Cisapride (R 51 619, Janssen Pharmaceutica) is a gastrointestinal prokinetic drug currently undergoing clinical trials. It is a derivative of cis-4-amino-3-methoxypiperidine and has many properties that may be of interest to the anaesthetist.

Cisapride increases lower oesophageal sphincter (LOS) pressure in both conscious volunteers and patients [1, 2]. It increases the rate of gastric emptying [3] and reverses the morphine-induced delay in gastric emptying in patients before anaesthesia [4, 5]. However, the rate of production and composition of gastric secretions are not affected by cisapride [6]. The drug also increases the motility of both the small and large intestines [7, 8].

There are several pharmacological differences between cisapride and the presently available gastrointestinal prokinetic agents metoclopramide and domperidone. Unlike these agents, cisapride has no anti-dopaminergic properties [9]. Consequently, extrapyramidal side-effects, a frequent problem with metoclopramide [10], have not been reported. Animal studies have shown that cisapride acts predominantly by enhancing the release of acetylcholine from the nerve endings in the myenteric plexus in the wall of the gastrointestinal tract [11]. The reversal of morphine-induced delay in gastric emptying by cisapride is of considerable interest, and the action of cisapride in this respect has been compared directly with metoclopramide in patients before surgery [5]. In this study, it was shown that cisapride was considerably more effective than metoclopramide. Finally, unlike metoclopramide and domperidone, cisapride enhances large bowel motility [8].

Cisapride has been administered by mouth, i.m., i.v. and rectally. The bioavailability of oral cisapride is 40–50% because of first-pass metabolism, with peak concentrations in the plasma at 1–2 h and an elimination half-life of 7–10 h in healthy subjects [12]. Absorption after i.m. administration is rapid and reliable [4]. An improved rectal formulation has been developed more recently. This cyclodextrine-based suppository is absorbed rapidly and therapeutic concentrations are maintained for at least 9 h [13].

The principal uses for cisapride are likely to be in the treatment of reflux oesophagitis [14], syndromes of delayed gastric emptying [15], intestinal pseudo-obstruction [16], functional post-prandial dyspepsia [17] and constipation [18]. What, therefore, is the potential for cisapride in anaesthetic practice?

The results of an important study of the possible use of cisapride in anaesthesia are published in this issue of the British Journal of Anaesthesia [19]. This study has investigated the effect of cisapride on LOS pressure when it was given before antagonism of neuromuscular blockade with atropine and neostigmine. Cisapride increased LOS pressure significantly before antagonism, but failed to prevent the decrease in LOS pressure after administration of atropine and neostigmine. These results are disappointing, as Corazziari and colleagues [20] found that cisapride increased oesophageal motility and LOS pressure in patients with oesophageal reflux and that atropine reversed the effects on peristalsis but had no effect on the increased LOS pressure. However, the patients in this study were not under anaesthesia. Cisapride may be useful, therefore, before induction of anaesthesia, especially in patients with reflux oesophagitis, but it has now been demonstrated that it will not be effective after antagonism of neuromuscular blockade with atropine and neostigmine [19].

It has been established that cisapride prevents
the delay in gastric emptying caused by morphine [4, 5]. Cisapride seems to be unique in this respect. There have been no reported studies on the delay in gastric emptying produced by other opioids, but it would be surprising if cisapride did not have the same effect. The inhalation of gastric contents is an important cause of anaesthetic mortality associated with surgery and obstetrics [21, 22] and the use of opioids before induction of anaesthesia probably makes inhalation more likely [23]. The preoperative use of cisapride, especially in emergency and obstetric anaesthesia, may well reduce the incidence of this complication. However, there are no data available at present on the effect of cisapride on the progress of labour and the condition of the neonate.

There is no current evidence of an effect on nausea and vomiting associated with anaesthesia. Postoperative gastric stasis may cause nausea and vomiting and it has been shown that cisapride is effective in the treatment of post-prandial nausea associated with gastroparesis [24]. The possible anti-emetic effect of cisapride is currently being investigated in animals. Gastric stasis may be an important cause of postoperative nausea and vomiting and cisapride may well be useful in this situation. However, this is only speculative, as clinical studies have not yet been performed.

The enhancement of gastrointestinal motility caused by cisapride may affect the absorption of drugs administered by mouth. For example, the rate of absorption of cimetidine and diazepam has been shown to be increased in patients receiving cisapride [12, 25]. This may be beneficial in the absorption of oral analgesics and studies are currently addressing this question, while others are examining the effect of cisapride on the absorption of oral paracetamol and opioids. Because of its effect on opioid-induced delay in gastric emptying, cisapride may be beneficial in the treatment of constipation caused by chronic opioid therapy. Studies investigating this problem are also in progress.

Gastrointestinal stasis is a common problem in patients in intensive therapy. There are no plans at the moment to investigate the use of cisapride in this situation, as the safety of a new drug should be established before it is used in the intensive therapy unit. Premature infants, intolerant of oral feeds associated with marked gastric stasis, have been treated successfully with cisapride [26].

Because of the adverse events associated with the i.v. administration of domperidone [27] and the peripheral vasodilating action of i.v. cisapride [25], caution is necessary in the use of the parenteral preparation of cisapride. It is recommended that parenteral cisapride should be given i.m.; if i.v. administration is essential, the drug should be given as a dilute solution slowly over 3 min [19]. At present, there are no plans to apply for a licence for the use of parenteral cisapride.

In conclusion, cisapride may well have a role to play in future anaesthetic practice, but considerably more investigation is needed. If cisapride is to be available for general use only as an oral preparation, its use in anaesthesia will be limited. However, the new rectal preparation is a promising development, as it may be a satisfactory method of administration of the drug in anaesthetic practice and the intensive therapy unit.

D. J. Rowbotham

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