Metabolic, hormonal and gastric fluid and pH changes after different preoperative feeding regimens

Mohamed Naguib MB BCH MSc FFARCSI MD,*
Abdulhamid H. Samarkandimb BS KSUF FFARCSI,†
Yasser Al-Hattab MB BCH MSc KSUFA,†
Ahmed Turkistani MB BS KSUF,†
Mohamed Bilal Delvi MB BS MD DA,†
Waleed Riad MB BCH MSc,†
Mounir Attia MB BCH MSc KSUF AB†

Purpose: To evaluate the metabolic, hormonal and gastric fluid and pH changes after administration of a small volume of different preoperative feeding regimens.

Methods: In a prospective, randomized, double-blind study 375 adult patients were allocated to one of five groups. Patients ingested 60 ml honey, glucose-fructose-sucrose-maltose mixture (GFSM), apple juice or water two hours before surgery or continued their overnight fast (controls). Blood samples were obtained from an indwelling venous catheter before the administration of feeding regimens and before induction of anesthesia for determination of glucose, triglycerides, insulin, epinephrine and norepinephrine concentrations. Before anesthesia induction, patients were asked to grade the degree of thirst and hunger. After tracheal intubation residual gastric volume (RGV) was suctioned through an orogastric tube.

Results: Administration of honey, GFSM, apple juice or water resulted in increases in RGV without changes in the gastric pH. The median RGV values were 15 ml in controls and 20-25 ml in other groups. Thirst was noted after administration of fluids containing sugars. Hunger was noted in the apple juice group. Plasma concentrations of glucose increased and triglycerides decreased after ingestion of fluids containing sugars. Plasma insulin concentrations decreased in GFSM and apple juice groups. Norepinephrine concentrations increased in the control, apple juice and water groups.

Conclusions: Small volumes of fluid increased RGV ($P < 0.05$). Apple juice resulted in increased incidence of thirst and hunger and plasma glucose and norepinephrine concentrations. Compared with GFSM or apple juice, honey had a gentler effect on plasma glucose and insulin concentrations.

Objectif : *Évaluer les changements métaboliques et hormonaux ainsi que les modifications des liquides et du pH gastrique suivant l'administration d'un faible volume de différentes prescriptions alimentaires.*

Méthode : *L'étude prospective, randomisée et à double insu a été réalisée auprès de 375 patients adultes répartis au hasard en cinq groupes. Les patients ont pris 60 ml de miel, d'un mélange de glucose-fructose-sucrose-maltose (GFSM), de jus de pomme ou d'eau, deux heures avant une intervention chirurgicale, ou ils sont restés à jeun toute la nuit (témoins). Du sang a été prélevé par cathéter veineux à demeure, avant de donner les liquides et avant l'induction de l'anesthésie, pour déterminer les taux de glucose, de triglycérides, d'insuline, d'adrénaline et de noradrénaline. Les patients ont gradué leur faim et leur soif avant l'induction de l'anesthésie. Après l'intubation endotrachéale, le volume gastrique résiduel (VGR) a été aspiré dans un tube orogastrique.*

Résultats : *L'administration de miel, d'un mélange de GFSM, de jus de pomme ou d'eau a fait augmenter le VGR sans changer l'acidité gastrique. Le VGR moyen a été de 15 ml dans le groupe témoin et de 20-25 ml dans les autres groupes. La soif a été notée après l'administration de liquides sucrés et la faim, avec l'ingestion de jus de pomme. Les concentrations plasmatiques de glucose ont augmenté et celles des triglycérides ont diminué après l'ingestion de liquides sucrés. Le taux plasmatique d'insuline a baissé avec le GFSM et le jus de pomme. Celui de la noradrénaline a diminué chez les témoins, et avec le de jus de pomme et l'eau.*

Conclusion : *Des volumes faibles de liquides augmentent le VGR ($P < 0,05$). Le jus de pomme provoque une incidence accrue de faim et de soif et une augmentation des concentrations plasmatiques de glucose et de noradrénaline. Comparé au GFSM ou au jus de pomme, le miel a un effet plus modéré sur les concentrations plasmatiques de glucose et d'insuline.*

IT was generally believed that restriction of liquid and solid food ingestion for a specified period before induction of anesthesia "NPO after midnight"; would limit the severity of the acid

From the Department of Anesthesia at the University of Iowa College of Medicine,* Iowa, USA and King Saud University,† Riyadh, Saudi Arabia.

Address correspondence to: Mohamed Naguib MD, University of Iowa College of Medicine, Department of Anesthesia, 200 Hawkins Drive, 6JCP, Iowa City, Iowa 52242-1009 USA. Phone: 319-353- 7783; Fax: 319-356-2940; E-mail: mohamed-naguib@uiowa.edu

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pneumonitis syndrome if pulmonary aspiration of gastric contents does occur. Fasting became popular after Mendelson reported the link between feeding and aspiration during labour in 1946.[1] In a retrospective review of 185,358 anesthetics, the incidence of pulmonary aspiration was < 0.01% (1 in 12,131 anesthetics), and mortality was 1 in 46,340 anesthetics.[2]

To minimize residual gastric volume (RGV), patients have been fasted traditionally for 4–6 hr before surgery. The actual fasting period may extend to >16 hr because the last meal may be eaten in the late afternoon on the day before operation. It has been shown, in humans, that this period of fasting could reduce hepatic glycogen content by 60%[3] and alter the hormonal and metabolic setting.[4] Results of animal experiments have also shown that even short periods of food deprivation resulted in reduction of carbohydrate reserves and in alteration in the hormonal and metabolic responses to stress.[5]

The influence of preoperative oral fluid intake on gastric fluid volume in an elective surgical patient has been the subject of several studies in children and adults.[6–9] Ingestion of oral fluids until 2-4 hr before the expected time of surgery, compared with an overnight fast of 12 hr or more, was found to have no effect on residual gastric fluid volume or pH at the time of surgery.[6–9] The necessity for an overnight fast has, therefore, been questioned.[6–10] In the aforementioned studies[6–9] participants received volumes of clear liquids ranging widely from 2 $ml \cdot kg^{-1}$ to unrestricted amounts. The Canadian Anesthesiologists' Society (CAS) guidelines for preoperative fasting indicate that the minimum duration of fasting should be two hours after clear fluid intake.[11] The American Society of Anesthesiologists task force on preoperative fasting reported in 1999 that the evidence is equivocal regarding the effect of clear liquid ingestion on gastric acidity for both adults and children.[12]

Honey is a source of "natural" sugars. There are several reports of the effectiveness of honey in gastrointestinal disorders, wound healing and as an antibacterial, antiinflammatory and antitussive agent.[13–16] The composition of a particular sample of natural honey will depend upon the composition of the nectar(s) and where it originates. Honey is composed mainly of fructose, dextrose, maltose, sucrose and moisture with other trace components. The main sugars in honey, fructose and glucose are absorbed directly into the blood, provide a rapid source of energy without the need of digestion.[13]

Although several recent publications have examined the influences of different preoperative regimens, none have looked at the use of honey or the efficacy of smaller volumes of fluids. In addition, most of these studies were carried out on a small number of patients and were using only one regimen.

This prospective, randomized controlled study was designed to investigate the effects of different preoperative regimens, including NPO after midnight, or ingestion of a small volume (60 ml) of either natural honey, glucose-fructose-sucrose-maltose (GFSM) mixture, apple juice or water two hours before surgery on the gastric fluid volume, gastric pH, the degree of thirst and hunger, and changes in epinephrine, norepinephrine, insulin, triglycerides, and glucose concentrations in adult patients.

Methods

After obtaining institutional approval and informed consent, 375 ASA physical status 1 patients undergoing elective surgery and scheduled as the first case were studied. Patients were excluded if factors known to affect the gastric contents were present - pregnancy, obesity, diabetes, gastrointestinal disease, emergency care, and the ingestion of alcohol, opioids, anticholinergics, histamine type-2 receptor antagonists or metoclopramide in the 24 hr before surgery and patients in whom airway management might be difficult. No premedication was given.

Patients were divided randomly into five groups (n = 75 patients in each). In group 1 (controls), patients fasted from midnight. Patients in groups 2 to 5 ingested 60 ml honey, glucose-fructose-sucrose-maltose mixture, apple juice or water, respectively, two hours (at 0600 am) before surgery was expected to begin (at 0800 am). Honey authenticity was confirmed by Saudi Arabian Standards Organization (see Appendix). A glucose-fructose-sucrose-maltose mixture (GFSM) was prepared by mixing these sugars together in the same proportions as they are found in the honey used in this study (see Appendix) *viz*: glucose 36.8 $g \cdot 100\ ml^{-1}$, fructose 39.9 $g \cdot 100\ ml^{-1}$, sucrose 1.3 $g.100\ ml^{-1}$ and maltose 7.3 $g \cdot 100\ ml^{-1}$. The pHs of honey, GFSM and apple juice used in this study were 3.5, 2.91 and 2.9, respectively. Blood samples were obtained from an indwelling venous catheter before the administration of any of the regimens and before induction of anesthesia. All samples were centrifuged immediately at 4°C for 10 min to separate the plasma. The plasma was stored at -70°C until measurements of glucose, triglycerides, insulin, epinephrine and norepinephrine could be performed. Plasma concentrations of catecholamines and insulin were measured in duplicate by radioenzymatic and radioimmunoassay, respectively, using WIZARD 1470 Automatic Gamma Counter, Wallac, Turku, Finland.

The sensitivity of the assay was 25 pg·ml^{-1} for epinephrine and norepinephrine. Intra- and inter-assay coefficients of variation were 8% and 12%, respectively. Normal values are up to 100 pg·ml^{-1} for epinephrine and up to 600 pg·ml^{-1} for norepinephrine. The sensitivity for insulin assay was 3 µU·ml^{-1}. Intra- and inter-assay coefficients of variation for insulin were 6.2% and 6.6%, respectively. The normal concentrations of insulin range from 5-25 µU·ml^{-1}. Plasma glucose and triglycerides were determined enzymatically using Dimension Clinical Chemistry System (DADE Behring Inc., Newark, DE 19714).

Immediately before induction of anesthesia, patients were asked by one investigator, blinded to group assignment, to grade the degree of thirst and hunger as nil, mild, moderate or severe. Anesthesia was administered according to the surgical requirements and the preference of the anesthesiologist in charge of the case. Two investigators performed aspiration of gastric contents for all patients. Immediately after induction of anesthesia and tracheal intubation, a multiorifice polyvinyl orogastric tube size 22F was inserted to 60 cm from the incisors, and its correct position was verified by air insufflation (5–10 ml) and auscultation. The tube was withdrawn under intermittent suction, and all aspirated fluid was collected in a mucus trap polyvinyl bottle, which collapsed at negative pressures exceeding -60 mm Hg. The procedure was repeated once, and total volume and pH were recorded. Gastric pH was measured using Sentran 1001 pH System, Sentron, Harbor, WA 98335.

Sample size

With the sample size of 64 in each of the five groups, a one-way analysis of variance was estimated to have 95% power to detect a difference at the 0.050 level

TABLE I Demographic Data, Gastric volume and pH ((mean ± SD) or median (range))

	Control (n = 75)	*Honey (n = 75)*	*GFSM† (n = 75)*	*Apple juice (n = 75)*	*Water (n = 75)*
Age (yr)	33.2 ± 10.7	31.6 ± 10.8	32 ± 7.1	31.9 ± 10.1	32.1 ± 13.3
Sex (M/F)	32/43	34/41	39/36	38/37	46/29
Weight (kg)	71 5 ± 15.2	72.6 ± 15.2	71.7 ± 8.5	69.5 ± 11.2	69.6 ± 13.6
Smoking (Yes/No)	17/58	21/54	22/53	18/57	20/55
Gastric volume (ml)	15 (3-87)	20 (3-120)	20 (5-60)*	25 (5-110)*	20 (5-100)*
Gastric pH	2.5 (1.7-7.1)	2.3 (1.2-7.5)	2.6 (1.5-6.8)	2.4 (0.97-6.8)	2.1 (1.4-7.5)

†GFSM = Glucose-fructose-sucrose-maltose mixture.
**P* < 0.05 compared with the control (Kruskal-Wallis test for multiple comparisons).

TABLE II Plasma concentrations of blood sugar, epinephrine, norepinephrine and insulin (median (25th-75th percentiles))

	Initial values					Pre-induction values				
Group§	*Plasma sugar (mmol·l⁻¹)*	*Epinephrine (pg·ml⁻¹)*	*Norepinephrine (pg·ml⁻¹)*	*Insulin (µU·ml⁻¹)*	*Triglycerides (mmol·l⁻¹)*	*Plasma sugar (mmol·l⁻¹)*	*Epinephrine (pg·ml⁻¹)*	*Norepinephrine (pg·ml⁻¹)*	*Insulin (µU·ml⁻¹)*	*Triglycerides (mmol·l⁻¹)*
Control	4.5 (3.9-5.2)	1 8 (14-24)	136 (72-196)	21.7 (15.8-30.4)	1.0 (0.73-1.72)	4.3 (3.9-5)‡	19 (13-22)	178 (66-252)†	18.3 (13.8-22.5)*	1.1 (0.73-1.76)
Honey	4.7 (3.9-5.4)	1 8 (16-24)	136 (41-226)	22.2 (15.2-28.8)	1.5 (1.1-2.1)	4.9 (4.2-5.6)*	17 (14-24)	182 (41-280)	20.5 (12-28.4)	1.4 (0.97-2.1)†
GFSM ¶	4.5 (3.7-4.8)	1 8 (16.3-22)	193 (155-223)	22.1 (17-34.6)	1.2 (0.79-1.95)	4.8 (4.3-5.2)†	18 (16.5-24)	194 (172-251)	20 (14.5-30.6)*	1.1 (0.73-1.9)†
Apple juice	4.5 (3.8-5.1)	1 8 (16-22)	154 (114-200)	22 (17-25.6)	1.26 (0.88-1.87)	4.8 (4.3-5.3)†	16 (14-22)	212 (180-280)†‡	16.7 (12.5-22.5)†	1.2 (0.85-1.8)†
Water	4.8 (4.5-5.2)	2 2 (18-29)	152 (113-197)	21.2 (14.2-24.9)	1.58 (1.1-2.2)	4.9 (4.4-5.2)	22 (16-30.5)	196 (124-374)†	15.1 (12.3-22.5)*	1.5 (1.1-2.2)

§ Number of patients in each group = 75.
¶ GFSM = Glucose-fructose-sucrose-maltose mixture.
Initial values were obtained prior to the administration of different regimens.
Pre-induction vales were obtained approximately 2 h after the administration of different regimens and prior to induction of anesthesia.
* *P* < 0.05 compared with the initial value (within group comparison; Wilcoxon signed-rank test).
† *P* < 0.01 compared with the initial value (within group comparison; Wilcoxon signed-rank test).
‡ *P* < 0.05 compared with the GFSM group (between group comparisons; Kruskal-Wallis test for multiple comparisons).

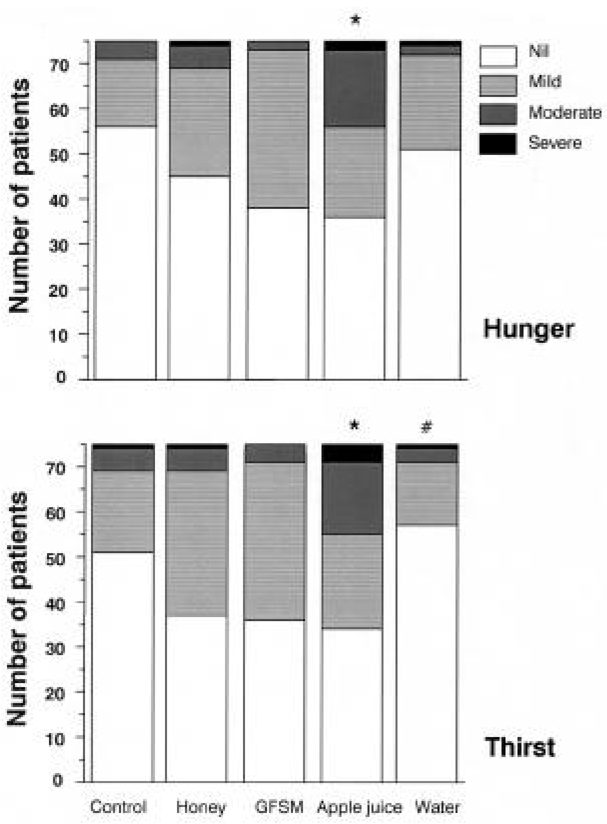

FIGURE 1 Incidence of hunger and thirst. GFSM = Glucose-fructose-sucrose-maltose mixture.
*$P < 0.05$ *vs* the control and water groups (Kruskal-Wallis test for multiple comparisons).
#$P < 0.05$ *vs* honey and GFSM groups (Kruskal-Wallis test for multiple comparisons).

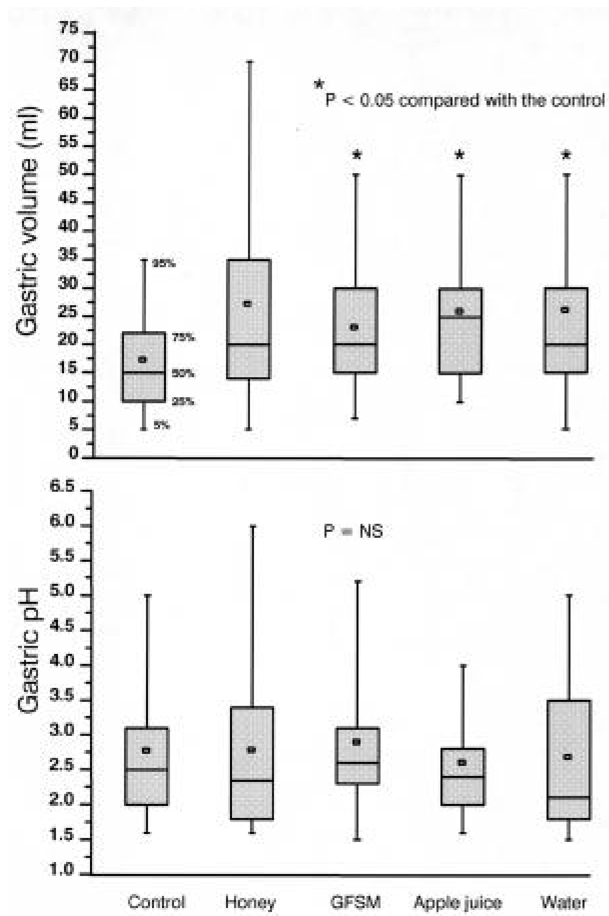

FIGURE 2 Gastric aspirate volume and pH. GFSM = Glucose-fructose-sucrose-maltose mixture.
Shaded areas = 25th to 75th percentiles; horizontal lines within shaded areas = medians, marking 50th percentiles; rectangular symbols in shaded areas = means; extended bars = 5th-95th percentiles.
*$P < 0.05$ compared with the control (Kruskal-Wallis test for multiple comparisons).

characterized by a Variance of means ($V=S(p_i-p_0)^2 / G$) of 13.360, assuming that the common standard deviation is 15.

Statistical analysis

All statistical analyses were carried out using BMDP statistical package, release 7.01 (University of California Press, Berkeley, California, 1994). Within group comparisons were carried out using Wilcoxon matched pairs signed-rank test. Between group comparisons were carried out using Kruskal-Wallis test for multiple comparisons. For multiple comparisons, the null hypothesis was rejected if ZSTAT was larger than the critical value ZC, where

$$1\text{-PHI}(ZC) = \text{ALPHA} / (K(K-1)),$$

PHI is the cumulative standard normal distribution function, ALPHA is the desired overall significance level, and K is the number of groups compared. Unless otherwise specified, results were presented as median (25th-75th percentiles) and were considered significant when $P < 0.05$.

Results

There were no differences in age, sex, weight, or smoking habit among the five groups (Table I). Patients in the apple juice group experienced more thirst and hunger than those in the control and water groups (Figure 1). In addition, patients in the honey and GFSM groups experienced more thirst than those in the water group (Figure 1).

Residual gastric volume (RGV) was greater ($P < 0.05$) in the GFSM, apple juice and water groups than in the control group (Table I, Figure 2). The increases in RGV observed in the honey group did not reach statistical significance due to the wide variations observed in this group. There were no differences among the groups with respect to gastric pH (Table I, Figure 2). No patient regurgitated or aspirated.

Plasma concentrations of glucose increased and triglycerides decreased two hours after ingestion of fluids containing sugars (Table II). However, plasma insulin concentrations decreased from the baseline value in all groups (Table II). Plasma concentrations of epinephrine did not change throughout the preoperative period (Table II). In contrast, plasma concentrations of norepinephrine increased in the control, apple juice and water groups (Table II).

Among group comparisons for the differences (preinduction minus initial value) in triglycerides, plasma sugar and hormones indicated that the changes in plasma sugar and norepinephrine were different in the GFSM group than in the control and in the apple juice groups, respectively (Table II).

Discussion

The results of this study indicate that administration of 60 ml of either honey, GFSM, apple juice or water to elective surgical patients two hours before surgery resulted in increases in RGV without changes in the gastric pH. Thirst was noted only in patients who ingested fluids containing sugars (honey, GFSM or apple juice). Hunger was noted in the apple juice group when compared with the control and water groups. Plasma concentrations of glucose increased and triglycerides decreased two hours after ingestion of fluids containing sugars (honey, GFSM or apple juice). Considerable reductions in plasma insulin concentrations were noted at the same time in GFSM and apple juice groups. Large increases in norepinephrine concentrations were noted before induction of anesthesia in the control, apple juice and water groups.

Several studies demonstrated that ingestion of different volumes of clear fluid (water, carbonated beverages, apple juice, tea and coffee), ranging from 150 ml for adults and 5 $ml \cdot kg^{-1}$ for children to unrestricted volumes, did not affect the volume or pH of gastric contents at induction of anesthesia.[6–9] In contrast, our results do not support this contention. This difference could be attributed to the smaller volume (60 ml) of fluid administered to our patients. Gastric emptying of liquids is influenced primarily by the volume of fluid in the stomach and by its energy density. Increasing the volume will speed emptying, but increasing the nutrient content will slow emptying.[17,18] Osmolality, temperature, and pH of drinks are of minor importance.[17,18] It should also be noted that gastric emptying time is a variable phenomenon in healthy subjects with significant inter- and intraindividual day-to-day differences.[19]

Our results have also shown that patients in the apple juice group experienced more thirst and hunger than those in the control and water groups (Figure 1). It seems, therefore, that apple juice would not be the ideal fluid to be used in the preoperative period.

Hepatic glucose metabolism, endocrine pancreatic secretion and adrenal medullary secretion are regulated by several mechanisms under the control of the autonomic nervous system. The ingestion of a carbohydrate-containing meal in a normal individual inhibits hepatic glucose output and facilitates insulin release from the pancreas.[20] The kinetics of insulin secretion is complex. For instance, the pancreas, when stimulated by a constant concentration of glucose, secretes insulin in two phases. The first and second phase peaks occur after a few minutes and at 60 min, respectively.[21] However, brief stimulation of glucose, sufficient to elicit first-phase release, often causes a temporary refractory period.[22]

In this study, we noted that increases in plasma glucose occurred two hours after ingestion of fluids containing sugars (honey, GFSM or apple juice) and were accompanied by concomitant reduction of insulin concentrations in GFSM or apple juice groups. This reduction could not be attributed to increased sympathetic activity since increases in norepinephrine concentrations were noted before induction in the apple juice group only. However, this reduction could be explained by the very short half-life of insulin (5.2 ± 0.3 min in normal subjects[23]) or the presence of fructose in excess of glucose in GFSM. Fructose, in comparison with other carbohydrates elicits a lower glucose and insulin response in healthy individuals and in individuals with diabetes. Fructose uptake and metabolism, which occur primarily in the liver, appear to be independent of insulin.[24] In addition, fructose is oxidized at a higher rate than glucose during suppression of endogenous insulin secretion, without any significant rise in glycemia.[25]

A glucose-fructose-sucrose-maltose mixture was used in this study in an attempt to discriminate between the effects of honey *per se* and the effect of its sugar. In accordance with our results (Table II), others have noted that the increases in blood glucose were higher after fructose or sucrose than after honey.[26] Similarly, Shambaugh *et al.*[27] noted that, unlike honey, sucrose administration resulted in glucose intolerance and increases in plasma sugar. Others have also demonstrated that honey was associated with consistently lower blood sugar concentrations on an oral glucose tolerance test.[28] Further, our results indicated that ingestion of honey –unlike GFSM- was not associated with any changes in insulin concentrations.

This study raises more questions than answers. The fact that 60 ml of fluids increased gastric fluid volume probably means that it should not be used on the morning of surgery. The published data indicate that at least 150 ml of fluids should be given to patients two to three hours before operation in order to minimize the RGV. This study also demonstrated that apple juice might not be the ideal fluid because it resulted in increases in the incidences of thirst and hunger and plasma glucose and norepinephrine concentrations preoperatively. Thirst was noted after fluids containing sugars (honey, GFSM or apple juice). Nevertheless, some still prefer honey because they like the flavor, even if thirst increases. The benefits of improved patient comfort by the alleviation of thirst and possible prevention of hypoglycemia, especially in children, should be considered in our practice. Nevertheless, active preoperative carbohydrate preservation has been shown to result in improvement of postoperative metabolism and reduction in the occurrence of postoperative insulin resistance.[28,29] Compared with GFSM or apple juice, honey had a gentler effect on plasma glucose and insulin concentrations.

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Appendix

Composition of honey used in this study as reported by Saudi Arabian Standards Organization

Water	16.7%
Sugars:	
Fructose	39.9%
Glucose	36.8%
Maltose	7.3%
Sucrose	1.3%
pH	3.5
Minerals:	
Sodium	9.5 ppm (part per million)
Potassium	68 ppm
Calcium	13.6 ppm
Iron	2.4 ppm
Copper	1.0 ppm
Zinc	8.8 ppm
Diastase activity	6