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Forum

An evaluation of gastric emptying times in pregnancy and the puerperium

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Summary

In a controlled study, gastric emptying was measured during the three trimesters of pregnancy and after delivery, using an indirect paracetamol absorption technique. The peak plasma paracetamol concentration, time to reach the peak, and the area under the plasma paracetamol concentration–time curve, were determined. As compared to nonpregnant controls, there were no significant differences in the gastric emptying times of women in the three trimesters of pregnancy and of mothers from 18 h after delivery onwards. Gastric emptying was significantly delayed in mothers within 2 h after delivery ($p < 0.01$); median (range) values of peak paracetamol concentration, time to reach the peak and the area under the paracetamol concentration–time curve for this group were 12.5 (0.2–30.5) mg.l^{-1}, 120 (30–120) min and 3.8 (0.1–16.6) mg.l^{-1}.h respectively, and 20.8 (8.6–64.5) mg.l^{-1}, 40 (10–120) min and 13.5 (5.5–28.8) mg.l^{-1}.h respectively, for the nonpregnant control group ($p < 0.01$). Repeated measurements of gastric emptying in these women on the second postpartum day showed no significant delay.

Key words

Gastrointestinal tract; gastric emptying.
Complications; aspiration pneumonitis.
Anaesthesia; obstetric.

Although the incidence of the pulmonary 'acid aspiration' syndrome has declined in recent years it still contributes to maternal morbidity and mortality [1]. The risk of regurgitation and pulmonary acid aspiration is exacerbated by a low intragastric pH and a large residual gastric volume [2]. The latter is determined by oral intake, gastric secretion, and the rate of gastric emptying. Whilst the physiological changes in maternal gastric secretion [3] and pH [4] are well documented, there is confusion about how pregnancy affects gastric emptying.

It is now widely accepted that gastric emptying is markedly delayed when opioids are administered during labour [5–7]. The effects of pregnancy and labour *per se* on gastric emptying are less clear and studies to date have produced conflicting results. This may be partly related to differences in measurement techniques which have included radiological studies with radio-opaque meals [5, 8], fluoroscopic examinations [9, 10], dye dilution methods with single [11], or double [12] gastric sampling, solute absorption e.g. paracetamol [6, 12, 13], and more recently impedance techniques [14], real-time ultrasonography [15] and applied potential tomography [16, 17]. Further difficulty with the interpretation of the results may have arisen, in some cases, from the selection of small sample sizes which are unrepresentative of the obstetric population as a whole, and lack of control group measurements. Furthermore, few controlled studies have investigated gastric function in the puerperium. This lack of information has prompted many anaesthetists to remain wary of the risks of pulmonary aspiration of gastric contents, not only in the immediate postpartum period but often well into the puerperium [18].

The aim of this study was to evaluate gastric emptying times during the first, second, and third trimesters of pregnancy and also in the postpartum period.

Methods

After obtaining local ethics committee approval and informed written consent, gastric emptying times were measured in the following separate groups of women: group 1: nonpregnant controls of reproductive age; group 2: women in the first trimester of pregnancy (8–10 weeks gestation) scheduled for vaginal termination; group 3: women in the second trimester of pregnancy (16–24 weeks gestation); group 4: women in the middle to late third trimester of pregnancy (34+ weeks gestation) in whom a vaginal delivery was anticipated; and group 5: mothers within 2 h after a normal vaginal delivery. Women in group 4 were investigated prepartum (not in labour) and again on two occasions postpartum, either on day 1, between 18–24 h postdelivery (group 4a), or day 2, between 24–48 h postdelivery (group 4b), and also on day 5 (group 4c); women within 2 h after a normal vaginal delivery (group 5) were reassessed on the second postnatal day.

All females were healthy, with no history of gastrointestinal disease or drug ingestion which might affect gastric motility. Oral contraceptive usage (control group), multiple pregnancy and gross obesity were exclusion criteria. Gestational age of pregnancies in groups 3 and 4 was confirmed by ultrasonography.

Gastric emptying times were measured indirectly using a paracetamol absorption technique. The rate of paracetamol absorption after oral administration is determined by the rate of gastric emptying because the drug is not absorbed to any extent from the stomach but is rapidly absorbed from the small intestine [19].

After a minimum 4 h fast, paracetamol 1.5 g in tablet form, was taken orally with 50 ml of water. Venous blood samples were obtained from an indwelling intravenous

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cannula in the forearm at the following times: 0 (pre-paracetamol) and 10, 20, 30, 40, 50, 60, 90, and 120 min post-paracetamol ingestion. During the sampling period all subjects remained recumbent [20] and no other oral intake was permitted. Plasma samples were frozen at −20°C and paracetamol concentrations were determined using the Cambridge Life Sciences enzymatic assay kit. In this assay, paracetamol is hydrolysed by aryl acyl amidohydrolase to acetate and 4-aminophenol. The latter is then reacted with o-cresol in the presence of ammoniacal copper sulphate to give a blue indophenol dye which is measured colorimetrically. The paracetamol concentrations were measured against standards of 10, 20 and 50 $mg.l^{-1}$ and known quality controls were run with the test samples. Precision runs of 10 measurements each were performed on two sets of plasma samples.

Differences in paracetamol absorption were assessed by determining the maximum plasma paracetamol concentration (P_{max}), the time taken to reach this concentration (T_{max}), and the area under the concentration-time curve (AUC), for the 2 h sampling period. Statistical comparisons were made using the unpaired *t*-test, the Mann–Whitney *U*-test or the Wilcoxon matched-pairs signed-ranks test, as appropriate. A level of $p < 0.05$ was considered significant.

Results

The numbers of women in each group and the mean (SD) age and weight are shown in Table 1. As compared to the control group, the mean age of women in the first trimester of pregnancy (group 2) was significantly lower ($p < 0.01$) and the mean weight of women in the third trimester of pregnancy (group 4) was significantly greater ($p < 0.01$). The mean weight of the women in group 5 (who were first investigated within 2 h after delivery) was calculated from the prepartum third trimester weight and was significantly greater ($p < 0.01$) than that of the control group. These patients were not weighed after delivery prior to entering the study. There were no other significant differences between groups.

All patients in groups 1, 2 and 3 completed the study. Postpartum measurements were not performed in six women from group 4 who had been assessed during the third trimester of pregnancy but who subsequently underwent emergency Caesarean section, thus leaving 30 women for re-evaluation after delivery. Twelve women (group 4a) underwent measurement of gastric emptying on day 1 after delivery (between 18 and 24 h after delivery) and 18 (group 4b) on day 2 (between 24–48 h after delivery). Eight of these 30 women (group 4c) were re-evaluated on the 5th postpartum day. Seventeen women (group 5) had gastric emptying times first measured within 2 h of delivery; 12 of these were re-investigated on the second postnatal day.

Table 1. Demographic Data. Values are expressed as mean (SD).

Group	No. of patients	Age; years	Weight; kg
Control (1)	32	28.4 (4)	58.3 (4.8)
1st trimester (2)	18	24.2* (5.1)	59.4 (6.0)
2nd trimester (3)	10	29.5 (2.6)	62.0 (6.6)
3rd trimester (4)	36	26.2 (5.5)	75.8 (14.4)**
Postdelivery (5)	17	27.6 (5.0)	72.9 (9.3)***

*$p < 0.01$ (unpaired *t*-test).
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***$p < 0.01$ (unpaired *t*-test).

Figure 1 shows the median plasma paracetamol concentration profiles over time for the control, first, second, and third trimester groups (groups 1, 2, 3, and 4, respectively). The median (range) values for P_{max}, T_{max}, and AUC for the 2 h sampling period are shown in Table 2. There were no significant differences between the groups for any of these measures of gastric emptying. The median gastric emptying time of 30 pregnant females predelivery (group 4) did not differ significantly from the postdelivery (18–48 h) values. Table 3 shows the numerical values of P_{max}, T_{max} and AUC for these groups. In this table the postdelivery data are given individually for day 1 (18–24 h) and day 2 (24–48 h) and also pooled together as days 1+2 (18–48 h). Gastric emptying times were similar for days 1, 2, and 5 postdelivery and did not differ significantly either from the prepartum or the control group values. Figure 2 shows the median plasma paracetamol concentration profiles over time for the control group, and 30 women pre- and postdelivery. As far as intrapartum analgesia was concerned, 11 of the females in group 4 received intramuscular pethidine during labour with three subsequently requiring epidural analgesia. A further 14 had epidural analgesia alone; no opioids were administered epidurally.

A group of 17 mothers studied within 2 h after delivery (group 5) showed significantly delayed gastric emptying compared to the control group ($p < 0.01$). Values of P_{max}, T_{max}, and AUC for this group (Table 4) were significantly lower ($p < 0.01$) than those of the control group. Four women had received intramuscular pethidine during labour while eight mothers had epidural analgesia.

Twelve of the 17 mothers in group 5 had gastric emptying times measured again on the second postpartum

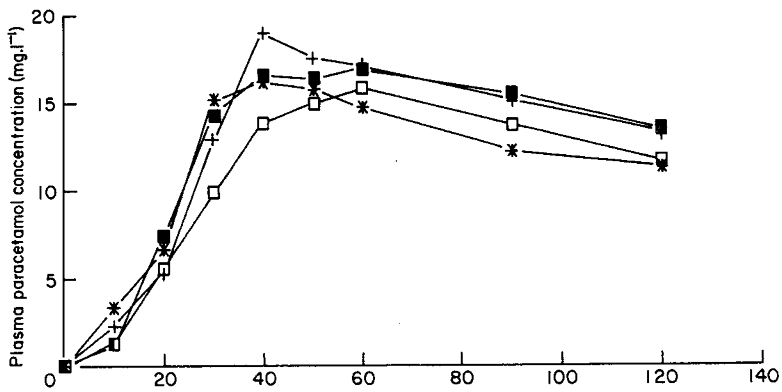

Fig. 1. Plasma paracetamol concentration vs time postparacetamol ingestion for the control (■), first (+), second (*) and third (□) trimester groups. Plasma paracetamol concentrations are expressed as median values.

Table 2. Control and pregnant values of maximum plasma paracetamol concentration, P_{max}, time to maximum concentration, T_{max}, and area under the concentration-time curve, AUC. All values are expressed as median (range).

Group	Control (1)	1st trimester (2)	2nd trimester (3)	3rd trimester (4)
Number of patients	32	18	10	36
P_{max}; mg.l^{-1}	20.8 (8.8–64.5)	21.3 (3.4–39.6)	25.7 (16.5–33.1)	21.0 (4.1–37.2)
T_{max}; min	40 (10–120)	45 (10–120)	30 (10–60)	40 (10–120)
AUC; mg.l^{-1}.h	13.5 (5.5–28.8)	14.2 (1.4–27.2)	13.6 (11.3–14.8)	12.6 (2.4–20.3)

Table 3. Maximum plasma paracetamol concentration, P_{max}, time to maximum concentration, T_{max}, and area under the concentration-time curve, AUC, for the control group and women in the third trimester of pregnancy, pre- and postdelivery.

			Postdelivery			
Group	Control (1)	3rd trimester (4)	Day 1 (4a)	Day 2 (4b)	Days 1+2	Day 5 (4c)
Number of patients	32	30	12	18	30	8
P_{max}; mg.l^{-1}	20.8 (8.6–64.5)	21.0 (4.1–37.2)	23.5 (11.3–41.8)	23.6 (12.1–49.0)	22.6 (11.3–41.8)	24.4 (11.7–31.4)
T_{max}; min	40 (10–120)	40 (10–120)	30 (20–120)	30 (10–90)	30 (10–120)	35 (10–90)
AUC; mg.l^{-1}.h	13.5 (5.5–28.8)	13.6 (2.4–20.3)	14.9 (10.8–19.0)	14.1 (8.9–19.1)	14.6 (8.9–19.1)	14.7 (5.92–33.1)

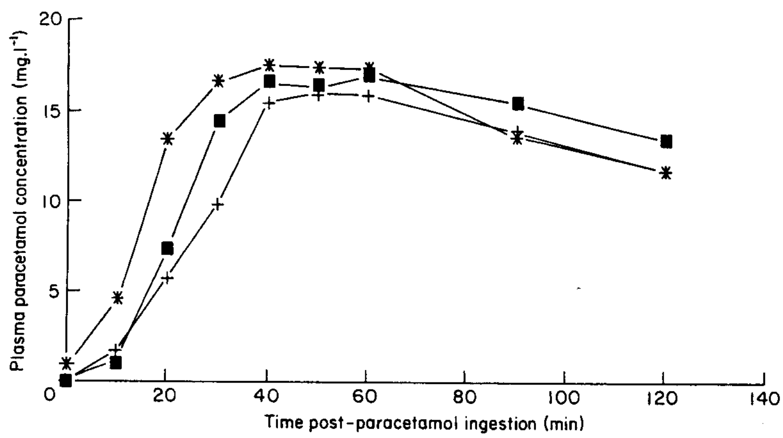

Fig. 2. Plasma paracetamol concentration vs time postparacetamol ingestion for the control group (■) and 30 females during the third trimester of pregnancy (+) and postdelivery between 18 and 48 h (*). Plasma paracetamol concentrations are expressed as median values.

Table 4. Maximum plasma paracetamol concentration P_{max}, time to maximum concentration T_{max}, and area under the concentration-time curve AUC for the control group, mothers within 2 h after delivery and on the second postpartum day.

Group	Control (1)	Postdelivery (2 h) (5)		Postdelivery day 2 (5)
Number of patients	32	17	12	12
P_{max}; mg.l^{-1}	20.8 (8.6–64.5)	12.5* (0.2–30.5)	10.1* (0.3–26.8)	36.6† (3.6–57.8)
T_{max}; min	40 (10–120)	120** (30–120)	120** (40–120)	40‡ (10–120)
AUC; mg.l^{-1}.h	13.5 (5.5–28.8)	3.8*** (0.1–16.6)	3.2*** (0.1–10.4)	17.5§ (2.0–31.1)

*p < 0.01 (Mann–Whitney *U*-test).
**p < 0.01 (Mann–Whitney *U*-test).
***p < 0.01 (Mann–Whitney *U*-test).
†p < 0.01 (Wilcoxon signed ranks sum test).
‡p < 0.01 (Wilcoxon signed ranks sum test).
§p < 0.01 (Wilcoxon signed ranks sum test).

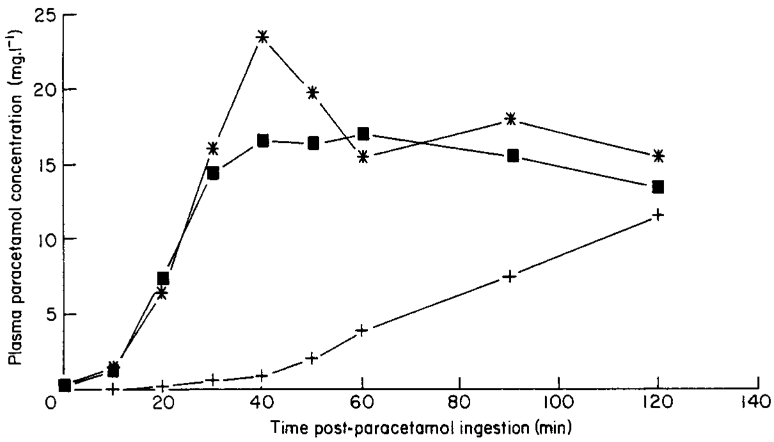

Fig. 3. Plasma paracetamol concentration vs time postparacetamol ingestion for the control group (■) and 12 mothers within 2 h postdelivery (+) and on the second postpartum day (*). Plasma paracetamol concentrations are expressed as median values.

day; P_{max}, T_{max}, and AUC values were significantly greater ($p < 0.01$) compared to their own postdelivery values (within 2 h) and were not significantly different from control results (Table 4). The 2-h postdelivery results are shown for the whole group of 17 women and also for the 12 from this group who were re-evaluated on the second postpartum day. Statistical comparisons were made of data obtained from the same individuals on two separate occasions. Thus, mothers who had delayed gastric emptying within 2 h after delivery, showed a return to normal by the second postpartum day. Figure 3 shows the median plasma paracetamol concentration profiles over time for the latter group within 2 h after delivery and on the second postpartum day compared to the nonpregnant control group.

Discussion

The emptying of gastric contents from the stomach to the duodenum is the result of highly complex interrelationships between hormonal, muscular and electrical influences and therefore any technique which simply measures the rate of transfer of liquids or solids from the stomach to the duodenum will not necessarily detect subtle changes in the pattern of emptying. Improvements in the assay techniques for gastrointestinal peptides, neurotransmitters and prostaglandins and the elucidation of the factors influencing such events as the migrating myoelectric complex further highlight the complexity of gastrointestinal motility. It is therefore not surprising to find that gastric emptying studies, including studies performed during pregnancy and labour have produced varying results.

Although X ray studies of gastric emptying during pregnancy and labour would be ethically unacceptable today, several such studies have been performed in the past [5, 8]. The results of these studies, the majority of which lacked control group comparisons, indicated that gastric emptying was 'normal' during pregnancy, while labour *per se* caused some delay in a certain proportion of females. Opioid administration during pregnancy and labour caused a marked delay in gastric emptying in these X ray investigations and this has been confirmed more recently using the paracetamol absorption technique [6].

Nonabsorbable marker techniques, although accurate, require nasogastric intubation and instillation of relatively large volumes of liquid meal [10]. The former may itself affect gastric motility as a result of both mechanical and psychological factors. Interpretation of the studies which have used these techniques in pregnancy and labour is compounded by the limited number of data points available and the small number of subjects studied.

Although there are now available several safe, noninvasive techniques for measuring gastric emptying including real-time ultrasound [15], epigastric impedance [14], and applied potential tomography [16, 17], the wealth of most recent studies in pregnancy and labour has concentrated on the use of the paracetamol absorption technique [6, 12, 13]. The popularity of this method is probably related to its simplicity, obviating the need for technical expertise, as well as patient acceptance and relative safety of use during pregnancy. Following an oral dose of paracetamol, a statistically significant correlation has been shown to occur between the half time of gastric emptying and the maximum plasma paracetamol concentration achieved, the time taken to reach this concentration and the area under the concentration-time curve [19].

The results of this study indicate that gastric emptying times are unchanged in pregnant females during the first, second, or third trimesters when compared with normal nonpregnant females. This is in agreement with a recent published study which employed the same technique [21]. Thus, it is likely that other factors such as gastro-oesophageal reflux, the pH of gastric contents and, in particular, difficulty with tracheal intubation, present more significant risk for the development of the acid aspiration syndrome in the pregnant population.

The control group data indicated a wide range of 'normal' gastric emptying times. Some evidence suggests that there is an interindividual variation in the gastric handling of paracetamol in tablet form [22]; normal subjects being classified as 'fast' or 'slow' absorbers and both modes of absorption being considered as normal. Where we attempted to look at differences in gastric emptying rates pre- and postdelivery, we ensured that the same women were investigated on both occasions, thus acting as their own 'controls'. Thus, the selection by chance of a group of women who, under normal circumstances, are 'slow' absorbers of paracetamol in tablet form would not lead to a misinterpretation of results in terms of delayed emptying. Ideally, the same women should have been followed throughout pregnancy and the puerperium with serial measurements of gastric emptying, but this was not feasible within the time scale of the study.

Gastric emptying was delayed in mothers investigated within 2 h of a normal vaginal delivery. Although these women were not evaluated during labour, but immediately postpartum, their emptying times on the second postpartum day were not significantly different from nonpregnant control values. Furthermore, data from the group of women investigated predelivery (third trimester) and again between 18 and 48 h postdelivery, showed no difference in gastric emptying times compared to normal nonpregnant controls. This is in agreement with data obtained from women 2–3 days postdelivery using applied potential tomography to measure gastric emptying [17]. The observed delay in gastric emptying during the immediate postpartum period may, in part, reflect intrapartum influences on gastric emptying including narcotic analgesic administration. In this investigation no measurements of gastric emptying were made between 2 and 18 h post-delivery, and thus further study is required to elucidate the pattern of gastric emptying in normal women at these times.

Hitherto, a relative lack of information regarding maternal gastric physiology after delivery has resulted in many anaesthetists remaining wary of the risks of pulmonary aspiration of gastric contents, not only in the immediate postpartum period but often well into the puerperium [23]. Requirements for anaesthesia during this time are not uncommon e.g. for evacuation of retained products of conception, perineal suturing, or drainage of breast abscesses. Provision of a regional anaesthetic technique, which would minimize the hazards of aspiration, is not always appropriate for the surgery in question. Uncertainty regarding the efficiency of gastric emptying in these patients has meant that they may still be treated as potentially having a 'full stomach'. Thus, regardless of the surgical procedure (which is often short and minimally invasive), the anaesthetic technique in this situation is tailored towards minimising the hazards of aspiration, with prophylactic administration of antacids and/or H_2 receptor antagonists as well as protection of the airway with the use of a rapid sequence induction and the insertion of a cuffed tracheal tube. The unnecessary placement of a tracheal tube may be hazardous when technical difficulty is encountered and could increase the risk of pulmonary aspiration under these circumstances.

The presence of delayed gastric emptying in the immediate (within 2 h) postpartum period confirms that strict precautions against acid aspiration as described above should be provided to mothers who are newly delivered and requiring anaesthesia. This study has also shown that gastric emptying is normal at 18–48 h after delivery. The incidence of gastro-oesophageal reflux, which is known to occur in a proportion of pregnant women at term [24], is significantly decreased by the second day after delivery [25]. Previous studies of intragastric pH and residual gastric volume have shown no difference between patients more than 8 h postpartum and nonpregnant females presenting for elective surgery [26].

Thus, the results of this study in conjunction with those which have measured gastro-oesophageal reflux, gastric pH and volume suggest that from the second postpartum day, the healthy mother would appear to be at no greater risk of pulmonary acid aspiration than the nonpregnant patient presenting for elective surgery. The pattern of gastric emptying between 2 and 18 h after delivery, however, remains to be elucidated.

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