state that the significance of the difference between the integrated 24 hour values were assessed using Wilcoxon’s matched pair signed rank test. Even in an ideal case in which all the after treatment values are lower or higher than the before treatment values, by definition a test of this type cannot provide a probability level lower than 2, k being the number of couples.⁶

With a sample size of k = 7, as that studied by Smith and Pounder, the minimum p value one can obtain is 2(1/128) = 0.008. Therefore, the authors could not have found a probability level lower than 0.001. Moreover, since in one of the seven cases the measured diurnal integral did not increase, it is incorrect to report a p value of less than 0.001.⁷

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Reply

Sir,—We reject three out of four of Mela et al’s criticisms.

(1) Twenty four hour intragastric acidity can be measured by either aspiration or the use of an intragastric probe. We have used the former method for the last 16 years,¹ and it has the advantage that aspiration is extremely reproducible,² and has produced reliable estimates of the effect of a range of antisecretory drug regimens,³ The use of a pH probe results in such an avalanche of data that Savarino and Mela have concluded that the “hourly” sampling is continuous intraluminal monitoring and those of simultaneous gastric aspiration appeared to be better correlated if the elimination of noise disturbing the in vivo pH-metry curves is obtained.⁴

(2) The use of the trapezoidal rule is another type of “smoothing” — certainly the integration of observed values of either acidity or gastrin provides an easily understood measure of individual 24 hour responses.

(3) The samples for 10:00 and 20:00 hours were not aspirated, because they occurred immediately after a main meal and oral dosing with either sufdotidine or placebo. We did not want to remove any active drug from the stomach. We know that intragastric acidity in either patients or healthy subjects is overwhelmed at these times by food buffer (see the similar value for 14:00 hours in the same experiments). The substituted values tend to underestimate the antisecretory effect of sufdotidine.

(4) The results of dosing with sufdotidine 600 mg b.d. to show that statistical analysis is almost superfluous, although we agree that the p values in Figures 2 and 4 are incorrect, and should be <0.01 and <0.05, respectively. A wide range of techniques can be used for the mathematical and statistical analysis of 24 hour data. We believe that the advantages of our technique are that it is simple to perform and the mathematical presentation produces a clear result — some statisticians tend to overinterpret 24 hour data.

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