

*Gut*, 1974, 15, 462-467

# The effect of metoclopramide<sup>1</sup> on gastric emptying of solid meals

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**SUMMARY** The effect of metoclopramide has been studied on the emptying of solid meals labelled with <sup>51</sup>Cr and monitored with a gamma camera.

Metoclopramide, 10 mg iv or a dummy injection, was given randomly and double blind to 10 normal subjects and to 10 patients within three months of a truncal vagotomy and pyloroplasty. All were tested in the recumbent position.

Metoclopramide had no effect on emptying rates in the normal subjects nor in four postvagotomy patients who had emptying within the normal range ( $T_{\frac{1}{2}}$  30-150 min). In six patients with abnormally delayed emptying (mean  $T_{\frac{1}{2}}$  369 min) metoclopramide produced a significant improvement (mean  $T_{\frac{1}{2}}$  194 min,  $P < 0.01$ ).

The actions of metoclopramide in stimulating gastric peristalsis and speeding up gastric emptying were first described by Justin-Besançon, Grivaux, and Watterz (1964). The influence of metoclopramide on the rate of emptying of liquids from the stomach has been studied by several investigators. Connell and George (1969), using a dye dilution technique, found that metoclopramide accelerated gastric emptying and that it was most effective when emptying was delayed. This technique was also used by Howard and Sharp (1973) who showed that the delayed emptying of a fluid meal in women during labour was significantly accelerated by metoclopramide. The rate of gastric emptying during a barium meal was found to be increased by metoclopramide (James and Hume, 1968; Kreel, 1970). The effect of metoclopramide on the gastric emptying of solid meals has not been reported, so we describe here the results of a double-blind trial of metoclopramide (Primperan) in normal subjects and in patients with duodenal ulcer soon after truncal vagotomy and pyloroplasty. We chose this group of patients as they have been shown in a previous study to have a slow emptying rate compared with normal subjects when

lying supine (Cowley, Vernon, Jones, Glass, and Cox, 1972).

The gastric emptying rate was estimated by a modification of the gamma camera technique described by Jones, Clark, Kocak, Cox, and Glass (1970) using an isotopically labelled solid meal.

## Materials and Methods

Ten normal subjects and 10 patients who had recently undergone truncal vagotomy and pyloroplasty were tested on two occasions, once after metoclopramide 10 mg and once after normal saline each as 2 ml intravenously. The preparations were given in a random double-blind manner and the interval between them ranged from four to 40 days (mean 12 days) in the normal subjects and from two to 20 days (mean three days) in the patients. One post-vagotomy patient was examined three months after the operation with an interval of three weeks between the two injections, but in the remaining nine patients the first test was performed at a mean interval of 15 days after surgery.

## Measurement of Gastric Emptying

While sitting down, subjects and patients ate a standard meal consisting of half a cupful of instant porridge (Redibrek), 250 ml of milk, half of which

<sup>1</sup>Primperan (Berk Pharmaceuticals)

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Received for publication 15 March 1974.

was used to make up the porridge, one thick slice of lightly buttered bread and marmalade. Radioactive sodium chromate ( $200 \mu\text{Ci}$  in 2 ml saline solution) was stirred into the porridge during its preparation. After finishing the meal, the subject lay on a couch under the gamma camera which was positioned so that the stomach appeared in the centre of the field of an oscilloscope display. Recording by the camera was then started and at the same time the subject was given an intravenous injection of either metoclopramide 10 mg in 2 ml normal saline or the saline alone. Recording of the radioactivity from the stomach area was recorded continuously for 90 minutes. The gamma camera was connected on-line to a PDP 12 computer and the activity from the area viewed by the camera was continuously recorded on magnetic tape. During the recording Polaroid photographs of the oscilloscope display each of 20 000 counts were taken at 30-minute intervals for record purposes (fig 1). The radioactivity in the field recorded by the camera during the first five minutes was projected on a television screen and the stomach outline, which could be clearly seen, was delineated by means of a light writing pen (fig 2). The information was fed to the computer which was programmed to print out the total radioactivity count within the delineated area for each of the subsequent five-minute intervals. Background activity was calculated and subtracted from the total, so that a falling count rate at each five-minute interval was representative of the rate of gastric emptying of the isotopically labelled meal. In order to check that the subject's

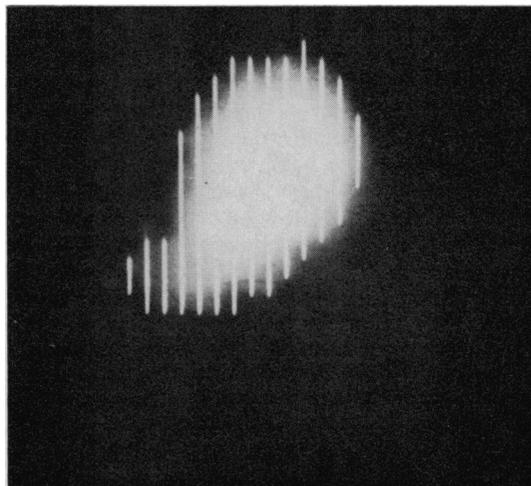


Fig 2 Gastric image shown on the television screen from integrated counts of the first five-minute recording period. Gastric outline marked with light pen.

stomach remained in the same position throughout the test period, pictures of the radioactivity were shown on the television screen at the end of each five minutes. In no test was the position of the stomach seen to alter significantly.

#### Analysis of Results

The results were expressed in two ways.

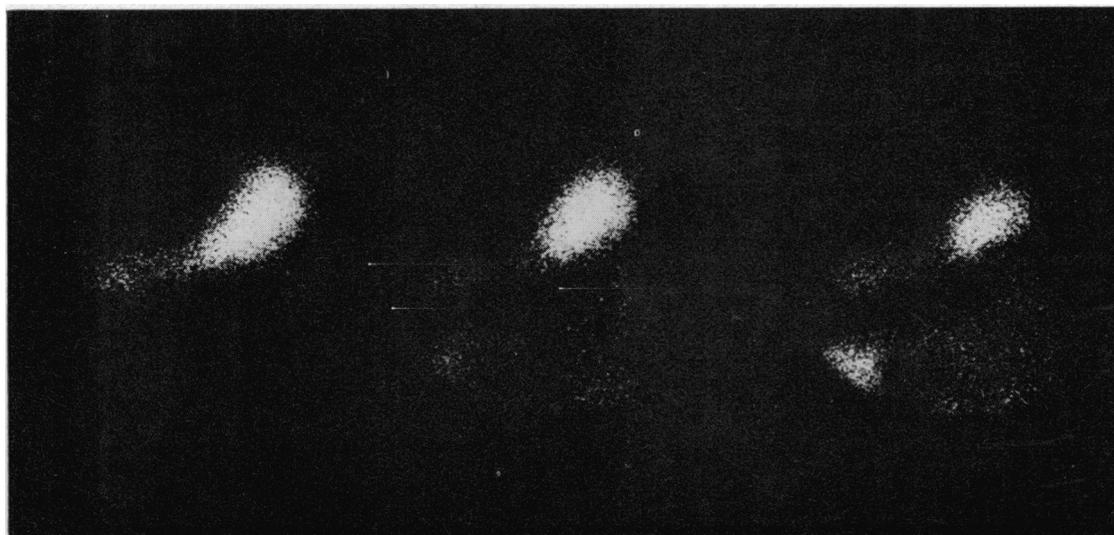


Fig 1 Normal pattern of gastric emptying seen on the oscilloscope display at five minutes, 35 minutes, and 65 minutes from the start of the recording.

1 The total radioactivity count in each five-minute period was calculated as a percentage of the initial five-minute count. Gastric emptying, expressed as this percentage, was calculated for convenience at 10-minute intervals for 90 minutes.

2 In order to compare the results with those of previous studies, the half emptying time ( $T_{1/2}$ ) was calculated in each subject from the regression line of the count rate plotted on a logarithmic scale against time on a linear scale. Although previous investigators had found that both liquid and solid meals appeared to empty exponentially, this was not always the case in the present study so that the function of  $T_{1/2}$  could be misleading. In fact, in only 33 of the total of 40 recordings could a mono-exponential pattern of emptying be assumed, and, in one extreme example, the calculated  $T_{1/2}$ s were identical after metoclopramide and saline injections, but when the percentage emptying in each 10-minute period was plotted, a marked difference in the emptying patterns became clear (fig 3).

**Results**

The time taken for normal subjects and postvago-

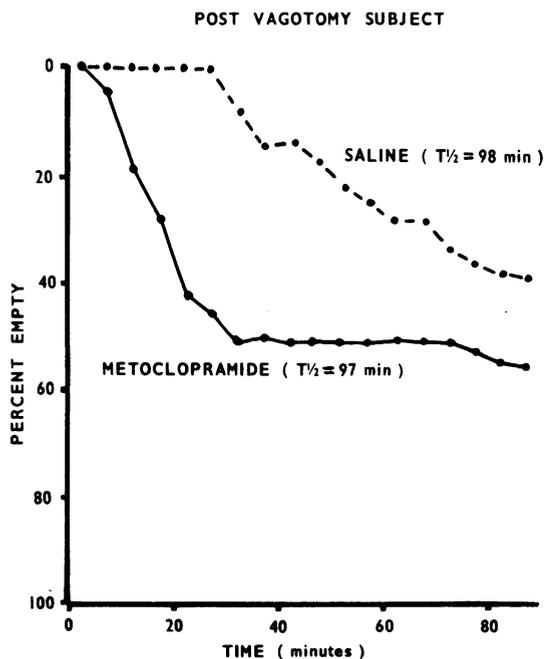


Fig 3 Percentage gastric emptying plotted against time in one subject shows a very different pattern of emptying with saline and metoclopramide. Calculated  $T_{1/2}$  was similar after both injections and was therefore very misleading.

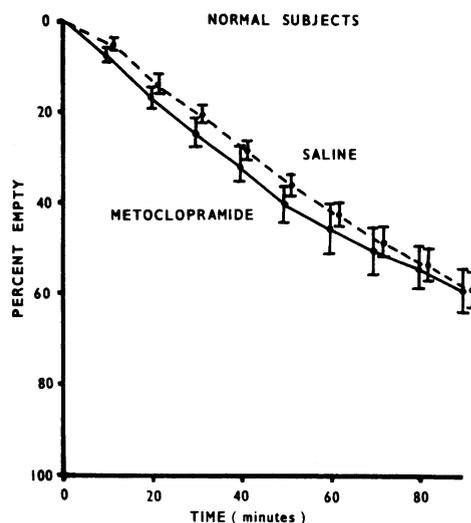


Fig 4 Percentage gastric emptying plotted against time in 10 normal subjects (mean  $\pm$  SEM).

tomy patients to complete the meal varied little, with a mean of 7.2 minutes for subjects and 9.3 minutes for patients.

**METOCLOPRAMIDE IN NORMAL SUBJECTS**

The mean percentage emptying at 10-minute intervals

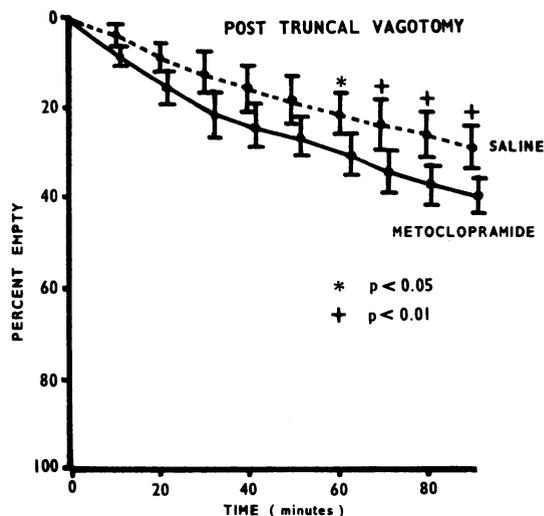


Fig 5 Percentage gastric emptying against time in 10 patients within three months of truncal vagotomy and pyloroplasty.

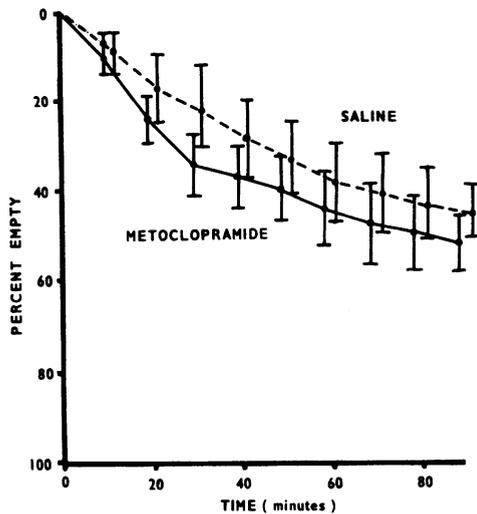


Fig 6 Percentage gastric emptying against time in four patients after truncal vagotomy and pyloroplasty with emptying times in the normal range.

in the 10 subjects is shown in figure 4. There was no significant difference between the metoclopramide and saline groups at any time. In one subject a  $T_{\frac{1}{2}}$  of 343 minutes after saline was reduced to only 78 minutes after the metoclopramide, but if these figures are excluded, the mean  $T_{\frac{1}{2}}$  values for the

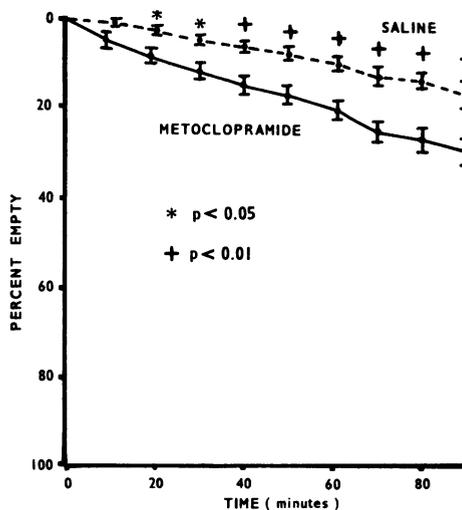


Fig 7 Percentage gastric emptying against time in six patients after truncal vagotomy and pyloroplasty with delayed emptying. The improvement with metoclopramide is clear.

remaining nine subjects were identical at 74.5 minutes after metoclopramide and 75.0 minutes after saline.

#### METOCLOPRAMIDE IN PATIENTS AFTER VAGOTOMY

The mean percentage emptying at each 10-minute interval in the 10 patients is shown in figure 5. The rate of emptying was greater after metoclopramide than saline at all times, the difference becoming statistically significant at 60 minutes ( $P < 0.05$ ) and thereafter more significantly ( $P < 0.01$ ). The mean  $T_{\frac{1}{2}}$  of 263 minutes after saline was significantly ( $P < 0.05$ ) reduced to 154 minutes by metoclopramide.

In view of the apparent inability of metoclopramide to speed up gastric emptying in the normal subjects, the observations in postvagotomy patients were separated according to whether gastric emptying was considered to be within the normal range ( $T_{\frac{1}{2}}$  30-150 minutes) or delayed. Thus metoclopra-

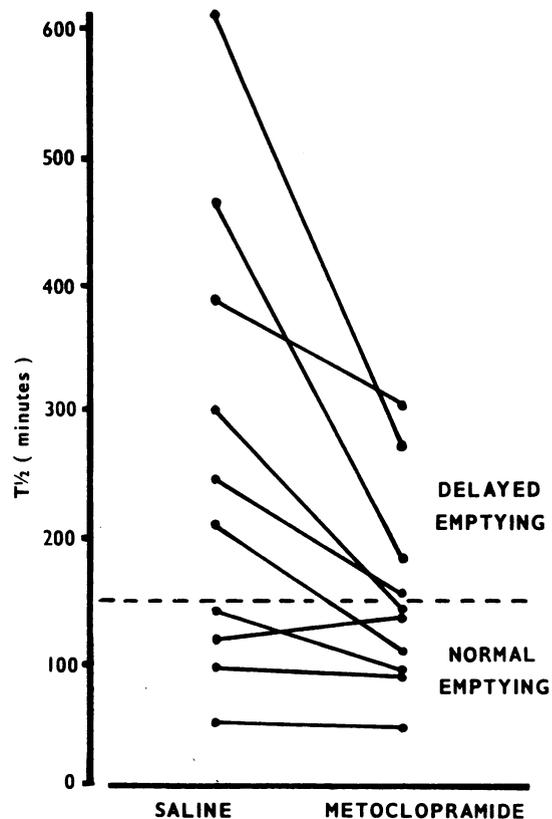


Fig 8 Gastric emptying with saline and metoclopramide in 10 postvagotomy patients expressed as  $T_{\frac{1}{2}}$ .

amide had no significant effect in four patients with emptying rates (fig 6), but in the six patients with delayed emptying the influence of metoclopramide was seen to be striking ( $P < 0.05$  at 20 minutes and  $< 0.01$  at 40 minutes and later) (fig 7). This difference is also clearly shown in fig 8 where the results before and after metoclopramide are expressed as  $T_{\frac{1}{2}}$ . The mean  $T_{\frac{1}{2}}$  of the six patients with delayed emptying before metoclopramide was 369 minutes and after the drug was 194 minutes ( $P < 0.01$ ).

### Discussion

The results of this study suggest that in subjects who have normal gastric emptying, the rate of emptying of solid meals is not affected by an intravenous injection of metoclopramide but the drug accelerates emptying when this is delayed. These findings are in agreement with those of Connell and George (1969) in their study of liquid meals and of Ramsbottom and Hunt (1970) who observed the effect of metoclopramide upon gastric emptying delayed by subemetic doses of apomorphine. Kennedy (1973) has observed the effect of metoclopramide 20 mg intravenously on the emptying of a water meal soon after vagotomy and found no improvement. Emptying of the water meal was not delayed in his patients and this may be why the drug had no effect. In the present series, the one healthy subject whose emptying time was grossly delayed, with a  $T_{\frac{1}{2}}$  well over twice the upper limit of normality observed in this and other laboratories (Griffith, Owen, Campbell, and Shields, 1968; Cowley *et al.*, 1972), gave a normal emptying time after metoclopramide, suggesting that the drug had been effective. In 10 patients who had undergone truncal vagotomy and pyloroplasty less than three months earlier, gastric emptying was considerably delayed in six but within normal limits in the remaining four. This finding is similar to that in a previous study in which six of 14 patients had normal emptying times two weeks after truncal vagotomy (Cowley *et al.*, 1972). In the present series metoclopramide halved the  $T_{\frac{1}{2}}$  of the patients with delayed emptying but had no apparent effect on those whose  $T_{\frac{1}{2}}$ s were already in the normal range.

The mechanism by which metoclopramide exerts its effect is not yet clear. Stadaas and Aune (1971) recorded intragastric pressure/volume relationships before and after vagotomy in 16 patients with duodenal ulcer and found that after vagotomy metoclopramide produced a marked elevation of the basal pressure, pressure peaks reappearing at the frequency of the normal stomach. These studies suggest that the stimulatory effect of metoclopramide upon gastric motility is not dependent upon the integrity of the vagus nerves. After vagotomy

well coordinated gastric motility disappears, with loss of adaptation to changes in gastric volume; metoclopramide apparently acts as a substitute for efferent vagal activity normally responsible for regulation of gastric motor function but lost by vagotomy. Intramural nerve plexuses may be an important part of the controlling mechanism for normal gastric peristalsis and these plexuses are present after vagal denervation. After vagotomy, peristaltic waves are recovered by metoclopramide but they remain insensitive to volume changes, suggesting that the drug may act on the intramural plexuses.

After vagotomy and pyloroplasty, the delay in gastric emptying which occurs in some patients does not appear to be related either to the completeness of vagotomy (Cowley *et al.*, 1972) or to the size or type of pyloroplasty (George, Royston, Cowley, and Spencer, 1973). Posture may be important, since McKelvey (1970) showed that liquids emptied more quickly after vagotomy when the patient was standing than when he lay on his left side. We have made similar observations with solid meals (Hancock, Bowen-Jones, Dixon, Testa, Dymock, and Cowley, 1974). It must be emphasized that in the present study all subjects were tested in the supine position throughout the observation period.

Although this delay in some patients has not been satisfactorily explained, it now seems likely that gastric emptying can be significantly accelerated by metoclopramide. Impaired emptying can lead frequently to distressing symptoms such as epigastric fullness and discomfort, nausea, and vomiting. The improved speed of emptying is presumably responsible for the relief of these symptoms produced by metoclopramide (Stadaas and Aune, 1972).

We would like to acknowledge the support of Berk Pharmaceuticals Limited in carrying out this study. We also wish to thank Professor B. Pullan for providing the facilities to record gastric emptying; Dr T. Testa for his advice, Mr Bell, consultant surgeon, Stepping Hill Hospital, for allowing us to study some of his patients; Professor R. A. Sellwood and Professor J. M. Evanson for their encouragement in the study.

### References

- Connell, A. M., and George, J. D. (1969). Effect of metoclopramide on gastric function in man. *Gut*, **10**, 678-680.
- Cowley, D. J., Vernon, P., Jones, T., Glass, H. I., and Cox, A. G. (1972). Gastric emptying of solid meals after truncal vagotomy and pyloroplasty in human subjects. *Gut*, **13**, 176-181.
- George, W. D., Royston, C. R., Cowley, D. J., and Spencer, J. (1973). Gastric emptying of a solid meal after long and short pyloroplasties. (Abstr.) *Brit. J. Surg.*, **60**, 307.
- Griffith, G. H., Owen, G. M., Campbell, H., and Shields, R. (1968). Gastric emptying in health and disease. *Gastroenterology*, **54**, 1-7.

- Hancock, B. D., Bowen-Jones, E. J., Dixon, R., Testa, H. T., Dymock, I. W., and Cowley, D. J. (1974) The effect of posture on gastric emptying of solid meals in normal subjects and patients after vagotomy (Abstr.) *J. Surg. Brit.*, **61**, 326.
- Howard, F. A., and Sharp, D. S. (1973). Effect of metoclopramide on gastric emptying during labour. *Brit. med. J.*, **1**, 446-448.
- James, W. B., and Hume, R. (1968). Action of metoclopramide on gastric emptying and small bowel transit time. *Gut*, **9**, 203-205.
- Jones, T., Clark, J. C., Kocak, N., Cox, A. G., and Glass, H. I. (1970). Measurement of gastric emptying using the scintillation camera and <sup>133</sup>Cs. *Brit. J. Radiol.*, **43**, 537-541.
- Justin-Besançon, L., Grivaux, M., and Wattez, E. (1964). L'épreuve au métoclopramide en radiologie digestive. *Bull. ;Soc. Med. Hôp.*, **115**, 721-726.
- Kennedy, T. (1973). Metoclopramide in the vagotomised stomach. I. Inman. *Postgrad. med. J.*, **49**, Suppl., 81-82.
- Kreel, K. (1970). The use of oral metoclopramide in the barium meal and follow through examination. *Brit. J. Radiol.*, **43**, 31-35.
- McKelvey, S. T. D. (1970). Gastric incontinence and post-vagotomy diarrhoea. *Brit. J. Surg.*, **57**, 741-747.
- Ramsbottom, N., and Hunt, J. N. (1970). Studies of the effect of metoclopramide and apomorphine on gastric emptying and secretion in man. *Gut*, **11**, 989-993.
- Stadaas, J., and Aune, S. (1971). The effect of metoclopramide on gastric motility before and after vagotomy in man. *Scand. J. Gastroent.*, **6**, 17-21.
- Stadaas, J., and Aune, S. (1972). Clinical trial of metoclopramide in postvagotomy gastric stasis. *Arch. Surg.*, **104**, 684-686.



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*Gut* 1974 15: 462-467  
doi: 10.1136/gut.15.6.462

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