EFFECTS OF THE ANTIEMETIC DRUG DOMPERIDONE ON THE RATE OF GASTRIC EMPTYING IN THE GUINEA-PIG

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Domperidone has been reported to increase the rate of gastric emptying in man (Reyntjens et al, 1978) although as yet its mechanism of action is undefined. We have investigated the effects of domperidone on guinea-pig isolated gastrointestinal tissue, (Ennis et al, 1978) and therefore it is necessary to confirm that domperidone has similar gastrokinetic properties in-vivo in the guinea-pig as it has in man.

Using an X-ray fluoroscopic technique we measured the rate of gastric emptying of 25 barium pellets orally fed to the guinea-pig after pretreatment with domperidone or metoclopramide. We have shown that metoclopramide (5mg kg^{-1} s.c.) administered at the time of feeding produced a significant increase in the rate of gastric emptying in the second hour after feeding. Therefore comparisons of drug effects were made during this time period. This effect of metoclopramide was not dose related since doses of 1mg kg^{-1} and 10mg kg^{-1} did not significantly alter the rate of gastric emptying from saline pretreated controls. Similarly domperidone (5mg kg^{-1} s.c.) produced a significant increase in the rate of gastric emptying ($p<0.01$) whilst doses of 1mg kg^{-1} and 10mg kg^{-1} were ineffective. See Table 1.

Table 1. Effect of drug pretreatment on the rate of gastric emptying in the guinea-pig during the second hour after feeding

Drug	Mean % ± s.e. of pellets leaving stomach
Saline	14 ± 4
Domperidone (5mg kg^{-1})	44 ± 12**
Metoclopramide (5mg kg^{-1})	52 ± 12**
Apomorphine (0.13mg kg^{-1})	7 ± 3*
Domperidone (5mg kg^{-1}) + Apomorphine (0.13mg kg^{-1})	1.2 ± 0.8*
Metoclopramide (5mg kg^{-1}) + Apomorphine (0.13mg kg^{-1})	16 ± 11

Significantly different from control *$p<0.05$, ** $p<0.01$, Mann Whitney U test, 2 tailed.

Apomorphine (0.13mg kg^{-1} s.c.) produced a significant decrease in the rate of gastric emptying ($p<0.05$) in the hour following the injection. Pretreatment with metoclopramide (5mg kg^{-1}) at the time of feeding followed one hour later by apomorphine (0.13mg kg^{-1}) prevented the response to apomorphine whereas pretreatment with domperidone (5mg kg^{-1}) was ineffective.

Thus we have shown that domperidone does increase the rate of gastric emptying in the guinea-pig as it does in man. Both domperidone and metoclopramide which increase gastric emptying are both dopamine antagonists (Reyntjens et al, 1978; Peringer et al, 1976). The only difference between these compounds is that domperidone does not readily cross the blood brain barrier. Thus since only metoclopramide could prevent the slowing effect of apomorphine it is possible that this effect of apomorphine may be mediated through central dopamine receptors.

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