Alcohol Consumption in Obese Patients Before and After Gastric Bypass as Assessed with the Alcohol Marker Phosphatidylethanol (PEth)

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Abstract

Introduction Roux-en-Y gastric bypass (RYGB) causes more rapid and enhanced absorption of alcohol. RYGB patients have also been reported to use more inpatient care for alcohol-related disease than do patients after other bariatric procedures. The present study was designed to evaluate alcohol consumption level before and after gastric bypass using a sensitive and specific alcohol biomarker.

Materials and Methods Two separate consecutive groups of patients and a group of healthy blood donors, as reference group, were included in the study. Alcohol intake was assessed using the alcohol marker phosphatidylethanol (PEth) at preoperative baseline and at 1 and 2 years postoperatively. In the first patient group ($n = 133$), neither surgeon nor patient was informed about the results of PEth testing. In the second group ($n = 214$), PEth results above $0.30 \mu\text{mol/L}$ were considered to indicate excessive alcohol consumption and led to preoperative alcohol counseling. The groups were followed for 2 and 1 year, respectively.

Results PEth results were significantly lower in both patient groups at baseline as well as postoperatively compared with the reference group. In both patient groups, there was a significant increase in PEth values at postoperative follow-up compared to baseline.

Conclusions Several physiological changes postoperatively have to be considered when interpreting PEth results in obese patients with dramatic weight reductions. According to results for PEth, obese patients treated with bariatric surgery would seem to have lower alcohol consumption compared with the reference group. Although slightly increasing their PEth values postoperatively, the RYGB patients did not reach the PEth values of the reference group.

Keywords Alcohol · Alcohol abuse · Alcohol marker · Gastric bypass · Phosphatidylethanol

Introduction

Roux-en-Y gastric bypass (RYGB) is a commonly performed bariatric procedure. In the USA alone, more than 50,000 RYGBs are performed each year, i.e., approximately 45% of all bariatric procedures [1]. RYGB is even more widely used in the Nordic countries and presently accounts for 82% of all bariatric surgery in the Scandinavian Obesity Registry, SOReg, [2]. Gastric bypass leads to profound changes in eating behavior and metabolism, in turn leading to dramatic weight reduction and often the disappearance of obesity-related comorbidities [3]. Although these effects lead to increased life expectancy and improved quality of life, the operation has also been reported to have side effects [4, 5]. RYGB has been reported to cause more rapid and enhanced absorption of alcohol resulting in a faster rise and higher peak blood alcohol concentrations [6–8]. In a retrospective population-based cohort study, Östlund et al. found that

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gastric bypass patients postoperatively used more inpatient care for alcohol-related disease compared with patients operated with gastric band or vertical banded gastroplasty [9]. In another prospective cohort study of RYGB patients, the presence of alcohol use disorders increased in the second postoperative year compared to the year prior to surgery [10].

So far, alcohol consumption in bariatric patients has been assessed with different questionnaires, e.g., the Alcohol Use Disorders Identification Test (AUDIT) [11]. Since self-reported alcohol consumption can be biased, an alternative approach would be to assess alcohol consumption with a specific alcohol marker, e.g., phosphatidylethanol (PEth). PEth is a collective term for a group of abnormal phospholipid homologs, the most prevalent being PEth 16:0/18:1, formed in the membranes of erythrocytes only in the presence of ethanol [12]. Being an alcohol metabolite, the theoretical specificity of PEth as an alcohol marker is 100% [12]. There is a correlation between alcohol consumed and PEth value [13, 14]. PEth has a half-life of approximately 1 week, thus reflecting alcohol consumption during several weeks before sampling [15, 16].

The present study was designed to examine alcohol consumption level in obese patients selected for RYGB and investigate whether gastric bypass induces a change in consumption level as estimated with a specific and sensitive alcohol marker.

Materials and Methods

Patient Selection and Outpatient Routines Patients were seen preoperatively by a bariatric surgeon and standard anthropometric data were obtained. The indications for gastric bypass followed the European guidelines on surgery of severe obesity [17]. Patients were informed at baseline about the pros and cons of surgery, including the accentuated and protracted effects of alcohol intake. All patients were informed in writing that a “standard battery” of laboratory tests was to be performed at baseline and at follow-up (FU). Two consecutive groups of gastric bypass patients were recruited into the study.

Group 1: During 1 year, 133 patients were included and followed annually for 2 years. The first year of FU was in our own outpatient unit and the 2-year FU was performed by the patients’ primary care physician. PEth results but no measured body weights were available at the 2-year FU.

Group 2: When all patients had been included in group 1, a second group of patients was recruited and followed for 1 year ($n = 214$).

In group 1, PEth testing was included but the results were blinded to the attending surgeon as well as to the patient. In group 2, patients were made aware that the test was taken and of its result. PEth results $> 0.30 \mu\text{mol/L}$ (indicative of excessive alcohol consumption) occurred in only two cases at the first visit and led to special counseling about alcohol intake.

Patients then had to show, by a second test 3 weeks later, that they were able to minimize their alcohol intake (which both patients successfully managed) before being accepted for operation.

Operative Procedure The surgical procedure has been described in detail previously [18]. In brief, a small gastric pouch (15 mL) is created, and the jejunum brought up, first as an “omega” loop in an antecolic and antegastric fashion. A gastrojejunostomy is created using linear stapling, then a side-to-side enteroanastomosis is likewise stapled, and finally, the omega loop is transected between the anastomoses. Routine limb lengths were 150 cm for the alimentary limb and 60 cm for the bilio-pancreatic limb. The mesenterial openings were closed.

Reference Values A matched group of 323 healthy blood donors of the same age range and from the same catchment area as that of the study groups was created for comparison. Blood samples for PEth were collected after informed consent during the first year of enrolment of patients in group 1. Neither the blood donors nor the patients knew in advance that blood sampling for PEth was to be performed upon inclusion in the study.

PEth Determination Whole blood concentration of PEth 16:0/18:1 was measured by liquid chromatography tandem-mass spectrometry, described in detail previously [19]. There is an agreement between Swedish laboratories on how to report and interpret a PEth value. Thus, no numerical results are reported $< 0.05 \mu\text{mol/L}$ and such values are interpreted as low (moderate) or no consumption, whereas values > 0.30 are interpreted as corresponding to excessive consumption [19, 20]. Hence, the limit of quantification was set to $0.05 \mu\text{mol/L}$ and used as cut off in the present study.

Statistics Data were prospectively stored in a proprietary database. Descriptive statistics and statistical evaluation were done with SPSS for Windows (version 22, IBM Corp., Armonk, NY). Friedman testing was performed for multiple comparisons. The Wilcoxon signed rank test, Fisher’s exact test, and the Mann-Whitney U test were used as appropriate for within and between groups analysis. Statistical significance was set at $p < 0.05$.

Results

All operations were performed according to standard protocols. There were no major complications and postoperative hospital time was 1.1 days. Patient anthropometric and weight loss data for both groups are shown in Table 1. There were statistical differences between the groups according to gender,

Table 1 Anthropometric and weight loss data for groups 1 and 2. In group 1, PEth result was blinded for the surgeon and the patient and in group 2, increased PEth result preoperatively lead to special counseling

	Group 1 (<i>n</i> = 131)	Group 2 (<i>n</i> = 214)	Reference group (<i>n</i> = 323)	Statistical difference (<i>p</i> value) ¹	
				Between groups 1 and 2	Between the reference group and groups 1 and 2 respectively
Gender, female <i>n</i> (%)	84 (64)	175 (82)	160 (50)	< 0.000	<i>p</i> = 0.005/ <i>p</i> < 0.000
Age (years) mean (SD)	47 (8.9)	42 (11)	40 (14)	< 0.000	<i>p</i> < 0.000/ <i>p</i> = 0.335
BMI at baseline (kg/m ²) mean (SD)	43 (6.3)	42 (5.7)		0.036	
BW at baseline (kg) mean (SD)	127 (22)	119 (21)		0.001	
BW at FU _{1y} (kg) mean (SD)	93 (17)	80 (16) ²		< 0.000	
BW loss first year (kg) mean (SD)	34 (14)	39 (12) ²		< 0.000	
%EWL first year mean (SD)	66 (22)	85 (22) ²		< 0.000	

SD standard deviation, BMI body mass index, BW body weight, FU_{1y} 1-year FU, EWL excess weight loss

¹ Gender is tested with Fisher's exact test; the rest of the parameters are tested with Mann-Whitney *U* test

² BW is missing for one patient

age, anthropometric, and weight loss data, but not in PEth results neither at baseline (*p* = 0.53) nor at 1-year FU (*p* = 0.41).

PEth Results in Groups 1 and 2 and Reference Group (Table 2 and Fig. 1) In both patient groups, a minority of the patients had PEth results ≥ 0.05 $\mu\text{mol/L}$ at all blood sampling occasions. In group 1, there was a number of drop-outs at the 2-year FU (*n* = 96 at 2-year FU, compared with *n* = 133 at baseline and *n* = 131 at 1-year FU); for further details *v.i.* and Table 3. Ninety-four patients in group 1 had complete FU, i.e., PEth results at baseline and at 1- and 2-year FU. In the reference group of blood donors, 44% had PEth ≥ 0.05 $\mu\text{mol/L}$, the same proportion for males and females.

In comparison with the reference group, both patient groups had a significantly lower proportion of PEth results

≥ 0.05 $\mu\text{mol/L}$, at baseline (*p* < 0.000) as well as at 1-year FU (*p* < 0.000). Likewise, group 1 had a lower proportion of PEth values ≥ 0.05 $\mu\text{mol/L}$ compared with the reference group at the 2-year FU (*p* = 0.012).

Comparison of PEth Results in Groups 1 and 2 The hypothesis that RYGB induces higher levels of alcohol intake in susceptible individuals was further tested by analyzing 1- and 2-year results stratified by their preoperative baseline values (Table 2). For group 1, Friedman testing indicated differences within the PEth values (*p* < 0.001). Further testing with Wilcoxon signed rank test showed no significant difference (*p* = 0.068) between baseline and 1-year PEth results, but showed significantly higher PEth results both at the 2-year FU compared with baseline (*p* = 0.016) and at the 2-year FU compared with the 1-year FU (*p* = 0.002). Twenty-eight percent of the patients in group 1 dropped

Table 2 Distribution of PEth results in the groups and statistical difference in PEth results between sampling occasions in groups 1 and 2 and the reference group

		Percentage of patients with PEth ≥ 0.05 $\mu\text{mol/L}$	Statistical difference (<i>p</i> value)		
			Over baseline values ¹	Between FU _{1y} and FU _{2y} values ¹	Between patient and reference groups ²
Group 1	Baseline (<i>n</i> = 133)	17			< 0.000
	FU _{1y} (<i>n</i> = 131)	21	0.068		< 0.000
	FU _{2y} (<i>n</i> = 94)	26	0.016	0.002	0.012
Group 2 (<i>n</i> = 214)	Baseline	12			< 0.000
	FU _{1y}	18	< 0.000		< 0.000
Reference group (<i>n</i> = 323)		44			

FU_{1y} 1-year FU, FU_{2y} 2-year FU

¹ Tested with Wilcoxon signed rank test

² Tested with Mann-Whitney *U* test

Fig. 1 Percentage of the individuals with PEth results $\geq 0.05 \mu\text{mol/L}$ in the three different groups: group 1 baseline $n = 133$, FU_{1y} $n = 131$, and FU_{2y} $n = 96$, group 2 $n = 214$, and reference group $n = 323$. FU_{1y} 1-year FU, FU_{2y} 2-year FU

out at the 2-year FU. Comparison between the patients that completed the study and those who dropped out at the 2-year FU is shown in Table 3. Drop-outs were younger ($p = 0.039$) and had a higher proportion of PEth results $\geq 0.05 \mu\text{mol/L}$ ($p = 0.003$) at 1-year FU.

In group 2, the frequency of PEth results $\geq 0.05 \mu\text{mol/L}$ was significantly higher at 1-year FU compared with baseline ($p < 0.000$).

Discussion

The obesity epidemic has made RYGB common since bariatric surgery is the only treatment achieving long-term weight reduction [21]. Considering the large number of patients operated, it is important to address possible drawbacks with the surgical procedure, e.g., altered alcohol metabolism and increased risk for alcohol use disorders.

Since self-reported alcohol consumption can be unreliable, there is a need for methods that can provide objective information about patients' alcohol use [22–24]. PEth is an alcohol marker with high sensitivity in groups with excessive alcohol consumption (96–100%) [13, 14, 25]. The clinical sensitivity has been more varied in groups with low or moderate alcohol consumption, largely due to differences in sensitivity between analytical methods [14, 16, 26, 27]. Hence, it has been reported that PEth can be used as a marker for low or moderate alcohol consumption using a method with improved analytical sensitivity [28]. In the present study, we used PEth as an objective marker of alcohol consumption level and of potential changes in its level after RYGB.

There is a correlation between PEth and alcohol consumption level, PEth likely reflecting the exposition to alcohol over time, i.e., average blood alcohol concentration during several weeks before sampling [13, 14]. However, in addition to the

Table 3 Comparison within group 1 between the patients with complete FU (baseline, 1- and 2-year FU) and the drop-out patients (drop-outs defined as patients missing PEth result at 2-year FU)

	Patients with complete FU in group 1 ($n = 94$)	Drop-out patients in group 1 ($n = 37$)	Statistical difference between patients with complete FU and drop-outs (p value) ¹
Gender, female n (%)	61 (65)	23 (62)	0.840
Age (years) mean (SD)	48 (8.5)	44 (9.3)	0.039
BW at baseline (kg) mean (SD)	129 (22)	123 (23)	0.164
BW at FU _{1y} (kg) mean (SD)	95 (17)	88 (18)	0.056
Percentage of patients with PEth $\geq 0.05 \mu\text{mol/L}$ at baseline	14	27	0.078
Percentage of patients with PEth $\geq 0.05 \mu\text{mol/L}$ at FU _{1y}	15	38	0.003
Percentage of patients with PEth $\geq 0.05 \mu\text{mol/L}$ at FU _{2y}	27		

SD standard deviation, FU_{1y} 1-year FU, FU_{2y} 2-year FU

¹ Gender is tested with Fisher's exact test; the other parameters are tested with Mann-Whitney U test

amount of alcohol consumed, body mass also influences blood alcohol concentration as indicated in the Widmark's formula [29]. Weight loss will lead to a reduction not only in adipose tissue but also in total body water, which was shown in a study on six obese women treated with bariatric surgery [30]. The weight development curves for our two patient groups show drastic reductions in body weight suggesting corresponding reductions in total body water as well. PEth values showed a significant increase between baseline and 1-year FU in group 2. Although not statistically significant ($p = 0.068$), a similar tendency between baseline and 1-year FU was seen in group 1 (Fig. 1). Since ethanol is distributed in total body water, the same amount of ethanol consumed will result in higher blood ethanol concentrations postoperatively and consequently to increased PEth values. The increased PEth results at 1-year FU can thus be due to the decrease in total body water and does not necessarily need to be a consequence of increased alcohol consumption. The weight reduction at 1-year FU was more pronounced in group 2 compared with group 1 (Table 1). This may at least partly explain the significant increase in PEth values at 1-year FU seen in group 2 but not in group 1.

In group 1, there is a significant increase in PEth results at 2-year FU, which is in line with King et al., where the alcohol consumption increased at the 2-year FU according to AUDIT [10]. Weight data for our 2-year FU are not available, but other studies show that weight reduction has ceased already at 1-year FU [4]. The results in group 1 suffer from 28% drop-out rate. The drop-outs had significantly higher PEth results at 1-year FU compared to the patients with complete FU (Table 3), so it is possible that the frequency of PEth ≥ 0.05 $\mu\text{mol/L}$ at 2-year FU would have been higher if more patients had completed the study. Hence, this may indicate an increase in alcohol consumption between 1 and 2 years postoperatively. Nonetheless, neither patient group reached the PEth values obtained in the reference group of healthy blood donors.

It seems reasonable that further changes postoperatively can contribute to increased blood alcohol concentrations, resulting in higher PEth despite unaltered alcohol intake. Gastric emptying of liquid seems to be faster after RYGB resulting in a faster absorption of alcohol [31]. In two different studies, RYGB patients were their own controls and were given the same dose of alcohol pre- and postoperatively. Increased peak alcohol level and longer time to reach zero concentration were seen postoperatively compared to preoperatively [7, 8]. Another possible mechanism that can contribute to an increased alcohol exposure is the decreased contact with gastric mucosa and thereby to the action of gastric alcohol dehydrogenase after RYGB. In a study on patients after total gastrectomy compared with controls, gastric alcohol dehydrogenase proved to be responsible for a significant part of the first pass metabolism of alcohol [32].

Almost half of the blood donors in the reference group had PEth results ≥ 0.05 $\mu\text{mol/L}$. In the study by Kechagias et al., study participants consumed 1 or 2 glasses of wine/day for 3 months. This consumption corresponds to 1.3 or 2.7 alcohol units/day (one unit = 12 g alcohol) and resulted in a median PEth concentration of 0.022 $\mu\text{mol/L}$ after 3 months [28]. Moderate alcohol consumption is defined slightly different in different countries. In the USA, the upper limit for moderate drinking is one drink (one drink = 14 g alcohol) per day for women and up to two drinks per day for men, while in Sweden, the corresponding limits are 9 and 14 units (12 g/unit) per week [33, 34]. This indicates that a significant proportion of the blood donors in the reference group consumed more than moderate amounts of alcohol.

It seems plausible that the weight of the blood donors reflects the "normal" weight in the Swedish population. The prevalence of BMI > 30 is estimated to be 15% in Sweden [35]. Most likely, there is a difference in body weight and total body water content between the patients and the reference group, probably less pronounced at FU as a consequence of the weight reduction. The proportion of PEth results ≥ 0.05 $\mu\text{mol/L}$ is at all time points lower in the patient groups compared with the reference group (Fig. 1). This must not necessarily mean that the patient groups have a lower absolute alcohol intake than the reference group, but rather that their average blood alcohol concentrations were lower.

There was no significant difference in the proportion of PEth ≥ 0.05 $\mu\text{mol/L}$ between groups 1 and 2 neither at baseline nor at the 1-year FU. It is not possible to evaluate whether the preoperative information on PEth in group 2 influenced the outcome.

There are some shortcomings of the present study such as the high drop-out rate and missing body weights at 2-year FU in group 1. Measurement of total body water pre- and postoperatively in the patient groups as well as in the reference group would have been of interest for the interpretation of PEth results. Another point of concern is the FU time; long-term follow-up is advantageous to fully elucidate patterns of alcohol intake after RYGB. However, the fact that we used an objective marker for assessment of alcohol intake provides support for the reliability of our results.

Conclusions

Several physiological changes postoperatively have to be considered when interpreting PEth results in obese patients with a dramatic weight reduction. According to results for PEth, obese patients treated with bariatric surgery would seem to have lower alcohol consumption compared with the reference group of healthy blood donors. Although slightly increasing their PEth values postoperatively, the RYGB patients did not reach the PEth values of the reference group.

Compliance with Ethical Standards

The present study was approved by the Institutional Review Board and the Lund University Ethics committee. It followed the guidelines of the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all patients.

Conflict of Interest Lisa Walther, Carl-Magnus Brodén, and Anders Isaksson declare that they have no conflict of interest. Jan Hedenbro reports personal fees from Medtronic and personal fees from Johnson & Johnson, outside the submitted work.

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