

The effect of spinal analgesia and surgery on peroperative drug absorption and gastric emptying in man

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Paracetamol 20 mg kg⁻¹ dissolved in 200 ml of water was given by mouth to seven patients undergoing minor orthopaedic surgery in spinal analgesia, and again 2 weeks later. The rate of paracetamol absorption was significantly delayed by spinal analgesia and surgery, indicating an inhibition of peroperative drug absorption and gastric emptying. The effect of spinal analgesia on gastric emptying was not able to normalize the delayed peroperative gastric emptying produced by surgery, and suggests that surgery is an important factor in peroperatively delayed gastric emptying.

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Spinal analgesia does not delay postoperative gastric emptying (1), and the patients are therefore able to drink and eat shortly after the operation. Furthermore, in comparison with general anaesthesia, spinal analgesia appears to decrease the loss of blood (2), the incidence of thromboembolic complications (3) and the metabolic stress response (4), presumably due to block of the sympathetic nervous system.

In the present study we investigated peroperative drug absorption and gastric emptying in patients undergoing minor orthopaedic surgery in spinal analgesia, using paracetamol absorption as an estimate of drug absorption and gastric emptying. Paracetamol like most drugs given by mouth, is normally not absorbed to any appreciable extent from the stomach, but is easily absorbed from the upper small intestine (5). In this way the rate of absorption of an oral paracetamol dose determines the rate of gastric emptying (6). Simultaneous measurements of paracetamol absorption and gastric emptying have confirmed measurements of the rate of paracetamol administered orally as a dependable expression of gastric emptying (7).

PATIENTS AND METHODS

The study was approved by the local Ethical Committee, and informed consent was obtained from each patient.

Seven men, otherwise healthy out-patients, age 20-51 years, body weight 55-88 kg and height 168-186 cm, undergoing minor surgery of the knee were studied.

Each patient was studied twice, the first time on the day of

operation and the second time 2 weeks later, so that each patient served as his own control. On each occasion they were investigated after an overnight fast. Fasting was continued until the end of the investigation.

On the day of operation, all patients were premedicated with diazepam 15 mg given orally together with 20 ml of water 1 h before surgery. Spinal analgesia was administered with a 22-gauge needle in the midline of the L₅-L₄ interspace with the patient in a sitting position. A single dose of 3.5-4.0 ml of bupivacaine 0.5% heavy was injected. All patients received an i.v. infusion of physiological saline (1-2 l) immediately before the injection to prevent a fall in blood pressure. Using an ethyl chloride swab, the spinal anaesthetic level was indicated by loss of cold sensation. The degree of pain during and after the operation was evaluated by means of a 4-point scale (no pain: 0, slight pain: 1, moderate pain: 2 and severe pain: 3). Symptoms of nausea and vomiting were recorded for each patient. Half an hour after establishment of spinal analgesia and immediately after the beginning of operation, the patients ingested paracetamol 20 mg kg⁻¹ with 200 ml of water. Venous blood samples were taken from an indwelling cannula before and 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, 240 and 300 min after paracetamol administration. Serum was separated and stored at -20°C until measurement of serum paracetamol concentration by high performance liquid chromatography was performed (8).

After 2 weeks, the control study was repeated. The patients remained at rest in bed in the recovery room in a supine position. The patients were premedicated with diazepam 15 mg orally, and given the same dose of paracetamol and water at the same time as on the operation day. Venous blood samples were taken at the same intervals as on the day of operation.

Paracetamol absorption was assessed from the plasma concentrations at each sampling time, the peak paracetamol concentration (C_{max}), the time to reach peak concentration (T_{max}), the area under the plasma concentration-time curve from 0 to 60 min (AUC-60) and the area under the plasma concentration-time curve from 0 to 120 min (AUC-120).

A paired Student's *t*-test was used; *P*-values less than 0.05 were considered statistically significant.

Table 1

Mean plasma paracetamol concentrations (\pm s.e. mean) and *P*-values (Student's *t*-test) and each sampling time on the operation day and again 2 weeks later. Patients received paracetamol 20 mg kg/body weight dissolved in 200 ml water.

	Mean plasma paracetamol concentrations ($\mu\text{g ml}^{-1}$)											
	15 min	30 min	45 min	60 min	75 min	90 min	105 min	120 min	150 min	180 min	240 min	300 min
Operation (<i>n</i> = 7)	2.6 \pm 0.9	6.6 \pm 1.1	8.3 \pm 0.8	9.4 \pm 1.1	9.8 \pm 0.7	10.4 \pm 0.9	11.1 \pm 1.1	10.1 \pm 1.0	8.8 \pm 0.9	7.9 \pm 0.9	5.5 \pm 0.8	4.7 \pm 0.8
Control (<i>n</i> = 7)	9.8 \pm 1.6	12.4 \pm 1.2	13.1 \pm 0.9	11.9 \pm 0.8	10.8 \pm 0.8	11.0 \pm 0.7	11.2 \pm 1.0	10.5 \pm 0.6	8.8 \pm 0.7	7.8 \pm 0.9	6.0 \pm 0.9	4.6 \pm 0.6
<i>P</i>	0.003	0.002	0.009	0.14	0.36	0.49	0.89	0.73	0.97	0.97	0.58	0.68

RESULTS

Both anaesthesia and operation were uneventful in all patients. The duration of the operation ranged from 35 to 85 min.

Cephalad extension of spinal analgesia had reached T₇₋₁₀ half an hour after ingestion of paracetamol, T₇₋₁₁ 1 h after, T_{10-L4} 2 h after and L_{3-S2} 3 h after.

One patient (no. 3) had a pain score of 1 point 1 h after ingestion of paracetamol and reached a maximum of 2 points 1 h later; pethidine 100 mg i.v. and supp. acetylate was therefore given. One patient (no. 7) had a pain score of 1 point for the first 3 h. Five patients had no pain at all.

The mean serum paracetamol concentrations measured from 15 to 45 min after spinal analgesia and operation differed significantly from control (*P* < 0.05). None of the values measured from 60 to 300 min differed significantly from control (Table 1).

After spinal analgesia and operation mean C_{max} was 12.3 \pm 0.6 $\mu\text{g ml}^{-1}$ (mean of 7 values \pm s.e. mean), mean T_{max} was 87.9 \pm 15.2 min, mean AUC-60 was 332 \pm 37 $\mu\text{g min ml}^{-1}$ and mean AUC-120 was 947 \pm 56 $\mu\text{g min ml}^{-1}$ (Table 2).

In the control study mean C_{max} was 14.7 \pm 1.1 $\mu\text{g ml}^{-1}$, mean T_{max} was 49.3 \pm 10.3 min, mean AUC-60

was 618 \pm 50 $\mu\text{g min ml}^{-1}$ and mean AUC-120 was 1280 \pm 69 $\mu\text{g min ml}^{-1}$.

Mean C_{max} after spinal analgesia and operation was not significantly different from control (*P* = 0.13). Mean T_{max}, AUC-60 and AUC-120 after spinal analgesia and operation were significantly different from control (*P* < 0.05).

DISCUSSION

Paracetamol absorption as a probe for gastric emptying has been demonstrated to correlate well with other methods used to estimate gastric emptying (7).

The rate of peroperative gastric emptying in man has never been measured. This study demonstrates that spinal analgesia and surgery were associated with delayed paracetamol absorption in patients undergoing minor orthopaedic surgery, indicating an inhibition of peroperative drug absorption and gastric emptying. Peroperative gastric emptying was moderately delayed in six patients and unaffected in one (no. 6).

Major surgery seems to delay gastric emptying (9, 10). The effect of spinal analgesia on the gastrointestinal tract is related to the extent of subarachnoid pre-ganglionic blockade of sympathetic B-fibres. Sym-

Table 2

The individual values of the peak serum paracetamol concentration (C_{max}), the time from administration of paracetamol to its peak concentration (T_{max}), the area under the plasma concentration-time curve from 0-60 min (AUC-60), the area under the plasma concentration-time curve from 0-120 min (AUC-120) and *P*-values on the operation day and again 2 weeks later.

Subject	C _{max} ($\mu\text{g ml}^{-1}$)		T _{max} (min)		AUC-60 ($\mu\text{g min}^{-1} \text{ml}^{-1}$)		AUC-120 ($\mu\text{g min}^{-1} \text{ml}^{-1}$)	
	Operation	Control	Operation	Control	Operation	Control	Operation	Control
	1	11.9	18.6	30	30	449	823	1058
2	13.1	12.4	105	45	273	527	851	1134
3	10.3	14.6	60	15	467	637	934	1226
4	10.0	15.1	150	45	191	675	665	1372
5	13.8	16.6	105	105	287	654	974	1524
6	13.2	9.8	60	60	351	399	1081	976
7	13.9	15.5	105	45	307	608	1065	1346
Mean \pm s.e. mean	12.3 \pm 0.6	14.7 \pm 1.1	87.9 \pm 15.2	49.3 \pm 10.7	332 \pm 37	618 \pm 50	947 \pm 56	1280 \pm 69
<i>P</i>	0.13		0.045		0.002		0.01	

pathetic nerves to the stomach serve to inhibit peristalsis and to contract the pylorus. It could be expected that spinal analgesia sufficiently high (T₅-T₁₁) to produce sympathetic block leading to increased peristalsis and relaxation of the pylorus could have normalized peroperatively delayed gastric emptying produced by minor surgery. This was apparently not the case. Our results could be explained by the fact that the extent of sympathetic blockade during spinal analgesia is less than the extent of analgesia and motor blockade (11).

Postoperative gastric emptying in patients undergoing minor orthopaedic surgery in spinal analgesia is not delayed (1), and therefore it appears that peroperative inhibition of gastric emptying is most likely due to factors other than spinal analgesia.

It is generally believed that stress, anxiety and pain delay gastric emptying. Our patients were studied twice under the same circumstances, so the contribution of stress and anxiety to the delay in gastric emptying should be reduced to a minimum.

Only two patients had slight pain peroperatively and it is therefore unlikely that pain was the reason for delay in gastric emptying. In fact, there seems to be no evidence to support the widely held belief that stress, anxiety and pain delay gastric emptying (10). The anaesthetic techniques included premedication with diazepam which has no effect on gastric emptying by diazepam *per se* (1, 12, 13, 14).

Opioid analgesic drugs are the major cause of delayed gastric emptying during the perioperative period (10). Our results show, as judged from the delay in paracetamol absorption, that surgery, also minor, is an important factor in peroperative delayed gastric emptying. The effect of spinal analgesia was not sufficient to normalize delayed peroperative gastric emptying.

Mean serum paracetamol concentrations measured postoperatively from 60 to 300 min were not significantly different from control and this seems to be in accordance with earlier studies which have shown that regional analgesia does not delay gastric emptying itself (1, 15, 16). As a consequence of delayed gastric emptying in patients undergoing minor surgery in regional analgesia, anorexia, nausea, vomiting, delayed absorption of drugs and so an increased risk of aspiration of gastric contents to the lungs may be expected peroperatively. It therefore seems advisable for patients to fast prior to surgery in regional analgesia.

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