Original Article

The relationship of gallbladder motility with mixed diets which contains various quality and quantity of fat

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Abstract

Purpose. To evaluate gallbladder motility on ultrasonography after the ingestion of different forms and quantities of fat.

Methods. After a fast, 111 volunteers underwent ultrasonography to measure gallbladder volumes before, 30 min, and 60 min after ingesting Calorie Mate Liquid®, Calorie Mate Jelly®, Terumeal 2.0®, or Terumeal 2.0 α ®, which are used as nutritional supplements. The Calorie Mate products contain 4.4 g of fat, while the Terumeal products contain 15 g of fat. Most of the fat in these products is composed of long-chain fatty acids except for Terumeal 2.0 α ®, in which 15% of the fat is composed of medium-chain fatty acids. Gallbladder volume and the ejection fraction were measured using the ellipsoid method.

Results. There were significant differences in gallbladder volume before, 30 min, and 60 min after taking Calorie Mate Liquid® and Terumeal 2.0 α ®, and in gallbladder volume before and 30 min after taking Calorie Mate Jelly® and Terumeal 2.0®. There were significant differences in the 30-min ejection fraction between Calorie Mate Jelly® and Calorie Mate Liquid® and Terumeal 2.0 α ®, and in the 60-min ejection fraction between Calorie Mate Jelly® and Terumeal 2.0® and Terumeal 2.0 α ®. There were no other significant differences.

Conclusions. Calorie Mate Liquid®, which contains 4.4 g of fat, can be used as an appropriate gallbladder stimulant. Gallbladder contractions were weaker with jellies than with others; thus, jelly meals are not appropriate for evaluating gallbladder contraction. There was no difference in gallbladder contraction between the meal containing a medium-chain fatty acid component of 15% and the other meals.

（Key words: gallbladder motility, medium-chain fatty acids, ellipsoid method, CalorieMate®, Terumeal®）

Introduction

It is important to evaluate gallbladder function in order to treat asymptomatic gallstone patients[1]. Gallbladder malfunction is also related to cholecystitis[2], adenomyomatosis[3], diabetes mellitus[4-5], chronic pancreatitis[6], and other conditions. Large-scale studies of gallbladder function in these diseases can be done

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if there are examinations that can easily evaluate gallbladder function. Ultrasonography[7], drip infusion cholecystography, and computed tomography[8] are currently used to assess gallbladder volume. Previous reports have shown that two egg yolks are a useful gallbladder stimulant[5]; however, there are concerns about egg-related taste and sanitation issues. Therefore, a safe and easy gallbladder stimulant needs to be identified, since there are no such commercially available products.

Few reports have shown that gallbladder contraction differs depending on the fat content[9], though in clinical practice, the acute cholecystitis patients' meal is usually fat-restricted.

The purpose of this study was to evaluate gallbladder motility using ultrasonography after the ingestion of nutritious foods that contain fat in different forms and quantities in order to identify an appropriate gallbladder stimulant. We reported a mixed diet, Calorie Mate Liquid®, produced by Otsuka Pharmaceutical group, is useful as a gallbladder stimulant in our preliminary report[10]. We reassessed it with more participants and compared with other products. Furthermore, differences in gallbladder contraction after long-chain and medium-chain fatty acid ingestion were assessed.

Methods

One hundred and eleven healthy volunteers (89 males, 22 females) were included in the study. Their mean age was 23.1 years (21-36 years). All participants gave their written informed consent. Institutional review board approval was obtained before the study began.

After a 12-hour fast, all volunteers underwent ultrasonography to measure gallbladder volumes before, 30 min, and 60 min after taking mixed diets. In previous studies, the gallbladder contraction peaked at 60 min after egg yolks administration[11-12] and at 35 min after ingestion of a liquid meal with 13g of fat[13]. Therefore, we chose these timing. Mixed diets are Calorie Mate Liquid®, Calorie Mate Jelly®, Terumeal 2.0®, or Terumeal 2.0 α®, which are used clinically as nutritional supplements. The former two are produced by Otsuka Pharmaceutical group and the latter two are produced by Terumo Corporation. The Calorie Mate products provide 200 kcal and contain 4.4 g of fat, while the Terumeal products provide 400 kcal and contain 15 g of fat (Table 1). Most of these fat consists of long-chain fatty acids except in Terumeal 2.0 α®, in which medium-chain fatty acids account for 15% of the fat.

Table 1. Mixed diets used as gallbladder stimulants

	Calorie Mate Liquid® (n=17)	Calorie Mate Jelly® (n=20)	Terumeal 2.0® (n=37)	Terumeal 2.0α® (n=37)
Volume	200ml	215g	200ml	200ml
Energy(kcal)	200	200	400	400
Fat(g)	4.4	4.4	15	15
Long-chain fatty acid(%)	100	100	100	85
Medium-chain fatty acid(%)	0	0	0	15
Protein(g)	10	7.6	14.5	14.5
Glucide(g)	28.6	32.5	52	52

During ultrasonography, longitudinal and cross-sectional diameters were measured twice, and then the means of the diameters were used to calculate the gallbladder volume using the ellipsoid method[7] with the formula below:

GB volume（ml）= 0.52 × GB length × GB width × GB height

The gallbladder ejection fraction（GBEF）was calculated 30 and 60 minutes after ingestion of the four products using the following formula:

GBEF（%）= ｛(GB volume before stimulant - GB volume after 30 or 60 min taking stimulant)/（GB volume before stimulant)｝× 100

Values are presented as mean ± SD. Paired t-tests were used to compare gallbladder volumes before and after product ingestion, and unpaired Student's *t*-tests were used to compare the gallbladder ejection fractions with the different products. A $P < 0.05$ was considered to be statistically significant.

Results

There were significant differences in the gallbladder volume before, 30 min, and 60 min after taking Calorie Mate Liquid® and Terumeal 2.0 *α* ®, while there were significant differences in the gallbladder volume before and only 30 min after taking Calorie Mate Jelly® and Terumeal 2.0®（Figure 1-4）.

The mean ± SD 30-min gallbladder ejection fractions after Calorie Mate Liquid®, Calorie Mate Jelly®, Terumeal 2.0®, and Terumeal 2.0 *α* ® were 52.6% ±27.9%, 19.1% ±33.8%, 51.6% ±62.7%, and 47.1% ±46.7%, respectively（Figure 5）, while the mean 60-min gallbladder ejection fractions were 49.5% ± 49.9%, 4.82% ±80.5%, 70.0% ±37.8%, and 59.2% ±28.3%, respectively（**Figure 6）. The 30-min gall**bladder ejection fraction after taking Calorie Mate Jelly® was significantly different from that after taking Calorie Mate Liquid®（p=0.002）and Terumeal 2.0 *α* ®（p=0.03）. The 60-min gallbladder ejection fraction after taking Calorie Mate Jelly® was significantly different from that after taking Terumeal 2.0®（p=0.0002）and Terumeal 2.0 *α* ®（p=0.0006）. There were no other significant differences.

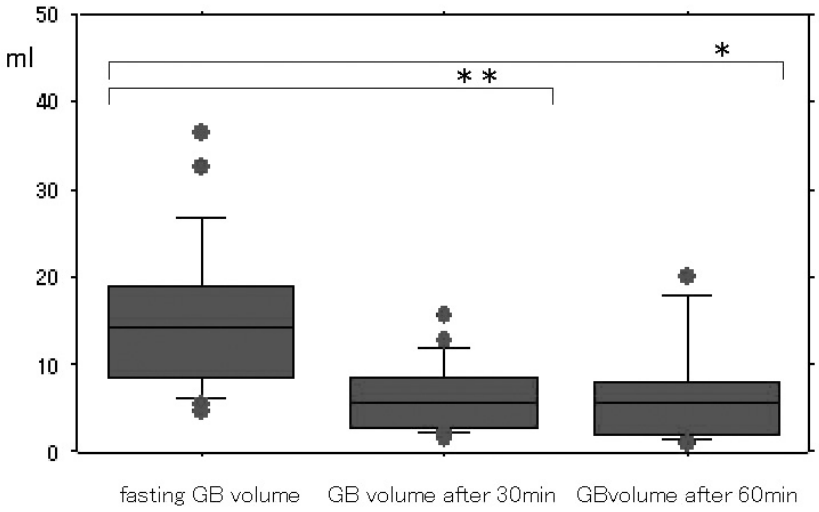

Fig 1. Gallbladder volumes before and after ingesting Calorie Mate Liquid®
*: P < 0.05, **: P < 0.01

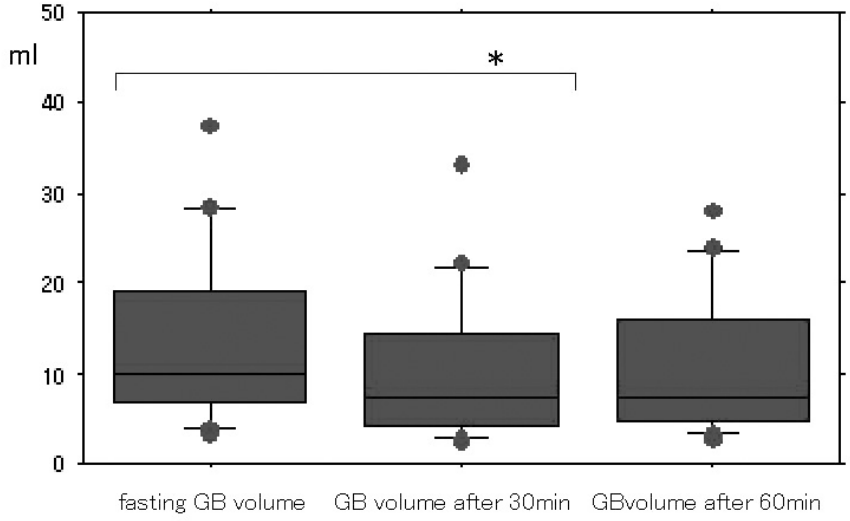

Fig 2. Gallbladder volumes before and after ingesting Calorie Mate Jelly®

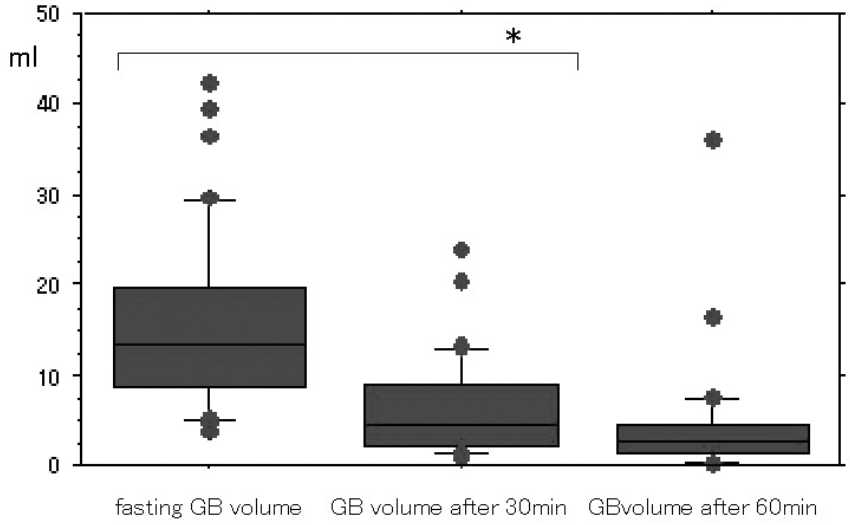

Fig 3. Gallbladder volumes before and after ingesting Terumeal 2.0®

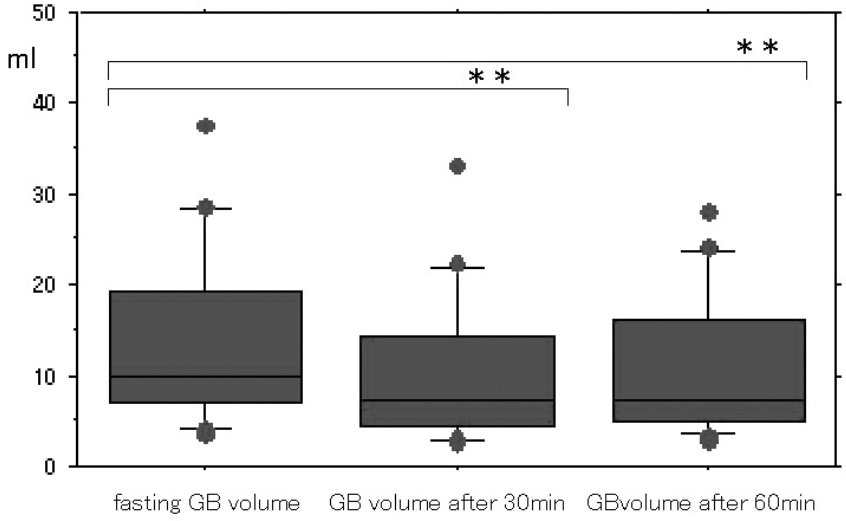

Fig 4. Gallbladder volumes before and after ingesting Terumeal 2.0α®

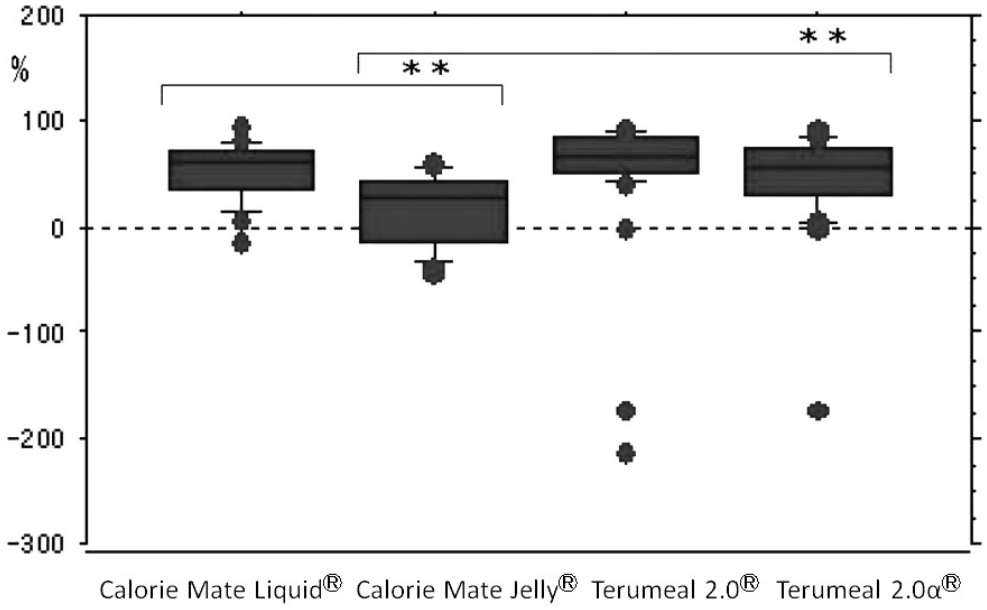

Fig 5. Gallbladder ejection fractions 30 min after ingesting gallbladder stimulants

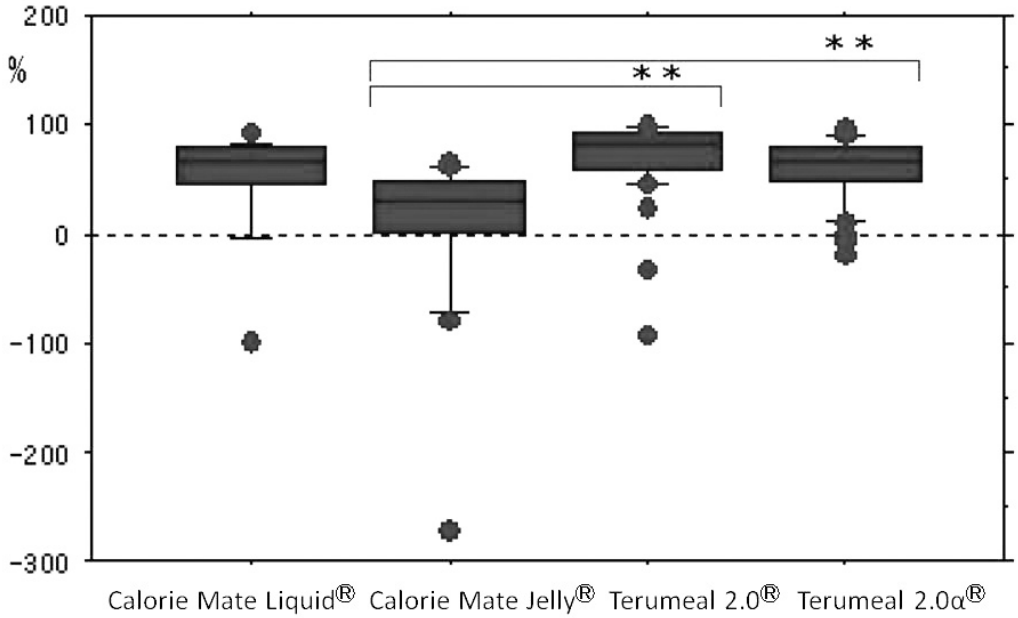

Fig 6. Gallbladder ejection fractions 60 min after ingesting gallbladder stimulants

Discussion

The present study found that Calorie Mate Liquid®, which contains 4.4 g of fat, is an appropriate gallbladder stimulant. Gallbladder contractions were weaker after the ingestion of jelly products than after other stimulants; thus, jelly-type meals are not appropriate for evaluating gallbladder contraction. There was no difference in gallbladder contraction between the meal containing a medium-chain fatty acid component of 15% and the other meals.

A previous report stated that, based on the ellipsoid method, the 30-min gallbladder ejection fraction was 30-48% and the 60-min gallbladder ejection fraction was 55-70% after the ingestion of two egg yolks[11-12]. In the present study, mixed diets that contained 4.4 g and 15 g of fat were used, and both of them caused gallbladder contractions as well as two egg yolks which contain an average of 11 g of fat. It has been reported that a meal containing 8 g of fat caused cholecystokinin release and gallbladder contraction, though a meal containing 25 g of fat caused greater cholecystokinin release and gallbladder contraction[14]. Another report found that even oral water or sham feeding caused significant gallbladder contraction without cholecystokinin release, which was eliminated by premedication with atropine[15]. These findings suggest that not only cholecystokinin but also the cholinergic pathway appear to play important roles in the control mechanism of gallbladder contraction. This notion is further supported by the fact that patients who had gastrectomy, particularly those with vagotomy, have an increased risk of gallbladder disease[16]. Therefore, the products that were assessed in the present study appear to have had a stimulant effect on the gallbladder. With respect to fat quantity, no difference in gallbladder contraction was found between 4.4 g and 15 g of the liquid products; this finding is not consistent with previously published studies[14-15].

Though Calorie Mate Liquid® and Calorie Mate Jelly® contained the same amount of fat, there were significant differences in the 30-min ejection fractions. The jelly needs stomach digestive movement to reach the duodenum, where cholecystokinin is released, before the gallbladder contracts. Thus, gallbladder contractions were weaker after the ingestion of jellies than after the ingestion of liquid stimulants. Thus, it would appear that a jelly-type meal is not an appropriate stimulant for the evaluation of gallbladder contraction.

Significant gallbladder contractions occurred 30 and 60 min after the ingestion of a liquid meal containing 4.4 g of fat. It might be of no use to restrict fat in the meal given to patients recovering from acute cholecystitis if it contains more than 4.4 g of fat, though we usually restrict the amount of fat in such meals to 20-30 g per day to prevent gallbladder contraction. Furthermore, given that weaker gallbladder contractions occurred after the jelly-type than after the liquid-type meals, usual meals may have different effects on gallbladder contraction. Further studies are needed to fully explore these issues.

Medium-chain fatty acids do not result in cholecystokinin excretion and gallbladder contraction[17-19]. However, in the present study, there was no significant difference in gallbladder contraction between the meal in which medium-chain fatty acids accounted for 15% of the fat and the other meals. Further studies involving meals with other proportions of medium-chain fatty acids are needed.

In conclusion, Calorie Mate Liquid® is as an appropriate gallbladder stimulant that can be used in large-scale studies of diseases associated with gallbladder malfunction.

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質および量の異なる脂質を含む食品による胆嚢収縮の評価

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要　約

【目的】質および量の異なる脂質を含む食品を摂取後の胆嚢収縮について評価する。

【方法】絶食後のボランティア111名を対象として，栄養補助食品であるカロリーメイト缶®，カロリーメイトゼリー®，テルミール2.0®，テルミール2.0α®の摂取前，摂取後30分，60分の胆嚢容積を腹部超音波検査にて求めた。カロリーメイト製品は脂質を4.4g，テルミール製品は15g含有し，テルミール2.0α®では脂質の15％が中鎖脂肪酸，それ以外はおおむね長鎖脂肪酸で構成されている。胆嚢容積はEllipsoid法で求め，胆嚢収縮率を算出した。

【結果】カロリーメイト缶®，テルミール2.0α®経口投与30分後，60分後の胆嚢容積は投与前に比して有意差を認め，カロリーメイトゼリー®，テルミール2.0®では30分後のみに有意差を認めた。30分後の胆嚢収縮率はカロリーメイトゼリー®とカロリーメイト缶®，カロリーメイトゼリー®とテルミール2.0α®の間でそれぞれ有意差を認めた。60分後の胆嚢収縮率ではカロリーメイトゼリー®とテルミール2.0®，カロリーメイトゼリー®とテルミール2.0α®の間でそれぞれ有意差を認めた。

【結論】カロリーメイト缶®は脂質を4.4gと比較的少量しか含有しないものの，胆嚢収縮剤として使用可能である。ゼリーを用いた場合胆嚢収縮は他に比較して弱いため，胆嚢収縮能評価には適さない。中鎖脂肪酸の配合が15％では胆嚢収縮に違いは見られなかった。

（キーワード：胆嚢収縮，中鎖脂肪酸，Ellipsoid法，カロリーメイト®，テルミール®）

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