GASTRIC EMPTYING AND DRUG ABSORPTION BEFORE SURGERY

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SUMMARY
The rate of paracetamol absorption following oral administration has been used as a model of drug absorption and as an indirect estimate of the rate of gastric emptying before and after elective or emergency surgery in 13 adult patients. The rates of paracetamol absorption before and after surgery were not significantly different and compared well with results obtained previously in normal volunteers. This suggests that preoperative anxiety and pain did not delay gastric emptying in this group of patients.

It has been accepted generally that gastric emptying is delayed by anxiety and pain (Kaufman, 1980). Thus, since patients awaiting surgery are frequently anxious (Norris and Baird, 1967) and, on occasions, in pain, it has been assumed that emptying of the stomach will be delayed and that this may interfere with the absorption of orally administered drugs and increase the risk of oesophageal regurgitation.

Most of the techniques available for the measurement of gastric emptying are unsuitable for use in patients awaiting operation. However, the rate of absorption of an orally administered drug that is not absorbed from the stomach can be used as an indirect index. Paracetamol is such a drug which, moreover, has the additional advantages that its plasma concentration can be measured accurately, and that its safety and familiarity make it acceptable to patients. The rate of its absorption after oral administration has been shown to correlate well with direct measurements of gastric emptying using isotope tracer techniques (Heading et al., 1973) and it has been used as an indirect index of gastric emptying in a number of clinical situations (Nimmo, 1976).

PATIENTS AND METHODS
Paracetamol absorption was studied in 13 patients (11 male) undergoing surgery under general anaesthesia. Ten patients (mean age 44.4 yr: range 22–64 yr) were undergoing minor elective procedures (repair of inguinal hernia or varicose vein surgery) and three patients (mean age 44.7 yr: range 19–70 yr) were undergoing emergency orthopaedic procedures for lower limb trauma (internal fixation of fracture, or débridement of wound).

Approval for these studies was obtained from the hospital Ethics Committee and all patients gave informed consent. They were free from any symptoms or history of gastrointestinal disease and were not in receipt of any medication. They had fasted for at least 4 h before the investigation. In each patient absorption was measured before surgery and then again shortly before discharge from hospital between 2 and 5 days after operation, so that each patient served as his own control. Approximately 3 h before surgery an indwelling venous cannula was inserted under local anaesthesia. After a baseline blood sample had been withdrawn paracetamol 1.5 g, in the form of three Panadol tablets, was administered with water 50 ml. Blood samples were taken at 15-min intervals for 90 min. Throughout this period the patients remained in a semi-recumbent position and refrained from smoking. Only after the last sample had been withdrawn was premedication administered. Anaesthesia and surgery were uneventful, and in all patients recovery was rapid and uncomplicated. Morphine 10 mg or pethidine 100 mg were given i.m. to provide analgesia in the postoperative period in some patients, but none received more than two doses. The study was repeated shortly before the patient's discharge from hospital. At this time no patient was nauseated or in pain and all had been receiving a normal hospital diet for at least 24 h. No analgesic had been given in the previous 24 h.

Concentrations of unchanged paracetamol in plasma were estimated by high performance liquid chromatography (Howie, Adriaenssens and Prescott, 1977). Paracetamol concentrations at each time interval after administration in the preoperative study were compared with the concentrations in
corresponding times in the postoperative study. The area under the plasma concentration–time curve from 0 to 60 min was calculated as a further index of paracetamol absorption. Since inspection of the data suggested that they did not follow a normal distribution, the non-parametric Wilcoxon rank pair test was used to assess the significance of the differences between the values before and after operation.

RESULTS

Absorption of paracetamol was similar before and after operation. There was a tendency for plasma paracetamol concentrations to be higher before operation, but the differences observed were small and none attained significance at the $P = 0.05$ level (table I, fig. 1). The area under the concentration–time curve up to 60 min was greater before surgery in nine of the 13 patients, but again this difference did not reach statistical significance. Before surgery the peak mean paracetamol concentration was $18.0 \pm 2.3$ (SEM) $\mu$g ml$^{-1}$ at 30 min compared with $15.4 \pm 2.9$ $\mu$g ml$^{-1}$ at 45 min in the postoperative study. Peak plasma concentrations were reached within 60 min in seven of the 13 patients both before and after surgery.

The small number in the group of patients undergoing emergency surgery did not allow the application of statistical methods. The results are shown in table II, and it can be seen that there was no evidence of delayed absorption in this group.

DISCUSSION

In these patients absorption of oral paracetamol was similar before and after elective and emergency surgery. The pattern of paracetamol absorption and the plasma concentrations obtained were almost identical to those observed in previous studies of normal volunteers in which the rate of gastric emptying was measured simultaneously (Clements et al., 1978). This would suggest that anxiety and pain before surgery do not cause any significant degree of slowing of gastric emptying.

<table>
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<tr>
<th>Table II. Paracetamol absorption before and after emergency surgery (mean values and range), n = 3</th>
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<tr>
<td>Plasma paracetamol concn (µg ml$^{-1}$) at time (min)</td>
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<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>Before op.</td>
</tr>
<tr>
<td>(3.9–20.3)</td>
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<tr>
<td>After op.</td>
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GASTRIC EMPTYING BEFORE SURGERY

No formal attempt to quantify anxiety was made in these patients, but all admitted to some anxiety when questioned before operation. In addition it was observed that venepuncture was more difficult, because of peripheral vasoconstriction, before operation than 2–5 days later. It has been shown that a majority of patients suffer some anxiety while awaiting operation (Norris and Baird, 1967) and there is no reason to suppose that our patients were exceptions to this rule.

Although anxiety has long been held to cause a delay in gastric emptying, there is little experimental evidence that this is so. Studies of patients with gastric fistula (Wolf and Wolff, 1947) showed that sudden surprise and fear caused a dramatic decrease in gastric motility, but that more chronic anxiety actually increased gastric secretory and motor activities. It seems probable that the anxiety preceding operation is of the chronic variety and may accelerate gastric activity. More recently, it has been shown that there is a direct relationship between neuroticism and the rate of diazepam absorption (Nakano, Ogawa and Kawatu, 1980), suggesting that anxiety may be associated with an increase in the rate of gastric emptying. On the other hand, paracetamol absorption and gastric emptying are slowed after the administration of adrenoreceptor agonists such as isoprenaline and salbutamol (Clark et al., 1980). However, plasma concentrations of catecholamines are not increased before operation (Butler et al., 1977) and it would appear that the sympathetic nervous system plays a relatively minor role in the control of gastric motility in this situation.

The effects of pain on gastrointestinal function have been little studied and interpretation of the results is complex. Gastric emptying has been shown to be delayed in dogs subjected to forelimb fractures (Zaricznyj et al., 1977) but most of these animals became shocked and hypotensive during the study. It seems probable that changes in splanchnic blood flow during the development of shock rather than the effects of pain were the main cause of delayed gastric emptying in this particular study.

In the present study, the three patients undergoing emergency surgery had painful but restricted injuries, without extensive tissue damage, and showed no sign of hypovolaemia or shock. All three had normal paracetamol absorption before and after surgery, which suggests that moderately severe pain has no effect on the rate of gastric emptying in adult patients.

These results provide no support for the widely held view that pain and anxiety cause significant slowing of gastric emptying before operation in adult patients with normal gastric function.

ACKNOWLEDGEMENTS

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REFERENCES


**LA VIDANGE GASTRIQUE ET L'ABSORPTION DE MEDICAMENTS AVANT LA CHIRURGIE**

**RESUME**

La vitesse d'absorption du paracetamol, après administration orale, a été utilisée comme modèle d'absorption médicamenteuse et comme stigmate indirect de la vitesse de vidange gastrique avant et après des actes chirurgicaux régis ou d'urgence chez 13 patients adultes. Les vitesses d'absorption du paracetamol, avant et après l'acte chirurgical, n'étaient pas significativement différentes entre elles et étaient tout à fait comparables aux résultats obtenus précédemment chez des volontaires normaux. Ceci suggère que l'anxiété et la douleur pré-opératoires ne retardent pas la vidange gastrique dans ce groupe de patients.

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**MAGENENTLEERUNG UND ABSORPTION VON MEDIKAMENTEN VOR DER OPERATION**

**ZUSAMMENFASSUNG**

Bei 13 erwachsenen Patienten wurde die Absorptionsgeschwindigkeit von Paracetamol nach oraler Gabe als Modell für Medikamentenabsorption und indirektes Maß für die Magenentleerung vor und nach elektiven oder Notfalloperationen verwandt. Die Absorptionsgeschwindigkeiten vor und nach Operationen unterschieden sich nicht signifikant voneinander und entsprachen gut den früher bei gesunden Probanden ermittelten Ergebnissen. Päraoperative Angst und Schmerzen scheinen die Magenentleerung bei dieser Patientengruppe nicht beeinflusst zu haben.

**VACIAMIENTO GASTRICO Y ABSORCION DE MEDICINA ANTES DE CIRUJIA**

**SUMARIO**

Se usó el ritmo de absorción del paracetamol por vía oral como modelo de absorción de medicina y como cifra estimativa indirecta del ritmo de vaciamiento gástrico antes y después de cirugía electiva o de emergencia en 13 pacientes adultos. Los ritmos de absorción del paracetamol antes y después de la cirugía no diferían de manera significativa y se comparaban bien con los resultados obtenidos previamente en voluntarios normales. Esto sugiere que la ansiedad y el dolor preoperatorios no demoraron el vaciamiento gástrico en este grupo de pacientes.