A Carbohydrate-Rich Drink Reduces Preoperative Discomfort in Elective Surgery Patients

Jonatan Hausel, MD*†, Jonas Nygren, MD, PhD*, Michael Lagerkranser, MD, PhD†, Per M. Hellström, MD, PhD‡, Folke Hammarqvist, MD, PhD§‖, Caisa Almström, RN*, Annika Lindh, MD, PhD¶, Anders Thorell, MD, PhD*, and Olle Ljungqvist, MD, PhD*§

*Center of Gastrointestinal Disease and ¶Department of Anesthesiology, Ersta Hospital; †Department of Anesthesiology and Intensive Care and ‡Department of Medicine, Karolinska Hospital; §Department of Surgery, Huddinge University Hospital; and ‖Clinical Research Laboratory at St. Görans Hospital, Karolinska Institutet, Stockholm, Sweden

We studied the effects of different preoperative oral fluid protocols on preoperative discomfort, residual gastric fluid volumes, and gastric acidity. Two-hundred-fifty-two elective abdominal surgery patients (ASA physical status I–II) were randomized to preparation with a 12.5% carbohydrate drink (CHO), placebo (flavored water), or overnight fasting. The CHO and Placebo groups were double-blinded and were given 800 mL to drink on the evening before and 400 mL on the morning of surgery. Visual analog scales were used to score 11 different discomfort variables. CHO did not increase gastric fluid volumes or affect acidity, and there were no adverse events. The visual analog scale scores in a control situation were not different between groups. During the waiting period before surgery, the CHO-treated group was less hungry and less anxious than both the other groups ($P \leq 0.05$). CHO reduced thirst as effectively as placebo ($P < 0.0001$ versus Fasted). Trend analysis showed consistently decreasing thirst, hunger, anxiety, malaise, and unfitness in the CHO group ($P < 0.05$). The Placebo group experienced decreasing unfitness and malaise, whereas nausea, tiredness, and inability to concentrate increased ($P < 0.05$). In the Fasted group, hunger, thirst, tiredness, weakness, and inability to concentrate increased ($P < 0.05$). In conclusion, CHO significantly reduces preoperative discomfort without adversely affecting gastric contents.

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Over the last decade, several anesthetic institutions have changed their guidelines regarding preoperative fasting before elective surgery. Often, intake of clear fluids such as water, black coffee, tea, or fruit juice without pulp is allowed until 2–3 h before the induction of anesthesia in patients without risk factors for pulmonary aspiration (1,2). Fasting times have been decreased to attenuate preoperative discomfort. Indeed, intake of such drinks reduces preoperative thirst (3–5). A reduction in mouth dryness also occurs (6), whereas the effect on preoperative hunger is inconclusive (3–5). Children allowed to drink before surgery are less irritable before anesthesia (5,7).

Studies have shown that performing surgery in fed, as opposed to overnight-fasted, patients, has several benefits. Central to the catabolic response to injury, including surgery, is the development of insulin resistance (8). The degree of insulin resistance after upper and lower gastrointestinal surgery and hip replacement is substantially reduced in patients treated with carbohydrates before surgery compared with those who are fasted (8,9). Insulin resistance is an independent factor explaining the variation in length of hospital stay (8). Indeed, a retrospective analysis showed that patients treated with preoperative carbohydrates were discharged from the hospital earlier than those who were fasted (10).

To facilitate the metabolic optimization of the elective surgical patient, a specially designed preoperative 12.5% carbohydrate drink (CHO) was developed (11). Gastric emptying of CHO was studied by using a scintigraphic method. A 400-mL single portion of this drink emptied from the stomach within 90 min after intake in both healthy subjects and patients about to

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Address correspondence and reprint requests to Olle Ljungqvist, Center of Gastrointestinal Disease, Ersta Hospital, PO Box 4622, SE-116 91 Stockholm, Sweden. Address e-mail to olle.ljungqvist@ersta.se.

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undergo surgery (11). This preoperative 50-g oral carbohydrate load stimulates insulin release to levels seen after a standard meal and changes the metabolic status of the patient before surgery (11).

The aim of this study was to investigate whether preparation with CHO could reduce preoperative discomfort in ASA physical status I–II elective abdominal surgery patients. CHO was compared with placebo (flavored water) or overnight fasting in a randomized, double-blinded setting. In addition, drink-related complications, residual gastric fluid volumes (GFVs) and gastric acidity (pH) were recorded.

Methods

A total of 252 consecutive adult patients scheduled for elective laparoscopic cholecystectomy (n = 174) or elective major colorectal surgery (n = 78) were included in the study (Table 1). Patients who were eligible for intake of preoperative clear fluids, according to the guidelines from the Swedish Association of Anaesthetists (1), were considered for inclusion. These guidelines are similar to the present recommendations given by the American Society of Anesthesiologists (ASA) (2). Consequently, exclusion criteria were conditions (including pharmacologic treatments) that might impair gastrointestinal motility, gastroesophageal reflux, pregnancy, and the potential for difficult airway management. In addition, patients with diabetes mellitus and patients in ASA physical status classes ≥III were excluded. The investigation was approved by the Research Ethics Committee at Karolinska Institutet. Before entering the study, the purposes and procedures of the study were fully explained to, and agreed upon by, each patient. Three hospitals in the Stockholm area took part in the study.

The patients were randomly assigned to one of three preoperative treatment groups: 1) preparation with CHO, 2) a placebo drink, or 3) fasting from midnight. The CHO and Placebo groups were double-blinded. To ensure that the taste of the drinks did not cause bias, a double-blinded pilot study (n = 26, healthy volunteers) was performed. Each participant was given either CHO or placebo (flavored water). Of 26 subjects, 12 (46%) could correctly identify the drink received.

During the evening before surgery, the CHO group consumed 800 mL of an iso-osmolar carbohydrate-rich drink (12.5% carbohydrates, 50 kcal/100 mL, 290 mOsm/kg, pH 5.0, Nutricia Preop®; Numico, Zoetermeer, the Netherlands) (11). The Placebo group was given the same amount of flavored water (0 kcal/100 mL, pH 5.0). There were no food or drink restrictions before midnight in any of the groups. After midnight, nothing by mouth was allowed, except a single morning dose of 400 mL of the respective drink in the CHO and Placebo groups. The morning drink was taken at least 2 h before premedication. The patients in the CHO (n = 80), Placebo (n = 86), and Fasted (n = 86) groups were comparable with regard to age, sex, and body mass index (Table 1).

Premedication was standardized to morphine 10 mg IM or ketobemidone 5 mg IM. The premedication was given at least 2 h after the morning drink in the CHO and Placebo groups (to avoid opioid-induced effects on gastric emptying) and at the corresponding time point in the Fasted group. No glucose-containing infusions were given before surgery. Unless contraindicated, patients in the colorectal group received a low-thoracic epidural catheter. Epidural analgesia was initiated before general anesthesia (GA) by using bupivacaine with epinephrine. GA was induced IV with fentanyl and thiopental after the administration of glycopyrrolate. Atracurium was given to facilitate endotracheal intubation, and GA was maintained with isoflurane and nitrous oxide in oxygen.

The patients scored their subjective sense of discomfort with 100-mm visual analog scales (VAS) repeatedly during the study. The scales were horizontal, ungraded, and anchored at both ends by vertical lines labeled as the extreme boundaries of the variable to be measured. Eleven different variables were evaluated: anxiety, depression, hunger, inability to concentrate, malaise, nausea, pain, thirst, tiredness, unfitness, and weakness.

The same VAS questionnaire was used on four different occasions: 1) as a baseline control approximately 1–2 h after lunch at the preadmission visit 1 wk before surgery (laparoscopic surgery) or at the corresponding time point on the day before the operation (colorectal surgery), 2) before intake of the drink on the morning of surgery (0 min, i.e., approximately 2 h before premedication), and at 3) 40 min and 4) 90 min after the morning drink. The Fasted group did the scoring at the corresponding time points. The patients did not have access to their previous results when scoring. The nurses administering the VAS scores were blinded to the CHO and Placebo groups, but for obvious reasons they were not blinded to the Fasted group.

The test-retest reliability (reproducibility) of the VAS in the preoperative situation was evaluated by using repeated determinations 5 min apart in the same individual (n = 41). These patients were not informed beforehand about the second test and did not have access to their first result when scoring the second time.

To study the effects of the various treatments on glucose and insulin concentrations, blood samples were taken in a standardized manner. Venous blood samples were drawn before and then 40 and 90 min after the morning drink (or at corresponding time points for the Fasted group) and at the induction of anesthesia. The samples were frozen immediately and analyzed after the decoding of the treatments. Plasma

Table 1. Demographic Data: Residual Gastric Fluid Volumes and pH

Type of surgery	Treatment group	No.	Sex (M/F)	Age, yr, median (IQR)	BMI, median (IQR)	Aspirated GFV, mL, median (IQR)	Gastric pH, median (IQR)
Laparoscopic cholecystectomy	Fasted	59	13M/46F	48 (37–59)	25 (23–26)	24 (15–40)	1.9 (1.6–2.3)
	Placebo	60	19M/41F	52 (34–58)	24 (22–26)	20 (10–35)	1.9 (1.8–2.3)
	CHO	55	14M/41F	49 (36–58)	24 (22–26)	18 (22–41)	2.0 (1.6–2.7)
Colorectal surgery	Fasted	27	13M/14F	52 (34–66)	25 (23–27)	18 (6–41)	2.0 (1.7–4.0)
	Placebo	26	15M/11F	56 (46–69)	24 (21–26)	22 (12–30)	1.9 (1.6–2.5)
	CHO	25	10M/15F	56 (50–67)	25 (21–27)	18 (7–39)	2.1 (1.7–2.4)

BMI = body mass index; CHO = carbohydrate-rich beverage; GFV = residual gastric fluid volumes; IQR = interquartile range (25th–75th percentiles). Differences between groups were nonsignificant.

glucose (n = 252) was measured with the glucose oxidase method (Yellow Springs Instruments, Inc., Yellow Springs, OH) (12). Serum insulin (n = 105) was analyzed by radioimmunoassay with an antibody developed in our laboratory (13).

Shortly after the induction of anesthesia and before the surgery commenced, a double-lumen nasogastric tube was inserted. The location in the stomach was confirmed by auscultation and aspiration of gastric fluid. Seven patients (Fasted, n = 3; Placebo, n = 2; CHO, n = 2) about to undergo laparoscopic cholecystectomy did, however, not receive a nasogastric tube (because of technical problems and patient wishes), and consequently the GFVs in these patients were not measured. Two methods were used to measure GFV. In 245 patients (Fasted, n = 83; Placebo, n = 84; CHO, n = 78), aspiration of gastric fluid was performed while the tube was manipulated into several positions. In a subset of 142 patients (Fasted, n = 50; Placebo, n = 50; CHO, n = 42), a single-marker dilution technique was also used (14). Ten milliliters of saline containing a known concentration of cyanocobalamin (vitamin B12, Behepan®; Pharmacia, Stockholm, Sweden) was instilled into the stomach. Ten minutes later, a 5-mL aspirate was drawn. The concentration of cobalamin was measured by spectrophotometry and the GFV calculated according to the equation:

$$\text{GFV} = \left(\frac{\text{amount of cobalamin given}}{\text{concentration of cobalamin in aspirate}}\right) - \text{volume of the marker} \quad (1)$$

The acidity of the gastric contents was measured in 127 patients (Fasted, n = 42; Placebo, n = 45; CHO, n = 40) and determined by automatic back-titration with NaOH 0.1 mol/L to pH 7 (Radiometer A/S, Copenhagen, Denmark).

VAS is by definition an analog scale with no predefined unit of measurement and in this study is treated as a nonmetric, ordinal (rank-ordered) scale. There are no direct methods for power analysis of ordinal data. With ordinal scales, statements about ranks can be made, but not statements about the relative sizes of the differences (15). Ordinal data should preferably be analyzed with nonparametric statistics (15). Unless otherwise indicated, data are presented as medians and percentiles. Friedman's test and the Page test (15) were used for within-group trend analysis of the VAS measurements, whereas the Kruskal-Wallis test and the Mann-Whitney U-test were used for testing between groups. Correlations were analyzed with the Spearman rank test. A P value of ≤ 0.05 was considered significant.

Results

There were no cases of apparent or suspected pulmonary aspiration or other drink-related complications before, during, or after surgery.

The mean (SD) time period between intake of drink and the induction of anesthesia in the CHO and Placebo groups was 218 (69) min and 215 (75) min, respectively (not significant). Overall, GFVs were small (Table 1). There were no differences in GFVs among treatment groups, between the Laparoscopic Cholecystectomy and Colorectal Surgery groups, or between sexes. The median volumes were similar regardless of preoperative treatment and mode of calculation (Fasted, 22 and 19 mL; Placebo, 20 and 17 mL; CHO, 20 and 16 mL for the aspiration and marker dilution methods, respectively). There was a significant correlation between the GFVs measured by the two methods (Spearman rank: Rho = 0.26, P = 0.002). No systematic difference between the methods was found. Of 245 patients, 239 (97.5%) had a GFV <100 mL obtained via the aspiration method. In three patients, no aspirate could be obtained. The maximum aspirated volumes were 287 (Placebo), 245 (CHO), and 103 mL (Fasted). By using the marker dilution method, the maximum GFV calculated was 163 mL (Fasted). There was no difference in gastric pH among the treatment groups at the induction of anesthesia (Table 1).

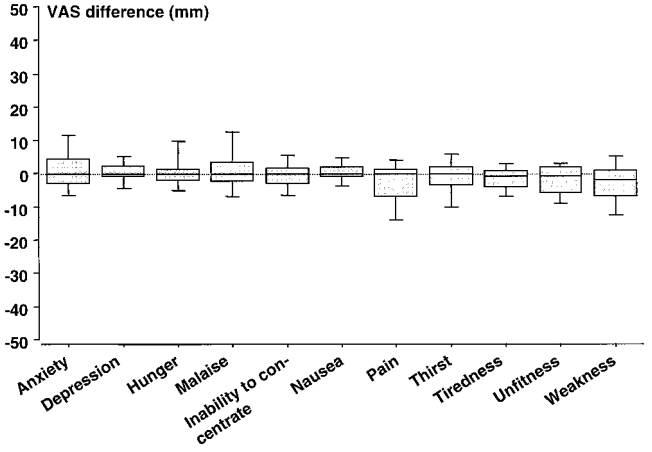

Figure 1. Reproducibility of the visual analog scale (VAS) in 11 discomfort variables. Box (25th–75th percentiles)-and-whisker (10th–90th percentiles) plots of differences between two VAS estimations 5 min apart in the same individual ($n = 41$).

In all 11 VAS variables, the median of the difference between the two scorings 5 min apart ranged from −2 to 0 mm (Fig. 1). The response frequency for all 11,088 VAS scores was 98.6%.

We were unable to detect any differences in VAS scores at any time point between the patient group scheduled for laparoscopic cholecystectomy and the Colorectal Surgery group, nor were there any consistent differences in discomfort between sexes. The highest median VAS scores were seen for hunger and thirst (Fig. 2). The VAS scores (median, 25th–75th percentiles) for depression and pain were low (less than 9, 3–30 and 5, 2–25, respectively) and not significantly affected in the preoperative situation.

In the Fasted group, trend analysis showed increasing preoperative discomfort over time in 5 of 11 VAS variables and no change in the other variables. Specifically, preoperative hunger ($P < 0.05$), thirst ($P < 0.001$) (Fig. 2), tiredness ($P < 0.0001$), weakness ($P < 0.01$), and inability to concentrate ($P < 0.05$) (Table 2) increased during the waiting period before surgery.

In contrast to the Fasted patients, the CHO-Treated group showed decreasing trends for preoperative discomfort in five of the variables and no change in the remaining variables. These patients became less hungry ($P < 0.05$), less thirsty ($P < 0.001$), and less anxious ($P < 0.01$) (Fig. 2) and experienced less malaise ($P < 0.01$) and unfitness ($P < 0.0001$) (Table 2) during the preoperative period.

Last, in the Placebo group, trend analysis showed decreasing unfitness ($P < 0.001$) and malaise ($P < 0.01$) (Table 2) over time. However, this group had a small but increasing nausea ($P < 0.0001$), increasing tiredness ($P < 0.001$), and an increase in inability to concentrate ($P < 0.05$) (Table 2). There was no consistent trend for hunger or thirst in this group.

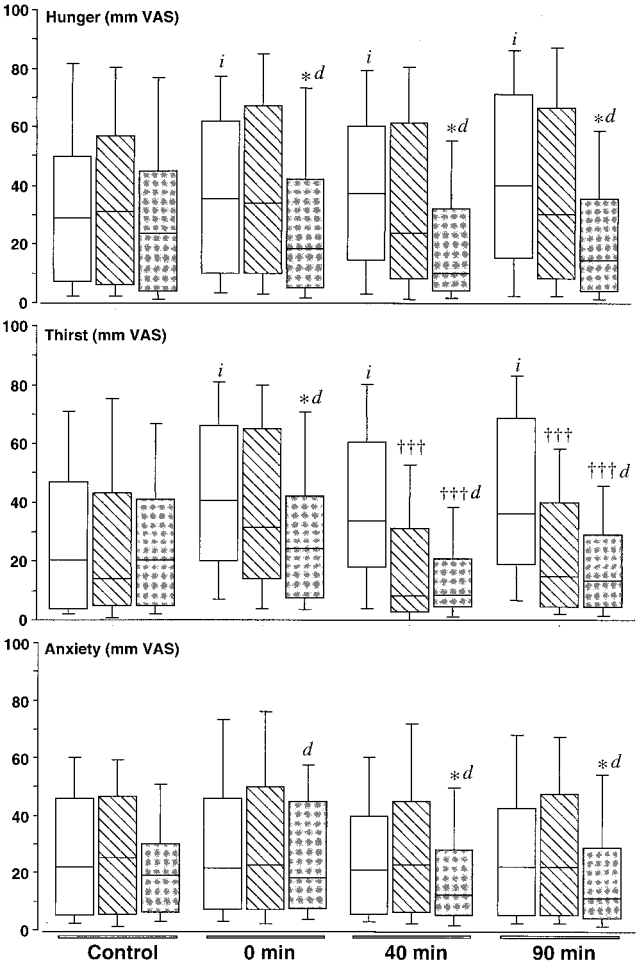

Figure 2. Visual analog scale (VAS) data for preoperative hunger, thirst, and anxiety. Box (25th–75th percentiles)-and-whisker (10th–90th percentiles) plots of VAS for hunger, thirst, and anxiety. Fasted group = blank boxes ($n = 86$). Placebo group = hatched boxes ($n = 86$). Carbohydrate (CHO) group = filled boxes ($n = 80$). Time axis: control = baseline control; 0 min = before intake of the morning drink; 40 and 90 min = time after the morning drink (corresponding times in the Fasted group). Trend analysis with Friedman's test and the Page test: hunger, thirst, and anxiety decreased (*d*) in the CHO group ($P < 0.05$), whereas hunger and thirst increased (*i*) in the Fasted group ($P < 0.05$). Between-groups analysis with the Kruskal-Wallis test and the Mann-Whitney *U*-test: less hunger, thirst, and anxiety in the CHO group (*$P \leq 0.05$ versus Placebo or Fasted), less thirst in the CHO and Placebo groups (†††$P < 0.0001$ versus fasted).

In the control situation, there were no differences among treatment groups in any of the 11 VAS variables. Before intake of the morning drink (0 min), the CHO group experienced less hunger ($P < 0.05$) and thirst ($P \leq 0.05$) than both the other groups (Fig. 2).

After the morning drink (40 and 90 min), the CHO group was less hungry ($P < 0.05$) and less anxious ($P \leq 0.05$) than the other groups (Fig. 2). Patients receiving either drink were less thirsty ($P < 0.0001$) than the Fasted group (Fig. 2). The CHO group felt less unfit ($P < 0.05$) after the morning drink (Table 2) compared

Table 2. Visual Analog Scale (VAS) Data for Preoperative Discomfort Variables

VAS variable	Treatment group	Control, mm, median (IQR)	0 min, mm, median (IQR)	40 min, mm, median (IQR)	90 min, mm, median (IQR)	Trend
Inability to concentrate	Fasted	20 (6–34)	21 (6–43)	15 (7–36)	25 (10–44)	*i*
	Placebo	17 (5–33)	18 (7–34)	20 (9–43)	23 (11–40)	*i*
	CHO	19 (6–33)	20 (8–32)	18 (9–27)	17 (8–32)	
Malaise	Fasted	16 (4–43)	14 (5–32)	12 (3–30)	10 (3–30)	
	Placebo	15 (4–33)	14 (3–31)	12 (4–28)	8 (3–26)	*d*
	CHO	14 (3–37)	15 (4–28)	8 (4–20)	7 (3–17)	*d*
Nausea	Fasted	4 (1–9)	4 (2–12)	3 (2–10)	4 (2–12)	
	Placebo	2 (0–7)	3 (1–10)	4 (1–13)	5 (1–13)	*i*
	CHO	4 (2–8)	4 (2–7)	4 (2–6)	3 (2–7)	
Tiredness	Fasted	19 (5–43)	31 (7–59)	29 (10–52)	35 (16–58)	*i*
	Placebo	20 (8–41)	24 (8–48)	22 (9–49)	33 (10–55)	*i*
	CHO	21 (9–50)	23 (8–45)	20 (11–37)	24 (12–46)	
Unfitness	Fasted	30 (18–49)	30 (14–49)	30 (14–48)	31 (14–53)	
	Placebo	35 (21–49)	30 (17–45)	27 (15–42)	27 (13–42)	*d*
	CHO	34 (20–48)	28 (14–42)	20 (12–33)*	22 (10–39)*	*d*
Weakness	Fasted	21 (9–43)	24 (12–46)	28 (10–44)	32 (12–51)	*i*
	Placebo	22 (12–41)	26 (15–46)	26 (14–38)	25 (12–44)	
	CHO	27 (13–45)	30 (14–46)	22 (12–34)	22 (10–39)	

CHO = carbohydrate-rich beverage; IQR = interquartile range (25th–75th percentiles); 0 min = before intake of the morning drink (corresponding time in the Fasted group); 40 and 90 min = time after the morning drink (corresponding times in the Fasted group); *i* = increasing trend ($P < 0.05$) according to Friedman's test and the Page test; *d* = decreasing trend ($P < 0.01$) according to Friedman's test and the Page test.

* $P < 0.05$ CHO versus Fasted. Other differences between groups were nonsignificant.

with the Fasted group, but there was no difference compared with the Placebo group.

Before intake of the morning drink, no differences were found in plasma glucose or serum insulin concentrations in the CHO and Placebo groups compared with the Fasted group (Fig. 3). As expected, glucose and insulin concentrations were increased in the CHO group ($P < 0.0001$) at both 40 and 90 min after the morning drink compared with the other groups. At the induction of anesthesia, a rebound effect was seen, and glucose concentrations were slightly, but significantly, smaller ($P < 0.01$), whereas insulin concentrations were still larger ($P < 0.05$) in the CHO group compared with the other two groups.

Discussion

This study shows that preparation with CHO increased preoperative well-being compared with intake of placebo (water) or overnight fasting. This treatment relieved preoperative thirst, hunger, anxiety, and, to some extent, malaise and unfitness. Furthermore, it was more effective than placebo in reducing hunger, thirst, and anxiety. The VAS proved to be a method with high reproducibility and patient acceptability in the preoperative situation. The administration of CHO two hours before premedication did not increase volumes of or affect the acidity of gastric contents, and no adverse events were noted.

Patients included in this study represent those typically allowed to drink clear fluids up to two hours before surgery, according to existing guidelines (1,2), i.e., patients without risk factors for pulmonary aspiration. In this study, patients in ASA physical status classes I–II were included. In one of the three hospitals in the study, the ASA classification for all surgical patients was kept on file. During the time period of the study, 80% of all acute and elective cases belonged to ASA status I–II. Thus, the preoperative treatment with CHO is potentially applicable and suitable for the majority of patients undergoing elective surgery.

There is no generally established method for a broader evaluation of perioperative morbidity or discomfort in elective surgery patients. In this study, 11 variables reflecting different aspects of subjective discomfort were used. The variables were chosen from clinical experience of common patient complaints in both the pre- and postoperative situation. The VAS method was chosen because of its general acceptance and ease of administration. VAS has previously been used in the preoperative situation to measure thirst (4,5), hunger (4,5), and different aspects of anxiety (16). VAS is widely used in pain estimations. Also, VAS has been used to evaluate nausea (17), tiredness (18), and up to 26 items of psychological symptomatology (19). In this study, the reproducibility of the VAS method in the preoperative situation was evaluated. High test-retest reproducibility and a high level of patient compliance, with an answer frequency of 98.6%, were found.

Thirst has been suggested to be the main determiner of preoperative discomfort, followed by anxiety, preoperative insomnia, and hunger (20). The preoperative

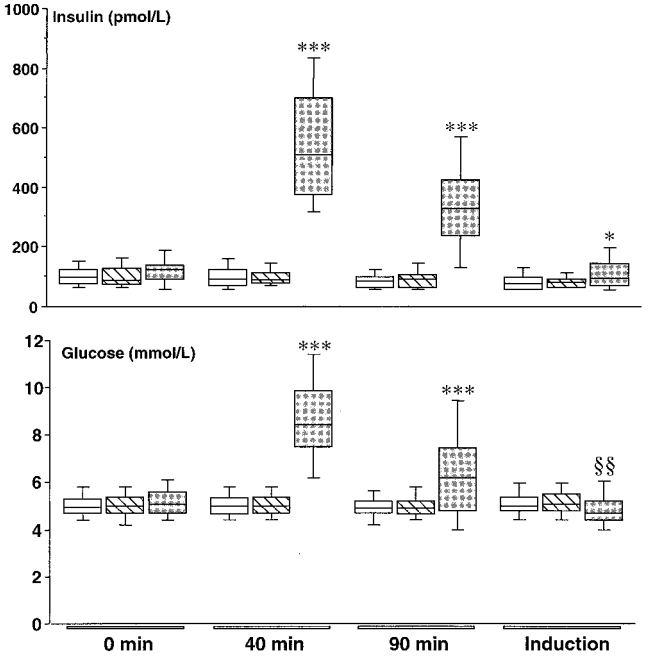

Figure 3. Serum insulin and plasma glucose concentrations. Box (25th–75th percentiles)-and-whisker (10th–90th percentiles) plots for insulin (n = 105) and glucose concentrations (n = 252). Fasted group = blank boxes. Placebo group = hatched boxes. Carbohydrate (CHO) group = filled boxes. Time axis: 0 min = before intake of the morning drink; 40 and 90 min = time after the morning drink (corresponding times in the Fasted group); induction = the induction of anesthesia. Between-groups analysis with the Kruskal-Wallis test and the Mann-Whitney U-test: larger insulin and glucose concentrations in the CHO group (***$P < 0.0001$, *$P < 0.05$ versus Placebo or Fasted), smaller glucose concentration at induction in the CHO group (§§$P < 0.01$ versus Placebo or Fasted).

waiting in itself also contributes to preoperative distress (16). In this study, the highest median preoperative VAS scores were seen for hunger and thirst. Preparation with CHO not only reduced preoperative thirst as efficiently as water (placebo), but it also reduced preoperative hunger. Furthermore, patients in the CHO group were less hungry and less thirsty than those in both the other groups, even before the morning drink. This is likely to be a remaining effect of the previous evening dose of carbohydrates (100 g) and thus supports that preoperative CHO treatment should be initiated on the evening before surgery. In addition, the CHO given in the morning was associated with a reduction in preoperative anxiety compared with both the other groups and a reduction in unfitness compared with the Fasted group. The positive effects on preoperative well-being by carbohydrates were accompanied by increases in glucose and insulin concentrations. The peak concentrations of insulin in the CHO group were similar to those previously recorded after CHO treatment and to those seen after a standard meal (11). The effect on hunger in the CHO group is probably directly related to the intake of energy. This may in turn have secondary effects on the experience of anxiety and unfitness by making patients feel more at ease. A wider testing of psychometric variables has previously not been made in studies of preoperative drinks.

In this study, GFV was determined by using blind aspiration as well as a marker dilution technique. Regardless of the method used, a median GFV of only approximately 20 mL was obtained in all three treatment groups. Seven of 245 patients had a GFV >100 mL identified by either of the two methods. The three patients with the largest volumes identified by the blind aspiration technique deviated slightly from the strict initial inclusion protocol, as found in a thorough postoperative review. In detail, one patient did not clearly reveal previous attacks of intestinal obstruction. The second patient had a too-short interval between intake of drink and premedication, and the third patient had a slightly increased fasted plasma glucose concentration. The occasional occurrence of outliers with GFVs >100 mL has been recorded previously in both fasting patients and those taking clear fluids before surgery (21). These results were obtained in patients given opioids as premedication. These drugs are often used for premedication but delay gastric emptying (22). However, with a two-hour interval between intake of drinks and the administration of opioids, there was no increase in GFVs compared with the Fasted group.

The relevance of gastric acidity to the clinical situation is still not known (23). Data from this study do not, however, support an increased acid secretion in the CHO group, because gastric pH was equal in all three groups. These findings are in accordance with a number of previous studies showing that intake of clear fluids up to two hours before elective surgery does not adversely affect gastric contents (3–5,21,23).

There are no large-scale prospective studies available to show that the reduction of fasting times does not affect the incidence and outcome of pulmonary aspiration (23). However, in a national survey performed in Norway (4.4 million inhabitants) three years after the introduction of the new fasting guidelines, none of the responding hospitals (91% response frequency) reported an increased incidence of aspirations or other side effects in patients taking clear fluids before elective surgery (24). In this study, no problems were encountered in 166 patients drinking 400 mL of clear fluid (CHO or flavored water) two hours before premedication.

In conclusion, the presently tested CHO had advantages over water (placebo) and overnight fasting by reducing preoperative discomfort in ASA I–II elective abdominal surgery patients. There were no adverse effects recorded from taking this drink in the preoperative period, GFVs were not increased, and gastric acidity was not affected. Thus, discomfort during the

waiting period before elective surgery can be significantly reduced in a majority of patients by the simple use of a CHO.

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