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Original Article

Dentistry Section

Extraoral Halitosis due to Exhaled Acetone in Patients Undergoing Sleeve Gastrectomy

HANADI G ALZAHRANI[1], MOHAMMED A ALSARHAN[2], ABDULLAH ALDOHAYAN[3], FAHAD BAMEHRIZ[4], HAMAD A ALZOMAN[5]

ABSTRACT

Introduction: Bariatric surgery is widely used and considered as one of the most effective treatments for morbid obesity, but it can be associated with medical and dental adverse side-effects. It is frequently associated with major metabolic changes that may lead to extraoral halitosis.

Aim: To assess the role of exhaled acetone produced as a result of weight loss in the production of extra-oral halitosis in patients undergoing bariatric surgery.

Materials and Methods: A prospective longitudinal cohort study was designed from October 2018 to November 2019 and monitored for six months postsurgery. The subjects were patients undergoing sleeve gastrectomy surgery with a Body Mass Index (BMI) of 35-50 kg/m^2. Subjects were divided into two groups of low BMI loss (<5 Kg/m^2) and high BMI loss (≥5 Kg/m^2) postsurgery, Breath samples were collected with a portable breath ketone analyser for measurement of acetone concentrations, and blood samples were taken for measurement of 3-hydroxybutyrate levels. Breath and blood samples were taken at baseline then at one month, three months, and six months postsurgery. All statistical analysis were performed using the SPSS version 22.0 with a significance value of p-value set at p<0.05.

Results: Out of 43 patients enrolled initially, eventually 39 patients completed the study. The mean level of breath acetone was 4.1, 3.4, and 3.8 ppm at one month, three months, and six months, respectively (*p*=0.018). There was a statistically significant increase in breath acetone at one month in patients with a high rate of BMI loss. At one month, the mean blood level of 3-hydroxybutyrate was higher in patients with a high rate of BMI loss than in those with a low rate of BMI loss (1.9 vs. 1.2 mmol/L; *p*=0.049). The levels of breath acetone and blood 3-hydroxybutyrate were significantly correlated at one month (r=0.6, p<0.05).

Conclusion: Rapid weight loss one month after gastric sleeve surgery resulted in high acetone levels suggestive of increased extraoral halitosis in such patients. Increased Acetone levels in breath and 3-hydroxybutyrate in blood are suggestive of increased extraoral halitosis in patients undergoing gastric sleeve surgery particularly within a month after surgery.

Keywords: Bariatric surgery, Breath tests, Ketones, Obesity

INTRODUCTION

Obesity is defined by the World Health Organisation (WHO) as a BMI greater than 30 Kg/m^2. It has been described as an unhealthy accumulation of body fat that occurs because of an imbalance between the amount of food eaten and energy expended [1]. It is considered a worldwide health problem, as it has nearly tripled since 1975 [1]. Obesity and overweight are major risk factors for a number of chronic diseases, including diabetes, cardiovascular diseases, and cancer [1,2]. According to a WHO report, obesity and overweight are dramatically increasing worldwide. Therefore, there has been a dramatic increase in the use of bariatric surgical procedures. The number of bariatric surgeries for adults in the United States increased from 20.1% in 2003 to 90.2% in 2008 [3]. The trend continued to grow, as the American Society for Metabolic and Bariatric Surgery reported that the number of bariatric surgeries performed in the United States increased by 10.8% in 2018 compared with 2017 [2]. Bariatric surgery can be associated with several unfavorable side effects, such as vomiting, vitamin deficiencies, nausea, and dehydration [4]. These adverse effects may lead to oral manifestations, such as reduction in salivary flow, dental erosion, unpleasant taste sensation, and halitosis [5]. The most frequent reported complaint after bariatric surgery was dry mouth (41.5%), followed by unpleasant taste sensation (38.5%) and halitosis (24.6%) [6]. Halitosis after bariatric surgery could be due to intra-oral or extraoral sources. Extraoral halitosis could be due to metabolic adaptations accompanying dietary restrictions that could lead to ketosis [7].

Ketosis is an increase in the number of circulating ketone bodies in the bloodstream as a result of fat metabolism processes. Several studies have reported increases in ketone bodies associated with weight loss and changes in nutrition [8]. When glucose levels are decreased, the liver starts to metabolise circulating free fatty acids to provide an alternative form of energy, which results in production of three ketone bodies: acetoacetate, 3-hydroxybutyrate, and acetone. Acetone is a volatile substance that can diffuse into the air spaces of the lung and be found in the exhaled breath [9]. Acetone in the breath is considered extraoral blood-borne halitosis that has been studied extensively under the old term 'fruity' smell [7,10,11]. Few studies have reported the association between bariatric surgery and exhaled acetone [6,10]. Only one study could be found in the literature that reported elevated levels of ketone bodies in subjects undergoing either Roux-en-Y gastric bypass or sleeve gastrectomy [10]. Boshier PR et al., reported that the levels of exhaled acetone increased following a low-carbohydrate diet (1396 ppb) and bariatric surgery (1693 ppb) compared with the preoperative level (410 ppb) [12]. The aim of this study was to assess the role of exhaled acetone produced as a result of weight loss in the production of extraoral halitosis in patients undergoing bariatric surgery.

MATERIALS AND METHODS

A prospective longitudinal cohort study was designed from October 2018 to November 2019 and subjects were monitored for a period of six months postsurgery. Ethical approval was obtained from the Institutional Review Board (approval number E-18-3071) and the College of Dentistry Research Center (approval number PR 0079) of King Saud University, Riyadh, Saudi Arabia. Informed consent was obtained from all participants.

The sample size was determined according to the method of Cohen (1988). At α=0.05 with an estimated standard deviation of 10 and an effect size of 0.8 and a power of 0.9 (90%), the number of subjects should be at least 30 in order to establish a statistically significant difference. Volunteers were recruited from the waiting list of patients eligible for sleeve gastrectomy surgery. Fifty subjects were initially selected in accordance with the following criteria.

Inclusion criteria: Obese patients with a BMI of 35 to 50 kg/m² and age ranging from 18 to 50 years of either sex.

Exclusion criteria: Patients with evidence of diabetes, smokers, pregnant or lactating women, and ketogenic diet.

Initially, 50 people were screened using the inclusion criteria and after applying the exclusion criteria 43 subjects were eventually enrolled in the study. Four subjects dropped out during the course of the study due to personal reasons. Finally, the study was completed over 39 subjects that gave a sample size above the minimum sample required for this study. [Table/Fig-1] represents the demographic characteristics of the sample. The study variables used were the acetone levels in the breath and 3-hydroxybutyrate levels in the blood of the subjects. Both these variables were the dependent variables used with independent variables of low BMI loss (<5 kg/m²) and rapid BMI loss (≥5 kg/m²) after the gastric sleeve surgery.

Variables	N=39 (100%)
Age (mean±SD) (years)	32.2±10.4
Gender	
Male	12 (31%)
Female	27 (69%)
BMI (mean±SD)	45.2±4.6 Kg/m²

[Table/Fig-1]: The demographic data of study participants and the Body Mass Index (BMI) along with the standard deviation (SD).

Baseline Visit

During the baseline visit, breath samples were collected for analysis of the concentration of exhaled acetone, and blood samples were taken for analysis of the concentration of 3-hydroxybutyrate.

Follow-Up Visit

Similar measurements were obtained at one month, three months, and six months postsurgery.

Breath Analysis

The level of acetone in the breath was measured by a portable breath ketone analyser (KETONIX®, Varberg, Sweden). The subjects were asked to breathe in and out normally and to indicate when they were approaching the terminal portion of their exhalation. At that point, they were asked to exhale via a disposable mouthpiece into the portable breath ketone analyser. The concentration of acetone in the breath was recorded in Parts Per Million (ppm).

Blood Tests

The level of 3-hydroxybutyrate in the blood was assessed with a portable ketone meter (StatStrip®, Nova Biomedical, Waltham, MA, USA). The patient's fingertip was cleaned with 70% isopropyl alcohol then wiped with dry gauze. Next, a skin puncture was performed using a finger stick device, and a droplet of blood was collected with the strip as shown in [Table/Fig-2]. The strip was then inserted into the portable ketone meter. The results were recorded in millimoles per liter (mmol/L).

Bariatric Surgery Procedure

All bariatric procedures were performed laparoscopically in the accredited Bariatric Surgery Center at King Khaled University Hospital. Sleeve gastrectomy procedures were performed in accordance with previous published studies from the Metabolic and Bariatric Surgery Center at King Khaled University Hospital [13-18].

[Table/Fig-2]: Shows the Statstrip® used for measuring the levels of 3-hydroxybutyrate in blood.

STATISTICAL ANALYSIS

All statistical analysis were performed using the Statistical Package for the Social Sciences (SPSS) version 22.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Descriptive statistics (mean, standard deviation, frequencies, and percentages) were presented for inferential statistics. Pearson correlation was used to identify the relation between two numerical variables. One-way ANOVA and the independent t-test were used to compare independent variables with two or more levels of numerical response variables. A p-value <0.05 was considered significant.

RESULTS

Thirty Nine (39) subjects completed the study eventually. There were 12 men and 27 women, with a mean age of 32.2 years (SD,±10.4) as shown in [Table/Fig-1]. The subjects were grouped according to their rate of BMI loss into group I, with a low rate of BMI loss (<5 kg/m²), and group II, with a high rate of BMI loss (≥5 kg/m²).

The overall mean level of breath acetone was 6.8 (±3.7) ppm at baseline before surgery, with 4.1±3.2, 3.4±2.4 and 3.8±2.7 ppm at one, three, and six months postsurgery, respectively. At one month, the level of breath acetone was higher in group II than in group I (4.90 vs. 2.81 ppm; p=0.018) [Table/Fig-3].

Months postsurgery	Group	N	Mean±SD (ppm)	Overall Mean±SD (ppm) (N=39)	p-value
1	I	16	2.81±0.92	4.1±3.2	0.018*
	II	23	4.90±3.82		
3	I	28	3.62±2.78	3.4±2.4	0.167
	II	11	2.72±1.22		
6	I	19	4.27±3.30	3.8±2.7	0.212
	II	20	3.17±2.01		

[Table/Fig-3]: Mean concentration of acetone in the breath. Group I with a low rate of Body Mass Index (BMI) loss (<5 kg/m²), and group II, with a high rate of BMI loss (≥5 kg/m²).
*Statistically significant (One-way ANOVA); SD: Standard deviation; p-value <0.05 considered significant

At baseline, the overall mean concentration of 3-hydroxybutyrate in the blood was 0.22±0.1 mmol/L. One month after surgery, the mean concentration increased to 1.6±1.2 mmol/L. The mean concentration then decreased significantly at three and six months to 0.8±0.8 mmol/L (p=0.001) and 0.4±0.3 mmol/L (p=0.003), respectively, as determined by one-way ANOVA.

When the level of 3-hydroxybutyrate in the blood was analysed based on the rate of weight loss, at one month subjects in group II had a statistically significant increase in the mean level compared with subjects in group I (from 1.93 to 1.21 mmol/L; p=0.049). At three months, the mean levels in groups I and II were 0.70 and 1.19 mmol/L, respectively; the difference was not statistically significant (p=0.078). At six months, there was no statistically significant difference between the two groups [Table/Fig-4].

Months postsurgery	Group	N	Mean±SD (mmol/L)	p-value
1	I	16	1.21±0.83	0.049*
	II	23	1.93±1.37	
3	I	28	0.70±0.68	0.078
	II	11	1.19±0.96	
6	I	19	0.46±0.36	0.816
	II	20	0.43±0.39	

[Table/Fig-4]: Mean concentration of 3-hydroxybutyrate in the blood. Group I with a low rate of Body Mass Index (BMI) loss (<5 kg/m²), and group II, with a high rate of BMI loss (≥5 kg/m²).
*Statistically significant (One-way ANOVA); p-value <0.05 considered significant

The Pearson correlation coefficient between breath acetone and blood ketone at one month was positive at 60.1% with p=0.001. [Table/Fig-5].

Time (N=39)	Pearson correlation (r)	p-value
Baseline	0.009	0.95
One month	0.601	0.001*
Three months	-0.142	0.38
Six months	-0.251	0.12

[Table/Fig-5]: Correlation between breath acetone and 3-hydroxybutyrate in the blood among the sample.
Pearson's Correlation (r) *significant correlation (Independent t-test)

DISCUSSION

Bariatric surgery has been used effectively for treatment of obesity. However, it has several side effects that can affect general and oral health. The aim of the present longitudinal clinical study was to assess the role of ketone bodies produced as a result of weight loss in the production of oral halitosis. To our knowledge and within the literature searched, this study is the first to compare the levels of acetone in the breath and 3-hydroxybutyrate in the blood at one month, three months, and six months after bariatric surgery (sleeve gastrectomy). The results showed that at one month after surgery, the level of acetone in the breath was higher in patients with rapid reduction of BMI (>5 kg/m²). There were no differences between patients with rapid and slow reduction of BMI in the level of breath acetone at three and six months. This indicates that halitosis as measured with the acetone breath or 3-hydroxybutyrate in the blood may not be dependent on rapid or low BMI loss over a period of time. Boshier PR et al., reported increased concentrations of exhaled acetone in subjects who underwent bariatric surgery compared with a control pre surgical group [12]. Although there is a similarity between this study and the current study, the current study reported an increase in acetone at one month in patients whose BMI decreased by ≥5 kg/m².

In the current study, the level of 3-hydroxybutyrate in the blood was high at one month after surgery then decreased significantly at three and six months. In a previous study, the 3-hydroxybutyrate level increased immediately after bariatric surgery, followed by a significant reduction at six months [19]. Tulipani S et al., have shown an increased level of 3-hydroxybutyrate in the first few weeks after bariatric surgery [20].

In the present study, there was a positive correlation between blood 3-hydroxybutyrate and breath acetone levels at one month after surgery. Several other studies have found strong correlations between blood 3-hydroxybutyrate and breath acetone levels, with correlation coefficients ranging from 0.54 to 0.94 [21-23]. In the present study, there were no significant correlations between blood 3-hydroxybutyrate and breath acetone levels at three and six months after surgery. This could be because weight loss is faster and greater in the first month than in the third and sixth months [24].

Several factors should be considered related to sampling, measuring, and interpreting breath acetone, such as exhaled air volume, breathing pattern, and breath temperature [24]. During a single exhalation, breathe acetone levels increase with exhaled volume. Thus, the greater the volume of air exhaled, the greater the acetone concentration [25]. Although bariatric surgery is currently considered the most effective treatment for morbid obesity, several studies have shown that patients may suffer from respiratory difficulties [26,27]. It has been noticed during breath sampling that patients cannot take long, deep breaths as they did preoperatively, which could explain the relatively low level of breath acetone immediately after surgery [26-28].

Limitation(s)

The study suggests that there is a relationship between extraoral halitosis and abrupt loss of BMI following gastric sleeve surgery. However, the sample size in the present study is small and may not be generalised for other study centres. Moreover, there might be confounding factors such as change in the diet after the surgery that needs to be taken into account. Studies involving other centres with different populations and larger sample size may give more insight of the relationship between extraoral halitosis and BMI loss after gastric sleeve surgery.

CONCLUSION(S)

The findings of the present study clearly suggest an increase of extraoral halitosis in patients with abrupt BMI loss for a month after gastric sleeve surgery. The findings also suggest a relationship with breath acetone and ketones in the blood for production of extraoral halitosis in patients who have undergone gastric sleeve surgery.

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PARTICULARS OF CONTRIBUTORS:

1. Graduate Program in Periodontics, Department of Periodontics and Community Dentistry, College of Dentistry, King Saud University, Riyadh, Saudi Arabia.
2. Associate Professor, Department of Periodontics and Community Dentistry, College of Dentistry, King Saud University, Riyadh, Saudi Arabia.
3. Professor, Department of Surgery, College of Medicine, King Saud University, Riyadh, Saudi Arabia.
4 Associate Professor, Department of Surgery, College of Medicine, King Saud University, Riyadh, Saudi Arabia.
5 Associate Professor, Department of Periodontics and Community Dentistry, College of Dentistry, King Saud University, Riyadh, Saudi Arabia.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Hamad A Alzoman,
Associate Professor, Department of Periodontics and Community Dentistry, College of Dentistry, King Saud University, P.O. Box 60169, Riyadh-11545, Saudi Arabia.
E-mail: halzoman@gmail.com; halzoman@ksu.edu.sa

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