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THE EFFECT OF ETHANOL AND ALCOHOLIC BEVERAGES ON GASTRIC EMPTYING OF SOLID MEALS IN HUMANS

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Abstract — Aims: The systematic study of the effect of pure ethanol, alcoholic beverages, and their non-alcoholic components on gastric emptying of solid meals in humans. **Methods:** 16 fasting healthy male subjects received once weekly 300 ml of the following solutions in random order: 4 and 10% (v/v) ethanol, beer, red wine, 5.5 and 11.4% (w/v) glucose, and water. The test solutions were given either together with a low caloric (270 kcal, $n = 8$) or a high caloric (740 kcal, $n = 8$) solid meal. Ultrasonography of the antrum was used to determine gastric emptying. **Results:** Gastric half emptying time (t(1/2)) of the high caloric solid meal with water was 131.3 ± 7 min. The ingestion of 4 and 10% (v/v) ethanol (158.8 ± 9.3 and 165.6 ± 6.2 min, respectively), beer (163.1 ± 11 min), and red wine (186.3 ± 8.4 min) resulted in a significantly longer t(1/2) than water. The lag phases after 4 and 10% (v/v) ethanol, beer, and red wine were not significantly different from that of water (48.1 ± 6.5 min). Compared with water, the ingestion of 5.5 and 11.4% (w/v) glucose resulted in a significantly longer t(1/2) (153.8 ± 5 and 168.1 ± 14.4 min, respectively) by increasing the duration of the lag phase. The high caloric meals resulted in a 2-fold prolongation of t(1/2) when compared with the low caloric meals. The effect of the solutions on the gastric emptying times, however, was similar for both test meals. **Conclusions:** (i) Ethanol in low concentrations of 4 and 10% (v/v) prolongs gastric emptying of solid meals; this inhibitory effect is not dose-dependent. (ii) Alcoholic beverages (beer and red wine) also result in a prolongation of gastric emptying. The inhibitory effect of red wine, but not of beer, is more pronounced than that of the corresponding ethanol concentration and amount. (iii) The inhibitory effect of ethanol and alcoholic beverages is mainly induced by a prolongation of the gastric emptying phase (without affecting the lag phase), whereas 5.5 and 11.4% (w/v) glucose prolong the lag phase in a dose-dependent manner. (iv) The inhibitory effect of ethanol, beer, and red wine on gastric emptying does not depend on the caloric content of the meal.

INTRODUCTION

Many individuals report effects of alcoholic beverages on gastrointestinal symptoms, ranging from relief from postprandial complaints to nausea or abdominal discomforts. Altered gastric emptying by alcoholic beverages may be responsible for these symptoms.

Recently, we have shown that the gastric emptying rate of pure ethanol solutions (4, 10 and 40% v/v) is significantly slower than that of water (Franke *et al*., 2004). Emptying of alcoholic beverages produced by fermentation (beer and red wine), but not those produced by distillation (whisky) required over 50% more time than their corresponding ethanol solutions (Franke *et al*., 2004). Because gastric emptying of liquids is mainly under the influence of the tone of the fundus, whereas gastric emptying of solids is regulated by the motor activity of the antrum, it remains unclear if these results can be applied to the effects of alcoholic beverages and ethanol solutions on the gastric emptying of solid meals. Until now, only few studies examined the effect of pure ethanol and commonly ingested alcoholic beverages on gastric emptying of solid meals. Delayed gastric emptying rates of solid meals by pure ethanol (Jian *et al*., 1986) and whisky were reported in one (Barboriak and Meade, 1970) and lack of an effect by red wine (Moore *et al*., 1981) was described in another study.

One reason for the scarcity of systematic studies in the literature could be the relatively large number of control solutions required in order to determine the effects of ethanol and alcoholic beverages on gastric emptying (Chari *et al*., 1993). A number of factors contribute to the complexity of designing an appropriate study on the subject, including caloric content (Hunt and Stubbs, 1975), volume (Mitchell and Voss, 1991), temperature (Fone *et al*., 1990), pH (Lin *et al*., 1990), chemical composition, physical state (Santangelo *et al*., 1998) and osmolality (Vist and Maughan, 1995).

Ethanol is a small molecule and exerts in contrast to its high 'theoretical' osmotic pressure as determined by an osmometer almost no osmotic pressure over biological membranes. This has to be considered when selecting isoosmotic control solutions for ethanol and alcoholic beverages. A detailed discussion on appropriate control solutions in studies of the effect of ethanol and alcoholic beverages on the stomach is given by Chari *et al*. (1993).

The aim of the present study was to determine the effect of some commonly ingested alcoholic beverages, their corresponding ethanol concentrations, and appropriate controls on the gastric emptying of solid meals by means of ultrasonography. Ultrasonography was chosen because it is a non-invasive, reliable method to determine gastric emptying parameters (Benini *et al*., 1999; Capello *et al*., 2000; Aoki *et al*., 2002). In this study, the following questions were addressed: (i) Do alcoholic beverages affect the gastric emptying of solid meals? (ii) Is gastric emptying dependent on the ethanol concentration? (iii) Does the effect of ethanol and alcoholic beverages depend on the total caloric content of the meal?

MATERIALS AND METHODS

Subjects

Sixteen healthy male volunteers (aged 29 ± 2.1 years, mean body weight 77 ± 1.7 kg) were enrolled in this study. All were

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Table 1. Test solutions with their volume, osmolality, ethanol, and caloric content

Test solutions	Volume (ml)	Ethanol concentration (v/v) (%)	pH	Osmolality (mOsm/kg)	Calories (kcal)
Ethanol 4% (v/v)	300	4	7.5	660	114
Ethanol 10% (v/v)	300	10	7.6	1650	284
Beer, 4.8% (v/v) Eichbaum Pilsener	300	4.8	4.2	1010	223
Red wine, 11% (v/v) Italian Medoc	300	11	3.9	2000	380
Water	300		7.4	10	0
Glucose 5.5% (w/v)	300		7.4	305	110
Glucose 11.4% (w/v)	300		7.4	630	228

non-smokers, did not consume alcoholic beverages on a regular basis, and took no medication. A written informed consent was obtained from each subject. The research protocol was approved by the ethics committee of the University Hospital and conformed to the revised declaration of Helsinki 1989.

Each subject was studied seven times, and had at the most one test per week. The sequence of the tests was randomized.

Study design

All examinations were performed in the afternoon. The subjects had fasted at least 8 h after a small breakfeast in the morning. Subjects were examined in a sitting position slightly leaned backwards. They had drunk 150 ml of the test solution (Table 1) during 5 min, and another 150 ml together with the solid meal during the following 5 min. Gastric emptying was measured for 3 (low caloric meal) or for 5 h (high caloric meal) by ultrasonography.

Solid test meals

Two solid test meals of different caloric content were used. The low caloric meal represented a snack and consisted of two slices of white bread and one baked egg totalling 270 kcal. The meal contained 11.9 g fat, 24.7 g carbohydrate, and 16.9 g protein.

The high caloric meal represented a lunch and consisted of 360 g commercially prepared ravioli with tomato sauce, one baked egg and 100 g ground meat fried with 5 g olive oil totalling 740 kcal. This meal contained 37.5 g fat, 54.7 g carbohydrate, and 46.1 g protein.

Test solutions

The test and control solutions are listed in Table 1 with their respective volumes, osmolalities, ethanol concentrations, and caloric content. In summary, 300 ml of the following solutions were used: pure ethanol (4 and 10% v/v), beer, and red wine. As controls the following solutions were given: 300 ml water (volume and isoosmotic control for ethanol), 5.5% (w/v) D-glucose solution (equicaloric control for 4% (v/v) ethanol) and 11.4% (w/v) glucose (equicaloric control for beer). Herein after the ethanol concentrations represent the volume of ethanol per 100 ml of water (v/v) and the glucose concentrations represent the weight of glucose per 100 ml of water (w/v) unless otherwise stated.

Ultrasonography

Realtime ultrasonography can be used to assess gastric emptying directly and has major advantages over scintigraphy as the gold standard. Ultrasonography is simple, non-invasive, and does not entail radiation which enabled us to repeat measurements with several different test solutions on the same subjects. Ultrasonography has been shown to be a reliable method to determine gastric emptying of solid meals (Benini *et al*., 1999; Capello *et al*., 2000; Aoki *et al*., 2002). Using a curved array scanner with a 3.25 MHz ultrasound transducer (Sonoline Sienna®; Siemens, Germany) a cross-sectional area of the antrum at the level of the superior mesenteric vein and the aorta was measured. These vessels served as landmarks to standardize the position of the scans. This antral area was scanned before, immediately after the meal was finished and then at 10 min intervals for 3 (low caloric meal) or 5 h (high caloric meal).

The inner echogenic layer corresponding to the interface between the gastric content and the mucosa of the gastric wall was outlined. The measurements were repeated twice and the mean value was considered representative. The areas of the antrum were traced by the internal calliper equipped with the ultrasound instrument. Lag time t(lag) represents the time from the end of the meal (time zero) until the maximal antral area was measured. Gastric half emptying time t(1/2) corresponds to the interval between the end of the meal and the moment when antral area was reduced to 50% of the maximal antral area. The gastric emptying phase [t(1/2)-t(lag)] represents the time from the beginning of the emptying process t(lag) until the time when antral area was reduced to 50% of the maximal gastric area t(1/2).

Serum ethanol concentrations

Blood samples (10 ml) for determination of serum ethanol concentrations were drawn at baseline and then every 15 min for 3 (low caloric meal) or 4 h (high caloric meal). The samples were centrifuged immediately at 4°C. Serum concentration of ethanol was determined using the alcohol-dehydrogenase method (Ethylalkohol, Roche Diagnostics GmbH, Mannheim, Germany).

Statistics

Data are expressed as the mean ± standard error of the mean (SEM) unless otherwise stated. Analysis of variance (ANOVA) for repeated measures was conducted to compare the gastric half emptying times and serum ethanol concentrations between the test solutions. The differences between the results were evaluated using Duncan's multiple range test and $P < 0.05$ was chosen as the level of statistical significance.

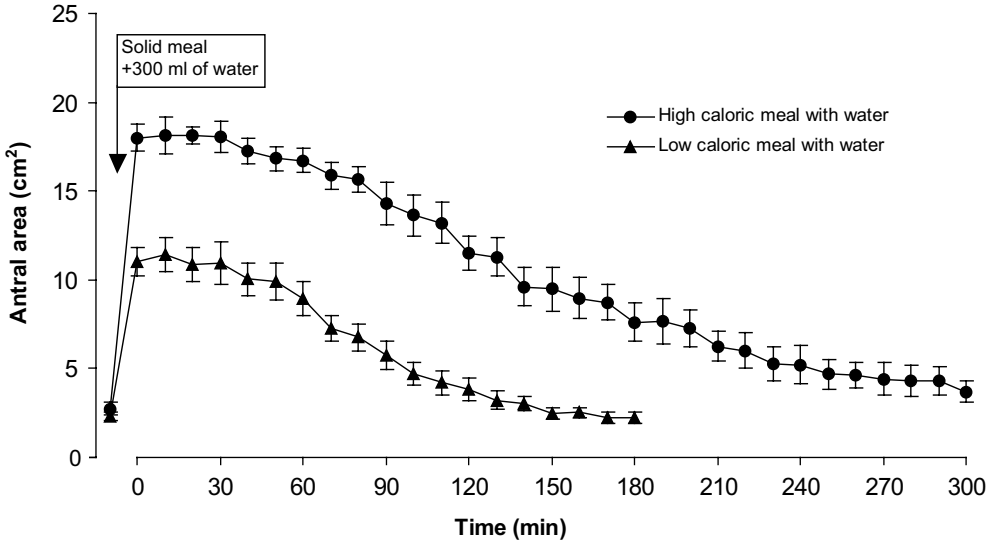

Fig. 1. Changes in antral area determined by ultrasonography after consumption of a low and a high caloric meal together with 300 ml of water. Results are means ± SEM of eight subjects for each meal.

RESULTS

Gastric emptying of high and low caloric solid meals with water

The changes in the antral area determined by ultrasonography after application of the low and high caloric solid meal with 300 ml of water are shown in Fig. 1.

Gastric half emptying time t(1/2) of the high caloric meal was significantly longer (131.3 ± 7 min) than that of the low caloric meal (75 ± 5.4 min). The lag phase t(lag) of the high caloric meal (48.1 ± 6.5 min) was also significantly longer than t(lag) of the low caloric meal (35.6 ± 4.1 min). The gastric emptying phase, the calculated time between the beginning of the emptying process t(lag) and the time when the antral area is reduced to 50% of the maximal gastric area t(1/2) was also significantly longer for the high caloric meal (83.1 ± 7.4 min) than for the low caloric meal (39.4 ± 3.2 min).

Effect of beer and 4% ethanol on gastric emptying of a high caloric meal

The gastric half emptying time t(1/2) with beer was 163.1 ± 11 min, and with a solution containing an equivalent ethanol concentration (4%) it was 158.8 ± 9.3 min (Fig. 2a). The gastric half emptying times with 11.4% glucose (isocaloric control for beer) and 5.5% glucose (isocaloric control for 4% ethanol) were 168.1 ± 14.4 and 153.8 ± 5 min, respectively. These solutions were emptied at a rate that was 17–28% below that of water (131.3 ± 7 min). The t(1/2) of the ethanol containing solutions and their isocaloric controls were not significantly different from each other.

The ingestion of both glucose solutions (5.5 and 11.4%) resulted in a significant prolongation of the lag phase (65 ± 2.5 and 80 ± 8.7 min, respectively) (Fig. 3a). However, there was no longer a difference between beer (54.4 ± 7 min), 4% ethanol (52.5 ± 6.2 min), and water (48.1 ± 6.5 min).

The emptying phases of the solid meals with the test solutions are shown in Fig. 4a. The emptying phase with beer

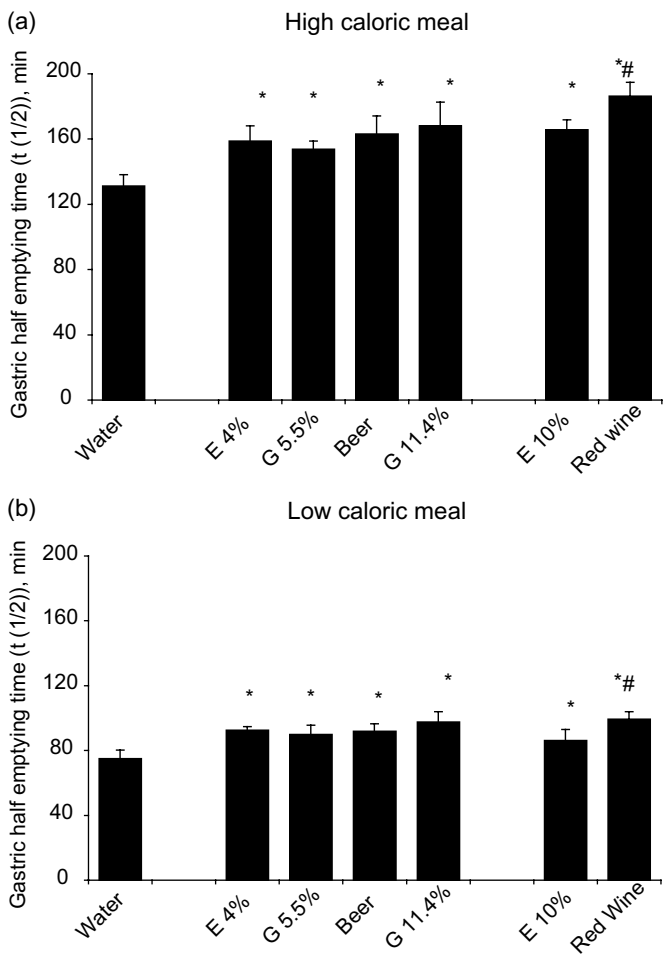

Fig. 2. Gastric half emptying time t(1/2) of the high caloric meal (a) and the low caloric meal (b) with the test solutions. Results are means ± SEM of eight subjects with each meal. G, Glucose (w/v); E, Ethanol (v/v). $^{*}P < 0.05$ compared with water, $\#P < 0.05$ compared with the corresponding ethanol solution.

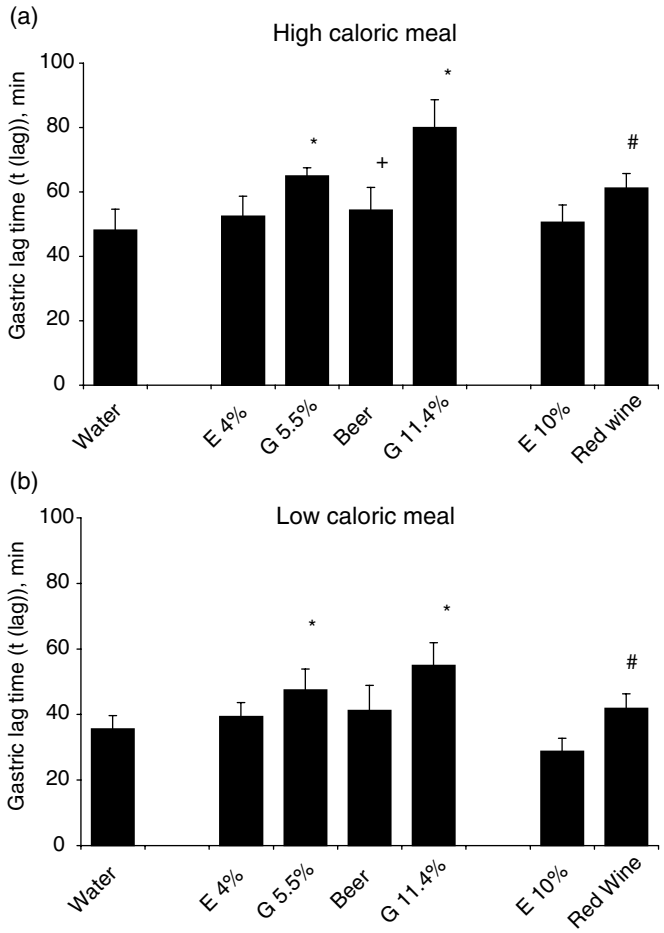

Fig. 3. Gastric lag time t(lag) of the high caloric meal (a) and the low caloric meal (b) with the test solutions. Results are means ± SEM of eight subjects with each meal. G, Glucose (w/v); E, Ethanol (v/v). $*P < 0.05$ compared with water, $\#P < 0.05$ compared with the corresponding pure ethanol solution, $+P < 0.05$ compared with isocaloric control.

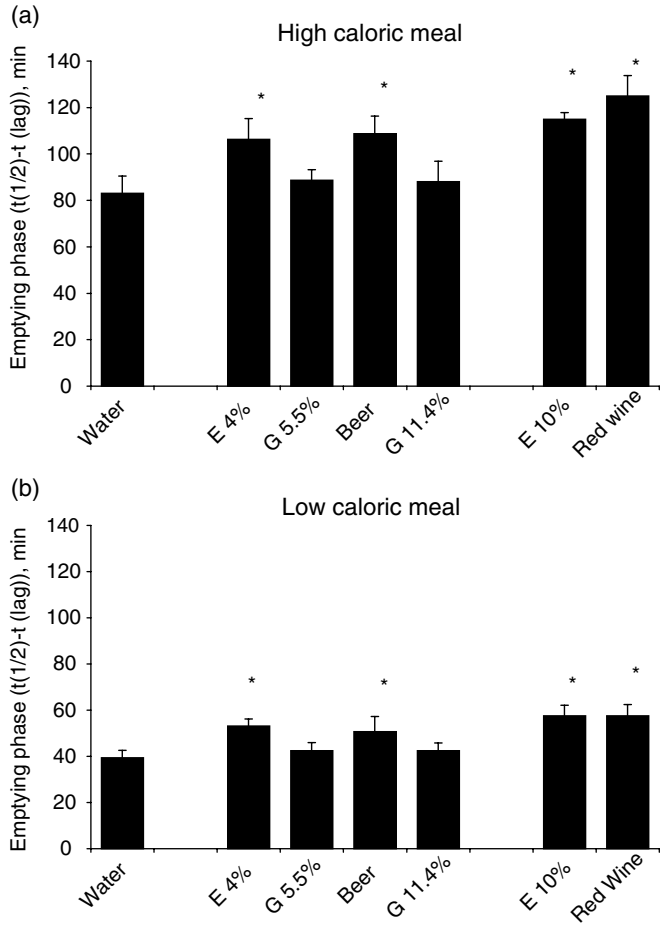

Fig. 4. Gastric emptying phase [t(1/2)-t(lag)] of the high caloric meal (a) and the low caloric meal (b) with the test solutions. Results are means ± SEM of eight subjects. G, Glucose (w/v); E, Ethanol (v/v). $*P < 0.05$ compared with water, $\#P < 0.05$ compared with the corresponding pure ethanol solution.

(108.8 ± 7.5 min) and 4% ethanol (106.3 ± 9 min) was significantly longer than that with water (83.1 ± 7.4 min) and the 5.5 and 11.4% glucose solution (88.8 ± 4.4 and 88.1 ± 8.7 min, respectively).

The effect of different ethanol concentrations on gastric emptying of high caloric solid meals

Gastric half emptying time of 10% ethanol was not significantly longer than that of 4% ethanol (Fig. 2a). However, red wine, which contains an equivalent concentration of 10% ethanol, resulted in a significant delay in t(1/2) compared with 10% ethanol (10% ethanol 165.6 ± 6.2 min, red wine 186.3 ± 8.4 min, $P < 0.05$).

This prolongation resulted from an increase in lag phase (Fig. 3a, 10% ethanol 50.6 ± 5.4 min, red wine 61.3 ± 4.5 min) as well as from an increase in the duration of the emptying phase (Fig. 4a, 10% ethanol 115 ± 2.8 min, red wine 125 ± 8.7 min). However, the increase in lag phase was statistically significant and that of the emptying time was not.

The difference between the emptying parameters for red wine and 10% ethanol were not due to differences in the resulting ethanol concentrations in the blood (Fig. 5).

The effect of the caloric content of the meal

On average the half emptying times of the low caloric meals were 70 min shorter than those of the high caloric meals (Fig. 2b). However, the effect of the different solutions on the gastric half emptying times was independent of the total caloric content of the meal; most importantly ethanol resulted in a significantly slower gastric half emptying time than water (75 ± 5.4 min). Beer (91.9 ± 4.6 min) resulted in an emptying rate similar to 4% ethanol (92.5 ± 5.3 min) and finally red wine (99.4 ± 4.6 min) slowed gastric emptying significantly compared with 10% ethanol (86.3 ± 6.7 min).

Similar to the high caloric meals the lag time of the low caloric meals (Fig. 3b) was significantly longer with the glucose containing control solutions (5.5% glucose 47.5 ± 6.4 min, 11.4% glucose 55 ± 6.9 min) than with water (35.6 ± 4.1 min). The lag time with ethanol and the alcoholic beverages was not significantly different from water (4% ethanol 39.4 ± 4.3 min, 10% ethanol 28.8 ± 4 min). However, red wine (41.9 ± 4.4 min) resulted again in a longer lag time than 10% ethanol.

Similar to the results with the high caloric meal, the emptying phase of the low caloric meal (Fig. 4b) was also significantly

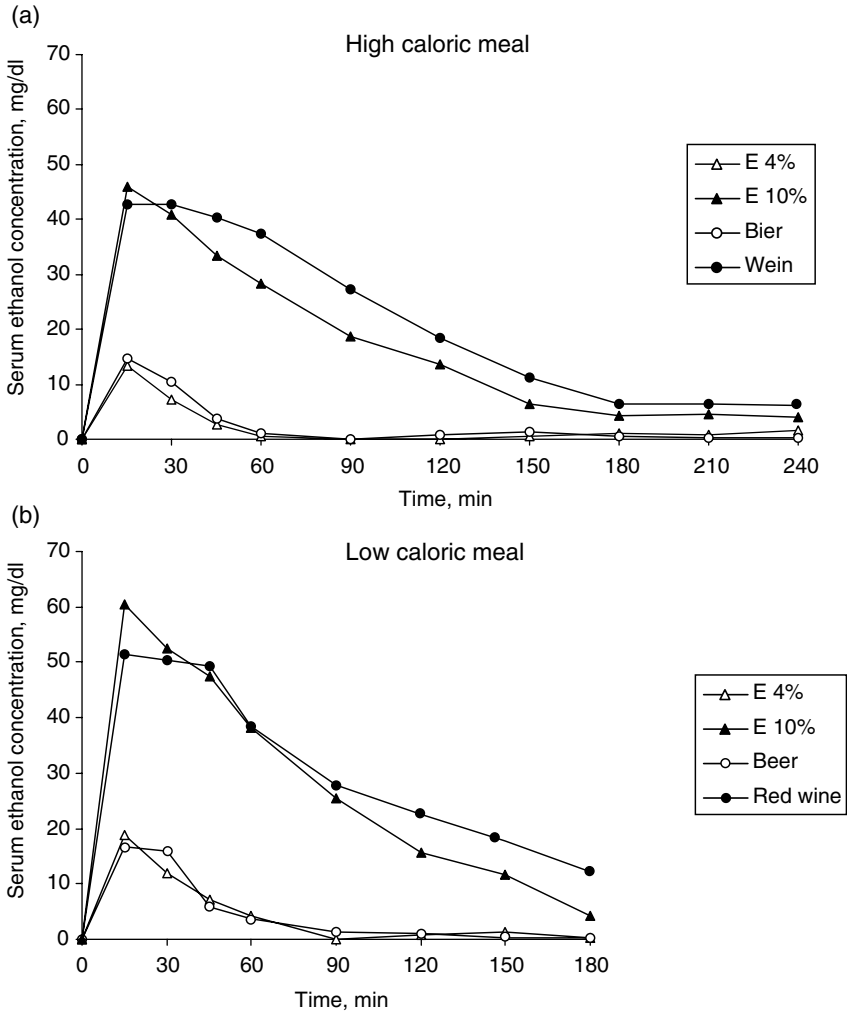

Fig. 5. Serum ethanol concentrations in response to a high caloric meal (a) and a low caloric meal (b) with different concentrations of pure ethanol or alcoholic beverages. Results are means of eight subjects for each meal.

longer after 4 and 10% ethanol, beer, and red wine as compared with that after water ingestion (water 39.4 ± 3.2 min, 4% ethanol 53.1 ± 3.1 min, beer 50.6 ± 6.6 min, 5.5% glucose 42.5 ± 3.4 min, 11.4% glucose 42.5 ± 3.3 min, 10% ethanol 57.5 ± 4.6 min, red wine 57.5 ± 4.9 min).

The effect of the caloric content of the meal on serum ethanol concentration

There was no significant difference between the serum ethanol concentrations after 4% ethanol and beer as well as after 10% ethanol and red wine (Fig. 5). However, the ethanol concentrations after consumption of the alcoholic beverages or pure ethanol were significantly higher when the solutions were consumed with the low caloric than with the high caloric meal.

DISCUSSION

The major results of the present study are: (i) 4% and 10% ethanol both prolonged the gastric half emptying time of solid meals as compared with water. (ii) Beer and red wine both prolonged the gastric half emptying time of solid meals as compared with water. Red wine, but not beer, was emptied at a significantly slower rate than the corresponding ethanol concentration. (iii) Ethanol solutions and alcoholic beverages resulted in longer gastric half emptying times of solid meals by prolonging the emptying phase, while 5.5 and 11.4% glucose prolonged the gastric half emptying time by prolonging the lag phase. (iv) The effect of ethanol and alcoholic beverages on gastric emptying was not dependent on the caloric content of the meals. (v) The same amount of ethanol and alcoholic beverages induced higher serum ethanol concentration when consumed with a low caloric than with a high caloric meal.

In the present study, the gastric half emptying time t(1/2) of the solid meals containing 270 and 740 kcal was prolonged with both ethanol solutions (4 and 10%) than with water. This was mainly caused by a slower gastric emptying rate, whereas the initial lag phase was similar to water. The result showing a longer t(1/2) with the ethanol solutions is similar to the observations by Jian *et al*. (1986), although they used ethanol at an approximate concentration of 25% (v/v). Thus, the

present study extends the observations by Jian *et al*. (1986) to lower concentrations of ethanol and gives an explanation for the delayed gastric emptying with use of ethanol solutions by showing a prolongation of the emptying phase.

Furthermore, we found that the effect of ethanol on gastric emptying of solid meals was not dose-dependent when given in concentrations of 4 and 10%. This is similar to what we have observed by examining the gastric emptying of 4 and 10% ethanol solutions in the absence of solid meals (Franke *et al*., 2004), and suggests the presence of a threshold above which ethanol no longer affects gastric emptying.

Unlike pure ethanol solutions, alcoholic beverages such as beer and red wine contain a number of non-alcoholic ingredients which are osmotically and calorically effective and are, for example responsible for the stimulatory effects on the gastrin secretion (Teyssen *et al*., 2003). Therefore, the ultimate effect of alcoholic beverages on gastric emptying is the result of the interplay of the effects of ethanol itself and these non-alcoholic substances. Compared with water both beer and red wine resulted in a longer t(1/2), and this was due to a significantly longer emptying phase.

An interesting study examining the effect of red wine (9.5%) on gastric emptying of a 337 kcal containing solid meal was performed by Moore *et al*. (1981). They compared pure red wine with a dealcoholised red wine (containing only 1.3% ethanol), in which major parts of the ethanol were exchanged by isocaloric amounts of medium-chain triglycerides. There was no significant difference in the gastric emptying rate of the solid meal when 9.5% red wine was compared with dealcoholised, isocaloric red wine. The present study compared the effect of red wine with that of the corresponding ethanol concentration (10%), and has shown that t(1/2) and t(lag) of solid meals when consumed with red wine were significantly longer than when consumed with the corresponding ethanol concentration (10%), whereas the emptying phase remained nearly the same. For the amount of liquid used, red wine contains ~100 kcal more than 10% ethanol. The difference in the effect on the t(lag) and t(1/2) could be explained by the difference in the caloric content. While Moore *et al*. (1981) showed that an ethanol containing red wine prolongs t(1/2) to a similar extent to that of an equicaloric solution of wine, we showed that the effect of wine on prolonging gastric emptying mostly depends on the non-alcoholic ingredients or the caloric content. One possible explanation is that wine contains ingredients that slow down gastric emptying. In this case, the prolongation in gastric emptying we have seen with red wine would not be related to the caloric content. Since there seems to be no difference between 4 and 10% ethanol in their effect on gastric emptying, there may be no difference between 1.3 and 10% ethanol either. In this case, the effect seen in the Moore study would also result from the additive effect of other ingredients to the baseline effect of ethanol itself.

The effect of beer, on the other hand, is different. The t(1/2) of beer was similar to that of the corresponding ethanol concentration (4%), even though beer, similar to red wine, contains ~100 kcal more than the equivalent ethanol solution (4% ethanol in this case), suggesting that the effect of beer on gastric emptying could be explained by the ethanol content alone. Furthermore, the caloric content of beer can itself induce the changes in gastric emptying seen (there was no difference between 11.4% glucose, 4% ethanol, or beer in their effect on gastric emptying). These findings suggest that in the case of beer the combined effect of the caloric content and the ethanol content are not additive, or alternatively, that there are non-alcoholic ingredients in beer that accelerate gastric emptying of meals.

Based on these findings we would expect that the difference in t(1/2) between beer and red wine is only related to the caloric content of the non-alcoholic ingredients. However, red wine is emptied at a slower rate than beer even though both contained ~100 kcal from non-alcoholic ingredients. We therefore propose that either beer may contain substances that accelerate gastric emptying, and/or red wine may contain substances that slow gastric emptying.

All the described effects were qualitatively similar between the high and the low caloric meals. The longer t(1/2) for all solutions seen in the high caloric meals might be explained by the difference in the caloric content between the high and low caloric meal. We therefore conclude that the effect of ethanol and alcoholic beverages on the gastric emptying of the solid meal does not depend on the caloric content of the meal. Interestingly, the serum ethanol concentration was lower when consumed together with the high caloric meals, supporting the common wisdom that the effect of ethanol is diminished when consumed with fatty meals.

Both glucose solutions (5.5 and 11.4%) induced dose-related prolongation in t(lag), suggesting that glucose solutions can be used in comparing the effects of ethanol solutions with the effects of equicaloric solutions on t(1/2), but not in comparing the two phases of gastric emptying with each other.

In conclusion, both ethanol concentrations (4 and 10%) had the same inhibitory effect on t(1/2), despite different caloric contents. Red wine and beer showed diverging effects on gastric emptying of solid meals that cannot be explained based on the difference in caloric or ethanol content. This suggests a role of other non-alcoholic ingredients on gastric emptying. The regulatory (neuronal and/or humoral) mechanisms by which ethanol and alcoholic beverages affect gastric emptying remain to be elucidated.

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