The incidence of maternal hypoglycaemia with prolonged fasting before elective caesarean section

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Background: Both national and international guidelines recommend that parturients fast from solids and clear fluids for six and two hours, respectively, prior to a caesarean section (c-section) in order to reduce the risk of pulmonary aspiration. The objective of this study was to evaluate whether fasting times conform to the current American Society of Anesthesiologists' (ASA) recommendations and whether prolonged fasting times are associated with metabolic sequelae, namely hypoglycaemia and ketonuria.

Methods: A total of 56 parturients were enrolled and interviewed at Tygerberg Hospital, a tertiary referral hospital in Cape Town, South Africa. Women who were unable to provide consent (below the age of 18) and/or women who were not scheduled for an elective c-section were excluded from the study. Whole blood glucose and urine ketone levels were measured immediately before anaesthesia.

Results: Fasting times for solids and fluids were 15 hours (IQR 12–18; 95% CI 14–17) and 14 hours (IQR 11–16; 95% CI 12–15), respectively. During the preceding week, 32% of the participants were subjected to repeated fasting periods with a median cumulative time (all the fasting periods added) of 40 hours (IQR 35–64; range 28–133). Hypoglycaemia occurred in 39.3% (95% CI 26.8–53.3) and significant ketonuria occurred in 51.8% (95% CI 38.1–65.1) of the participants, with both conditions associated with longer fasting times ($p < 0.001$). A sigmoid relationship was observed between fasting time and the probability of hypoglycaemia. Hypoglycaemia was unlikely to occur before nine hours of fasting, and thereafter, the risk of hypoglycaemia increased 1.5-fold per hour (95% CI 1.2–1.8).

Conclusion: Fasting times before an elective c-section were longer than what is recommended by the ASA guidelines and were associated with statistically and clinically significant metabolic consequences. Maternal glucose should be checked after nine hours of fasting, since the incidence of hypoglycaemia exceeds 5% after nine hours of fasting. Adherence to outdated fasting practices should also be addressed. Fasting time may be a simple, useful healthcare quality indicator.

Keywords: caesarean section, fasting, hypoglycaemia, ketonuria, parturient

In recognition of the suffering and distress that a prolonged fast can cause, there is mounting pressure to stop ignoring this silent epidemic of iatrogenic suffering.

Ragg[1]

Introduction

The historic 1946 article titled *'The aspiration of stomach contents into the lungs during obstetric anaesthesia'* described the eponymous Mendelson syndrome.[2] Awareness of the associated significant morbidity and mortality was heightened, and the era of universal preoperative fasting was ushered in.[2] The latest guidelines from the World Health Organization (WHO) as well as the American Society of Anesthesiologists (ASA) both recommend that all patients scheduled for elective surgery be fasted[3] for six hours from solids and two hours from clear fluids.[4] This includes pregnant women prior to an elective caesarean section (c-section).

The prevalence of c-section has doubled over the last 15 years, with c-section now being one of the most commonly performed operations worldwide.[5] Tygerberg Hospital, a tertiary referral hospital, is located in an upper-middle-income economy and has a high c-section delivery rate (47%).[6] Such high surgical delivery rates stretch hospital logistics, since operating theatre time is regarded as a scarce resource. Parturients waiting for elective c-section are fasted before surgery, often without intermission until they are operated on, to avoid wasting theatre time. On several occasions, one of the authors had noted clinical signs compatible with hypoglycaemia in parturients scheduled for elective c-section and upon questioning these parturients, prolonged fasting times were suggested. Therefore, a study was initiated to investigate the fasting times before a c-section and the metabolic consequences.

Methods

The Stellenbosch University Human Research Ethics Committee reviewed and approved this cross-sectional, observational study. All participants freely provided informed consent. Women who were over the age of 18 years and who were scheduled for an elective c-section were included. Diabetic parturients were also included in the study.

The null hypotheses were firstly that the fasting time complied with international recommendations (six hours from solid food and two hours from clear fluid) and secondly, that fasting time was not associated with either hypoglycaemia or significant ketonuria. Hypoglycaemia was defined as whole blood glucose ≤ 3.9 mmol/L and significant ketonuria as urine ketones ≥ 4.0 mmol/L.

To ascertain fasting times, the anaesthetist administered a questionnaire in the pre-anaesthetic room (Appendix 1). The questionnaire distinguished between clear fluid intake and solid intake. Non-clear fluids or milk-containing fluids were grouped with solids as the ASA fasting recommendations are six hours for both of these categories. Often more patients are scheduled for c-section than can be accommodated, due to a high turnover in the labour ward. This results in the frequent postponement of procedures to theatre lists on subsequent days. Therefore, the questionnaire also ascertained whether participants had been fasted on any other occasion during the preceding seven days.

A blood sample was taken at the time of insertion of the intravenous cannula in theatre. This blood sample was used to measure whole blood glucose (BG) concentration (Accu-check® Active Glucometer, Roche, Manheim, Germany). Appropriately coded test strips were used. Protocol specified that if hypoglycaemia was diagnosed, it was to be treated immediately with intravenous dextrose (Appendix 2). A urine sample for ketone measurement was obtained after urine catheter insertion, immediately prior to the surgery (RightSign® Urinalysis dipsticks, Hangzhou Biotech, Hangzhou, China).

Statistics

The sample size estimation for this study was based on a similar 2015 Brazilian study,[7] which investigated the fasting times for oral fluids before c-section. We derived a standard deviation (SD) of 6.9 hours for fasting time by averaging the calculated SDs for fasting times for both clear liquids and solids in the above paper. Our calculations indicated that 25 patients would be needed to provide 90% power to determine a difference in fasting time of four hours, when compared to the recommended six hours for solids. To improve the robustness of the study and to account for missing data, we planned to enrol 60 patients in the study.

Parametric data were described as mean ± SD and 95% confidence interval (95% CI). Non-parametric data were described as median, interquartile range (IQR) and 95% CI. The non-parametric Mann–Whitney test was used to compare the distribution of hours since intake of solids and clear fluids with recommended fasting times, as well as the number of cumulative fasting hours between those with and without ketonuria/hypoglycaemia. Logistic regression analysis was used to estimate the odds of hypoglycaemia with increasing hours of fasting. The software used for data collection and analysis were Excel (Microsoft Corporation, Redmond, USA), SSPS Version 25 and EpiCalc® 2000 (Version 1.02), the latter being used exclusively for the calculation of the confidence intervals.

Results

Data were collected over four consecutive weeks, on weekdays only. There were 60 elective c-sections performed during this four-week period. Four of these patients were not included due to lost data. All of the patients met the inclusion criteria. Eight patients had diabetes, however, none of them were insulin dependent. Inspection of their prescription charts confirmed that none of the diabetic patients had received either oral anti-diabetic medications or insulin on the day of surgery.

Fasting times

Fasting times for solids and clear fluids were 15 hours (IQR 12–18; 95% CI 14–17) and 14 hours (IQR 11–16; 95% CI 12–15), respectively (Figure 1). These times were significantly longer, both statistically and clinically, than the current six- and two-hour fasting time recommendations for solids and clear fluids, respectively ($p < 0.001$).

In total, 32% of the participants were subjected to repeated fasting periods. The median cumulative fasting time (all fasting periods added) was 40 hours (IQR 36–66; 95% CI 37–62), with a range of 28–133 hours.
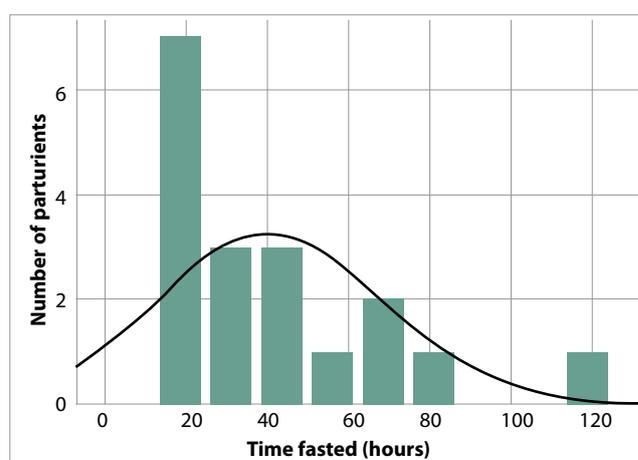

Figure 1: Histogram of cumulative hours fasted by participants exposed to repeated fasting times

Table I: Relationship between whole blood glucose, ketonuria and fasting times

	Overnight fasting times (hours)	
	Solids	**Fluids**
Normoglycaemia (whole blood glucose ≥ 4–10 mmol/L)	12.3 (IQR 11–15; 95% CI 12–15)	11.5 (IQR 10–14; 95% CI 11–13)
Hypoglycaemia (whole blood glucose ≤ 3.9 mmol/L)	17.0 (IQR 15–18; 95% CI 16–18)	16.0 (IQR 15–18; 95% CI 15–18)
No significant ketonuria (urine ketones < 4 mmol/L)	13.0 (IQR 11–15; 95% CI 11–16)	11.5 (IQR 10–14; 95% CI 11–13)
Significant ketonuria (urine ketones ≥ 4 mmol/L)	17.0 (IQR 14–18; 95% CI 15–19)	15.0 (IQR 12–18; 95% CI 14–17)

Hypoglycaemia

The mean (SD) whole blood glucose level was 4.05 (0.67) mmol/L (95% CI 3.8–4.2). Hypoglycaemia occurred in 39.3% of the participants included in this study (95% CI 26.8–53.3). Hypoglycaemic participants were subjected to longer overnight fasting periods than those with normoglycaemia ($p < 0.001$) (Table I).

The comparison between the number of hours fasted from fluids for participants with normoglycaemia and participants with hypoglycaemia can be seen in Figure 2.

The use of a logarithmic representation displayed that a sigmoid relationship existed between fasting time and the probability of hypoglycaemia (Figure 3). This relationship indicated that the first nine-hour period of fasting was not associated with an increased risk of hypoglycaemia. Thereafter, however, the relative risk of hypoglycaemia increased linearly 1.5-fold (95% CI 1.2–1.8) per additional hour fasted. The relationship indicates that there are 10%, 50% and 100% probabilities of hypoglycaemia at 11, 16 and 36 hours, respectively. Inspection of the raw data supports these results, with the earliest hypoglycaemia being documented after an 11-hour overnight fast, and both participants with the lengthiest fasts (36 and 38 hour) were hypoglycaemic.
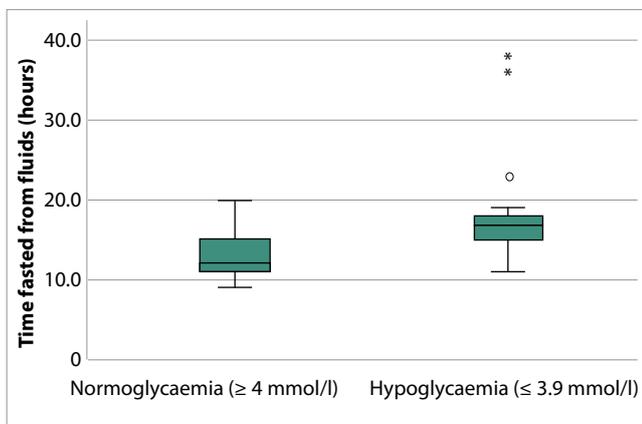

Figure 2: Box and whisker plot comparing the fasting times from fluids, of both participants with normoglycaemia and participants with hypoglycaemia
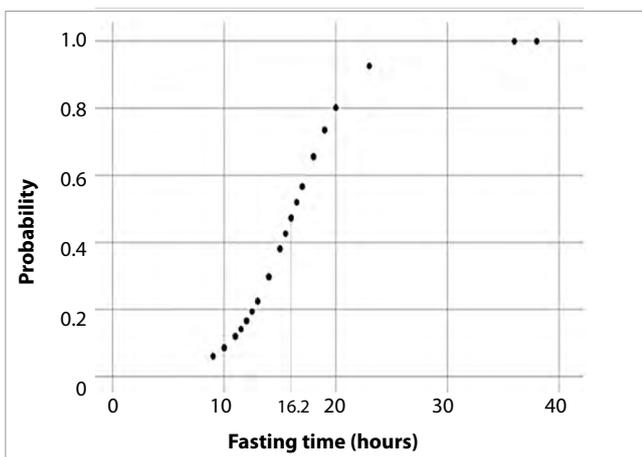

Figure 3: Probability of hypoglycaemia per hour of fasting from fluids

Diabetic patients

One of the eight diabetic participants enrolled in this study was found to be hypoglycaemic. The incidence of hypoglycaemia was 12.5% (95% CI 0.66–53.6) and 43.75% (95% CI 29.77–58.75) in the diabetic group and non-diabetic group, respectively ($p = 0.13$).

Ketonuria

Significant ketonuria occurred in 51.8% of the participants (95% CI 38.1–65.1) and was associated with longer fasting times ($p < 0.001$) (Table I). Participants with ketonuria were fasted for significantly longer periods: 17 hours (IQR 14–18; 95% CI 15–19) versus 13 hours (IQR 11–15; 95% CI 11–16) in the group without ketonuria ($p < 0.001$).

Hypoglycaemia with ketonuria

Hypoglycaemia and ketonuria coincided in 30.4% (95% CI 19.1–44.26) of the participants. There was a significant association between these metabolic abnormalities ($p < 0.001$). The hypoglycaemia–ketonuria combination was associated with longer fasting times ($p < 0.001$) and was more likely to occur (2.9-fold; 95% CI 1.2–6.4) than hypoglycaemia without ketonuria.

Discussion

The results indicate two salient points. Firstly, median fasting times for solids and clear fluids (15 hours and 14 hours, respectively) before an elective c-section were excessive. These fasting times were significantly longer than what is proposed in the ASA guidelines. One-third of participants were subjected to repeated fasting periods during the preceding seven days, with the median and the longest cumulative fasting times of 40 hours and 133 hours, respectively. Secondly, the relationship between fasting time and hypoglycaemia was sigmoid. This indicated that fasting for less than nine hours was safe with respect to hypoglycaemia. However, after nine hours, the relationship indicated that the risk of hypoglycaemia increased 1.5-fold per hour.

Current guidelines indicate that it is safe for patients to consume non-fatty foods and clear carbohydrate-containing fluids until six and two hours preoperatively, respectively. Nonetheless, this study, together with other research studies, indicate that prolonged preoperative fasting still occurs.[7-11] A Royal London NHS Trust study reported that more than 50% and 85% of participants were fasted from fluids and food for longer than 10 and 12 hours respectively before c-section.[11] Despite not even coming close to the prolonged fasting times revealed in this study, the Royal London NHS Trust study suggested that outdated fasting practices are also entrenched in high income countries.

All participants who were interviewed reported that they were instructed not to consume solids or fluids after 22h00 on the day before surgery. This indicates adherence to outdated practices. Non-anaesthetist physicians and nurses are perhaps unaware of recommended fasting times, and the associated discomfort and

distress that patients endure. Such practice is also not innocuous and may have multiple deleterious and costly metabolic consequences, including hypoglycaemia and dehydration, as shown in this study. Further potential complications include spinal hypotension, poor wound healing, an increased incidence of surgical wound complications, impaired return to normal bowel function, and ultimately a prolonged duration of hospital stay.[5,9,12-15]

A significant percentage of the participants were fasted on repeated occasions. Interviews suggested that this was prompted by a recurring scenario. Patients were instructed to cease all oral intake the night before the intended procedure. However, not all elective c-sections were performed the next day due to an over-booked theatre list. If the procedure was postponed, participants were fasted again in preparation for the theatre list on the following day. For some participants, this cycle repeated a number of times.

During early fasting, the primary source of glucose is hepatic glycogenolysis.[16] Prolonged fasting depletes the glycogen stores and promotes the use of alternative energy sources, generated by hepatic gluconeogenesis and lipolysis. Lipolysis is accompanied by ketogenesis.[17] Pregnant women are in a persistent state of "accelerated starvation",[13] which can be attributed to their pregnancy-associated increased metabolic rate and their altered physiological function, which prioritises fetal metabolic needs. However, parturients do not have a concomitant increase in glycogen stores. This accelerates "starvation-induced" onset of hypoglycaemia and ketonuria.

A high incidence of hypoglycaemia in fasted participants was documented. The high incidence of ketonuria, and in particular the combination of hypoglycaemia and ketonuria, is further evidence for the severe metabolic derangements induced by the recorded fasting practices. In each case of hypoglycaemia, the patient was immediately treated with intravenous dextrose (Appendix 2). We did not investigate whether hypoglycaemic participants were symptomatic, or whether the fetus and/or neonate showed either cardiotocographic or metabolic signs of stress. This represents a limitation of this study, and this aspect indicates an important future research question. Diabetic parturients were included in the study, since diabetic medications were omitted on the morning of the procedure, thus not influencing the incidence of hypoglycaemia. There was inadequate statistical power for a comparison of the incidence of hypoglycaemia between diabetic and non-diabetic patients, and this vulnerable group of patients requires further focussed study.

A valuable observation was that the risk of hypoglycaemia could be quantified as fasting time increased. Fasting for up to nine hours was not associated with hypoglycaemia, likely reflecting the magnitude of hepatic glycogen stores. At first glance, the observation of a steadily increasing risk of hypoglycaemia when fasting for periods longer than nine hours appears to contradict the findings of Tauhid-Ul-Mulk et al.,[18] who reported that fasting time was not associated with hypoglycaemia. However, the

longest fasting time in their study was nine hours.[18] We are of the opinion that a probability of hypoglycaemia exceeding 5% represents a clinically significant risk to both fetus and mother. As such, we recommend that the glucose levels of all parturients should be tested at and beyond nine hours of fasting from all intake.

As the saying goes, "[c]ulture eats strategy for breakfast", implying that traditional protocols are not easily given up in order to reset strategy and, hence, clinical practice. In the context of this study, this aphorism refers to the outdated fasting 'culture' that obstructs the implementation of the current fasting guidelines. Table II outlines simple interventions recommended to appropriately reduce fasting times before c-section.

Table II: Proposed interventions to curtail fasting time

1. Clear fluids: Provide patients with a clear carbohydrate-containing beverage at 6 am, to interrupt their overnight fasting. A further drink could be provided at midday, for patients who are expected to enter theatre in the afternoon.
2. Education of personnel: Educate personnel regarding safe, modern practices that encourage parturients to consume clear carbohydrate-containing fluids up to two hours before the procedure.
3. Educating patients: Create wall posters for the elective c-section wards, with a guide to appropriate fasting.
4. Clarifying the order of theatre lists: Allow patients to drink fluids and reduce their fasting period from clear fluids to two hours.

Conclusion

Fasting times before elective c-section were excessive and significantly longer than those recommended in the ASA guidelines. One-third of participants were subjected to repeated, extreme fasting periods during the preceding seven days. There exists a sigmoid relationship between fasting time and hypoglycaemia, which revealed that fasting for less than nine hours conferred low risk for hypoglycaemia. Thereafter, the risk increased considerably every hour. Prolonged fasting was due to the adherence to outdated fasting practices and organisational challenges in an overburdened, tertiary referral hospital. Simple remedial action is required for lessening fasting times before elective c-section. These fasting periods could act as an indicator of quality of healthcare.

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Appendices available online