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Research Article

Beta-Hydroxybutyrate Ketone Salt Supplement Alters Energy Metabolism, Blood Glucose and Ketone Levels But Not Appetite or Energy Intake

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Abstract

The purpose of this study was to determine the acute effect of Beta-Hydroxybutyrate (BHB) Ketone Salt (KS) on blood glucose and ketone levels, appetite profile, energy metabolism and intake, affect, and cognitive function. Twenty-two healthy females (age: 26 ± 7 y, Body fat %: 28 ± 8.2, Body Mass Index: 26 ± 8.6 kg/m^2) were recruited to participate in a single-blind crossover study design. Participants were randomly assigned to consume either 0.25g/kg of KS or flavor matched Placebo (PL). During each visit, participants blood glucose and ketone levels were measured at pre-, 0, 45 and 90 minutes. Indirect calorimetry was used to measure the thermic effect of the supplement at 30-45 and 75-90 minutes. Participants completed an appetite profile survey at pre-, 0, 30, 60 and 90 minutes. Affect and cognitive function were measured pre-, 0 and 45 minutes. Energy intake following an *ad libitum* breakfast was recorded. A significant supplement effect was observed for blood glucose (KS: 91±10, 83±10, 84±8, 82±8 mg/dL and PL: 91±8, 88±10, 89±8, 86±9 mg/dL, p=0.04) and ketone levels (KS: 0.3±0.2, 0.5±0.2, 0.4±0.2 Mmol/L and PL: 0.3±0.3, 0.2±0.2, 0.2±0.2 Mmol/L, p < 0.001) at pre, 0, 45 and 90 min, respectively. A significant difference over time (p<0.001) but not between supplements (p>0.05) was observed for appetite profile including satiety, hunger, fullness and desire to eat and cognitive function. Greater oxygen consumption was observed in KS (p=0.007) compared to PS (p>0.05). However, no significant difference in energy intake at breakfast (p=0.94) was observed between KS: 200±116 kcals and PL: 203±107 kcals. KS supplement caused modest elevation in blood ketone levels and reduced glucose, suggesting improved glycemic control, however, did not influence perceived satiety or energy intake.

Keywords: Ketogenic Diet; Metabolism; Cognitive Function; Blood Glucose

Abbreviations

KS	:	Ketone Salt
PS	:	Placebo Supplement
TMT	:	Trail Making Test
BHB	:	Beta-Hydroxybutyrate
BIA	:	Bioelectrical Impedance Analysis
RMR	:	Resting Metabolic Rate
SET	:	Stroop Effect Task
BW	:	Body Weight
QS	:	Questionnaires
BD	:	Blood Draw
TED	:	Thermic Effect of Drink
RER	:	Respiratory Exchange Ratio

Introduction

Diet strategies that include calorie restricting, carbohydrate depletion, and juicing lifestyles have been popular for weight loss achievement. Ketogenic diets have become increasingly popular and were the most googled diet in the world in 2018 (Google's Year in Search - Google Trends). Ketogenic diets may decrease

appetite and reduce calorie intake and are often advertised to burn fat as fuel to achieve endogenous ketosis and weight loss through increasing blood ketone levels [1]. Ketogenic diets normally consist of about ~75% of daily energy intake from fats, 10% from protein, and 5% from carbohydrates. Blood ketones are produced by the liver because of reduced carbohydrate availability due to prolonged fasting, starvation or ketogenic diet and can be used by the body as an alternative source of energy [2].

Prolonged starvation and adherence to the ketogenic diet may be difficult due to its restrictive properties, which is why exogenous ketone supplements might be a practical solution to achieving dietary ketosis [3]. Ketone salts and ketone esters are the two types of commercially available exogenous ketone supplements that have been previously used to achieve dietary ketosis. Administration of ketone esters have been effective in resulting short-term dietary ketosis, yet they are very expensive and may not be suited for long-term supplementation [3]. Ketone salts are marketed as a less expensive way to increase blood ketone levels, fat burning, and cognitive/athletic performance. Despite this, some studies suggest that these may be relatively ineffective and should be further investigated [4].

A limited number of studies have evaluated the effects of these supplements in humans compared to rodents. In previous studies, it has been observed that exogenous supplementation with Beta-Hydroxybutyrate (BHB) ketone esters and salts were found to produce acute nutritional ketosis (defined as having a blood ketone level of 0.5-3.0 Mmol/L), suppress appetite, lower plasma ghrelin levels and perceived hunger [2,5,6]. This may suggest potential benefits for weight loss through appetite due to increased perceived satiety and potentially reduced energy intake. Additional benefits of exogenous ketones supplementation may include altered energy metabolism, improved physical performance, and cognitive function [7,8]. In one study, despite an increase in fat oxidation, lower cycling time trial power output was observed following an ingestion of a ketone salt supplement [5]. On the other hand, ketone ester supplements improved an executive function multitasking test but not shuttle run time or sprint times in male team sport athletes [9]. Therefore, this may suggest that exogenous ketone supplements may alter energy metabolism and cognitive function but may not have an effect on high-intensity exercise performance.

The purpose of this study was to determine the acute effect of a commercially available Beta-Hydroxybutyrate (BHB) Ketone Salt (KS) on blood glucose and ketone levels, appetite profile, energy metabolism and intake, affect, and cognitive function in healthy females. It was hypothesized that consuming Beta-Hydroxybutyrate (BHB) ketone salt supplement would increase metabolic rate, decrease hunger, lower energy intake, and improve cognitive function compared to a placebo.

Methods

The study was approved by the local Institutional Review Board before data collection. A consent form was provided prior to testing to explain study procedures. Participants had to meet inclusion criteria of being female, between 18-45 years of age, healthy with no known risk factors for metabolic or heart disease.

Study Design and Participants

This randomized, single blinded, crossover study examined the acute effect of a BHB Ketone Salt and placebo on appetite profile, mood, thermogenesis, and energy intake in healthy female participants (*n=22*) between the ages of 18-45 years.

All the following procedures were described to participants prior to their commitment to the study. All participants completed a general health/education history, allergies, menstrual cycle, and breakfast habits questionnaire. Height, weight, age, race/ethnicity, and body composition were measured at the beginning of each lab visit. Weight was assessed using standardized procedures using a digital scale (BF-679W/BF-680W, TANITA, Arlington Heights, IL) and total body composition was assessed using a hand-held Bioelectrical Impedance Analysis (BIA) (OMRON HBF 306, Bannockburn, IL). Participants were asked to maintain similar food consumption and physical activity levels for 24 hours and to avoid participating in high intensity exercise, as well as consuming alcohol, tobacco, and caffeine for at least 12 hours before each session. To ensure participants compliance participants were asked to record energy intake using MyFitnessPal (MyFitnessPal Inc., San Francisco, CA) for the day before the initial lab visit, the day of the visit, and the day after the visit. In addition, habitual breakfast consumption was assessed to ensure that it did not deviate from their typical day. To control for hormone fluctuation participants were tested between 7-21 day of their menstrual cycle as it can influence energy metabolism and substrate utilization [10]. After baseline screening and familiarization with testing procedures, participants were randomly assigned to the order of the supplement.

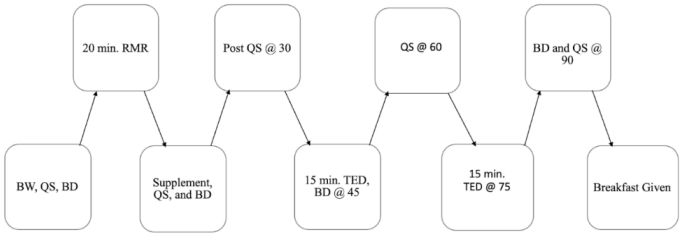

Figure 1: Study Timeline. RMR: resting metabolic rate, TED: thermic effect of drink, TMT: trail making test. RMR - Resting Metabolic Rate , BW - Body Weight, QS - Questionnaires, BD - Blood Draw, TED - Thermic Effect of Drink

Laboratory Visits

Participants came to the laboratory between 0530-0700 and fasted for at least 8 hours. Each session lasted between 2.5-3 hours. Preliminary data collection of resting metabolic rate (RMR) was assessed using the ventilated hood technique with a computerized open-circuit indirect calorimeter (Parvomedics, Truemax 2400, Salt Lake City, UT). RMR was measured in a supine position for 20 minutes prior to liquid preload (only last 10 minutes were used for analysis) followed by a visual analog scale (VAS-100mm) via Qualtrics for appetite profile including how hungry, satisfied, and full the participant felt, as well as how much desire they had to eat, and their perceived desire to eat something sweet and salty. These questionnaires were repeated at 0, 30, 60, and 90 minutes after preload.

Participant alertness and arousal was assessed using the Stanford Sleepiness Scale (1- wide awake; 7-sleep onset soon), a 6-point Felt Arousal Scale (FAS) (1 - low arousal, 6 - high arousal) [11] and a 20-item multidimensional self-report Activation-Deactivation Adjective Checklist (AD-ACL) on a scale (1 - not at all, 2 - somewhat, 3 - moderately So, 4 - very much so) [12]. The scale assessed energetic (ranging from tiredness - energy) and tense (ranging from calmness - tension) arousal. State anxiety was measured using the 10-item state version of the State Trait Anxiety Inventory [13].

In addition, to assess the effects of ketone supplement on cognitive function, timed Stroop Effect Task (SET) [14] and Trail Making Test (TMT) [15] were administered before and 45 minutes after supplement consumption to test letter and number recognition, mental flexibility, visual scanning, and motor function.

Blood glucose and ketone levels were measured following appropriate blood collection procedure using capillary sampling method via Precision Xtra Blood Glucose and Ketone Monitoring System (Abbott, Abbott Park, IL) at increments before, 0, 45, and 90 minutes after preload.

Participants were randomly assigned to either ™ Beta-Hydroxybutyrate (BHB) ketone salt supplement (Keto Drive, Zhou Nutrition, Park City, UT)) or placebo (True Orange Mango Orange, True Citrus, Middle River, MD). Both supplements were in a form of powder and diluted with 500 ml of water prior to consumption. BHB Ketone Salt supplement was administered based on body weight (0.25g/kg). Participants were given 10 minutes to consume the assigned supplement, followed by a palatability questionnaire using a visual analog scale (VAS-100mm) via Qualtrics to assess pleasantness of taste, after taste, sweetness, bitterness, sourness, visual appeal, and smell. Participants were also assessed on their levels of thirst in the administered survey before and after supplement consumption (1 - not thirsty at all, 2 - not very thirsty, 3 - somewhat thirsty, 4 - thirsty, 5 - very thirsty). The Thermic Effect of a Drink (TED) was measured at 30 minutes and 75 minutes following the preload for 15 minutes (only the last 10 minutes were used for analysis). Substrate utilization rates were determined using Respiratory Exchange Ratio (RER) and oxygen consumption (VO_2) was recorded. After the last TED, participants were provided with *ad libitum* breakfast meal including banana, cereal (Honey Nut Cheerios, General Mills, Minneapolis, MN) and cow's low fat (1%, generic brand) or almond milk (Almond Breeze Unsweetened, Blue Diamonds Growers, Los Angeles, CA) and were instructed to eat until they felt comfortably full. The amount of food consumed was measured and recorded, and macronutrient composition was analyzed based on Nutrition Fact Labels (Food and Drug Administration).

Data Analysis

Repeated measures ANOVA was performed (SPSS Version 24.0, SPSS Inc, Chicago, IL, USA). A 2x5 repeated measures ANOVA was used to analyze hunger, satiety, desire to eat, fullness, and perceived food consumption. A 2x3 repeated measures ANOVA was used to analyze RQ and VO_2, and a 2x4 repeated measures ANOVA was used to analyze blood glucose and ketones. A Repeated Measures Generalized Linear Model was used to analyze energetic and tense arousal. A 2x2 repeated measures ANOVA was used to analyze Stroop and trail making test results, and a paired sample T-Test was used to evaluate the pleasantness of taste. Data are presented as mean ± standard deviation, with a significance level set at $p < 0.05$.

Results

Physical characteristics of participants are presented in Table 1. Participants were tested on 14 ± 7 day of their menstrual cycle. Participants habitually consumed breakfast during the week. Based on a 24-hour dietary recall (n=22) there was no significant difference ($p>0.05$) before testing sessions in energy intake (EI) and macronutrients between KS (EI: 1411±411 kcals/day, CHO: 173±80g, FAT: 54±27g, PRO: 63±30g) and PS (EI: 1390±380 kcals/day CHO: 163±88g; FAT: 57±36g; PRO: 60±34g). In addition, no significant difference ($p>0.05$) in pleasantness of taste, aftertaste, sweetness, bitterness, sourness, palatability, and thirst was observed between KS and PS supplements.

A significant difference in blood glucose ($p = 0.01$) and ketone ($p = 0.02$) levels observed between KS and PS (Figure 2 and 3). Higher blood ketone and lower glucose levels were observed after KS compared to PS. A significant time effect for hunger, satiety, fullness, and desire to eat ($p<0.05$) but not supplement effect was observed for hunger ($p=0.51$), satiety ($p=0.48$), fullness (0.83) desire to eat ($p=0.69$), and amount ($p=0.94$) (Figure 4). Hunger significantly decreased at 0- and 30-min post supplement consumption and increased significantly ($p<0.05$) at 90-min compared to pre-supplement consumption. Satiety and

fullness increased significantly ($p<0.05$) at 0-, 30-, 60-min post supplement consumption and came back down to pre-supplement levels at 90-min. Desire to eat and amount decreased significantly ($p<0.05$) at 0-min post supplement consumption and increased at 90-min compared to pre-supplement consumption. In addition, there was no significant difference in energy intake at breakfast (KS: 218±108kcal and PS: 211±106kcal, p=0.84) or over 24-hours (p=0.79) between KS (EI: 1246±401kcals/day, CHO: 151±62g, FAT: 45±21g, PRO: 59±33g) and PS (EI: 1212±427 kcals/day CHO: 163±88g; FAT: 47±30g; PRO: 56±29g). A significant interaction of supplement and time observed for oxygen consumption ($p = 0.01$), but not for RER (p=0.28) (Figure 5 and 6). KS showed a greater increase from pre- to post- supplement consumption between 45-60 minutes and then remained elevated between 75-90 minutes, while in PS oxygen consumption increased and then declined over time. Furthermore, a significant time effect ($p<0.001$), but not supplement or interaction of time and supplement ($p>0.05$) was observed for FAS and Stanford Sleepiness Scale (Table 2). In addition, a significant time effect ($p = 0.01$), but not supplement or interaction of time and supplement ($p>0.05$) was observed for energetic and tense arousal. This effect was attributable to an increase in energetic arousal ($p = 0.005$). For state anxiety, it was found that there was an effect for condition ($p = 0.04$) with PS reporting higher anxiety, but no effect for time or interaction between condition and time. The affective and state anxiety results can be found in Table 2. Stroop and Trail Making Test results are presented in Table 3. Both test scores improved over time ($p = 0.004$ and $p = 0.009$, respectively), however, were not significantly different between KS and PS ($p>0.05$).

Measurement	Mean ± SD
Age (y)	25.6±5.6
Weight (kg)	70.2±16.8
Height (cm)	164 ± 3.9
BMI (kg/m^2)	26.1±6.2
BF (%)	28.6±8.0
y - years, kg - kilograms, cm - centimeters	

Table 1: Physical Characteristics of Participants (n=22).

	PRE	POST	POST-30	POST-60	POST-90
FAS-KS	2.0±1.0	3.1±0.8*	3.0±0.8*	3.3±0.8*	3.2±1.0*
FAS-PS	2.3±1.2	3±1.4*	3.0±1.4*	3.2±1.2*	3.1±1.4*
Sleepiness-KS	3.2±1.1	2.8±1.0*#	2.7±0.7*	2.6±1.3*#	2.8±1.4*
Sleepiness-PS	3.5±0.9	2.9±1.1*#	2.6±0.9*	2.5±0.9*#	2.5±1.1*
KS = ketone salt, PS = placebo supplement; * $p<0.05$ (time effect between pre-and post- supplement consumption); # $p<0.05$ (time effect between at 0-min and 60-min)					

Table 2: Effect of liquid supplement on FAS and Stanford Sleepiness results presented as Mean ± SD.

Test	Measurement	KS - Pre	KS - 45	PS - Pre	PS - 45
Stroop	WS (sec)	48±7.2	46±5.5*	49±11	47±11*
	CS (sec)	64±11	60±11*	64±16	61±14*
	WCS (sec)	92±18	83±15*	94±26	87±21*
Trail Making	A (sec)	18±5.2	16±4.2*	18±5.5	16±4.2*
	B (sec)	35±11	33±12	37±8.9	32±10
Energetic Arousal		18.2±5.4	19.4±5.9*	16.0±3.5	19.9±5.2
Tense Arousal		17.5±3.3	18.1±3.6	18.9±4.0	19.1±4.1

State Anxiety		16.4±4.1	16.2±3.6	17.8±3.9	17.5±4.2
WS - word specific; CS - color specific; WCS - word and color; A - numerical; B - numerical and alphabetical; KS = ketone salt; PS = placebo supplement; * p<0.05 (for time between pre-and post- supplement consumption)					

Table 3: Effect of liquid supplement on Stroop, Trail Making Test and AD-ACL results presented as Mean ± SD.

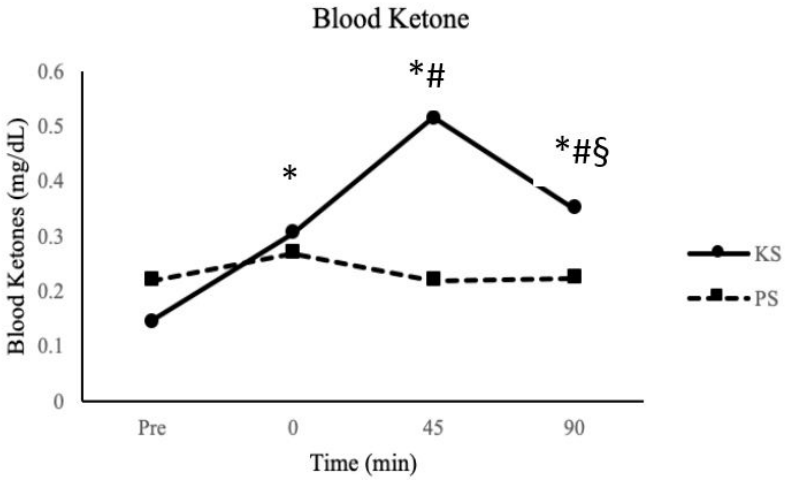

Figure 2: Effect of a liquid supplement on blood ketone levels over time.

** p<0.05 (time effect between pre-and post- supplement consumption)*

 # p<0.05 (time effect between 0-min and 45-min)

§ p<0.05 (time effect between 45-min and 90-min)

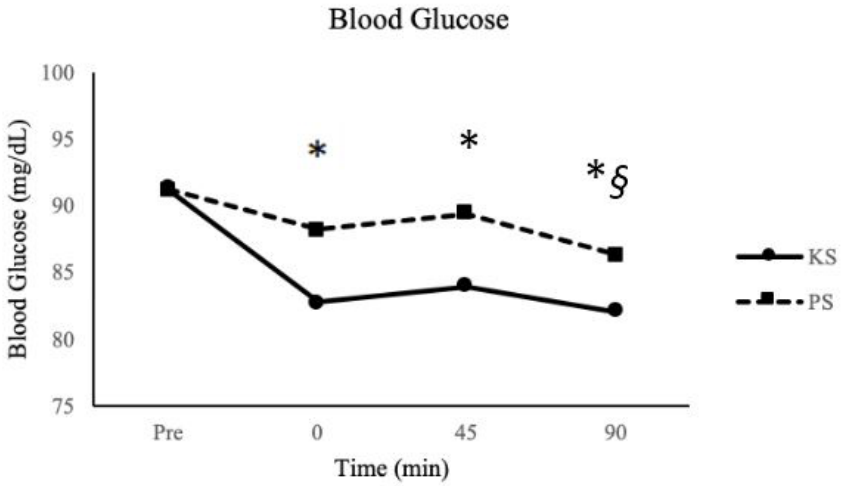

Figure 3: Effect of a liquid supplement on blood glucose levels over time.

** p<0.05 (time effect between pre-and post- supplement consumption)*

§ p<0.05 (time effect between 45-min and 90-min)

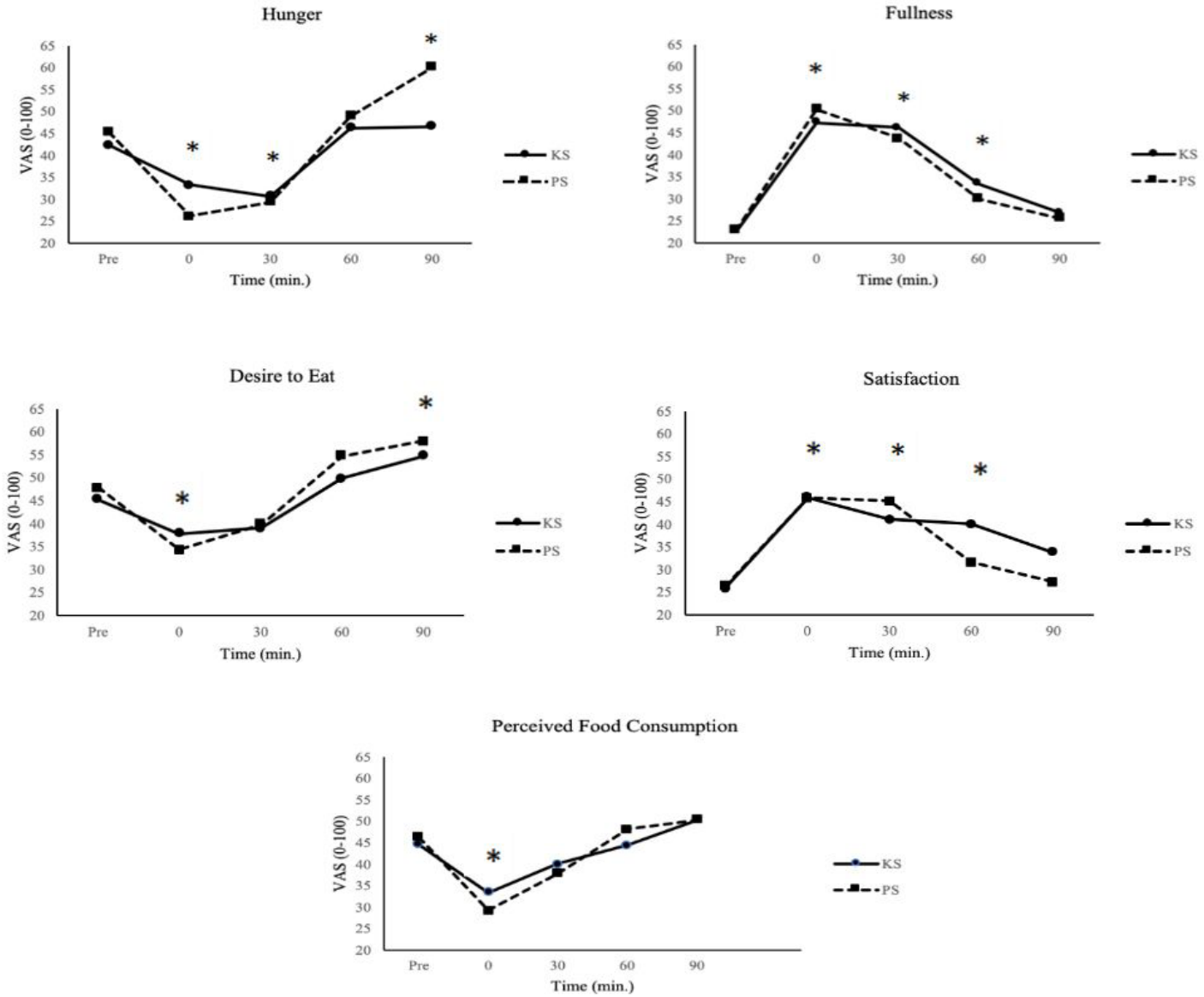

Figure 4: Effect of liquid supplement on subjective appetite ratings. Changes in perceptions of hunger (a), fullness (b), satisfaction (c), desire to eat (d), and perceived food consumption (e) over 90 minutes.

** p<0.05 (time effect between pre-and post- supplement consumption*

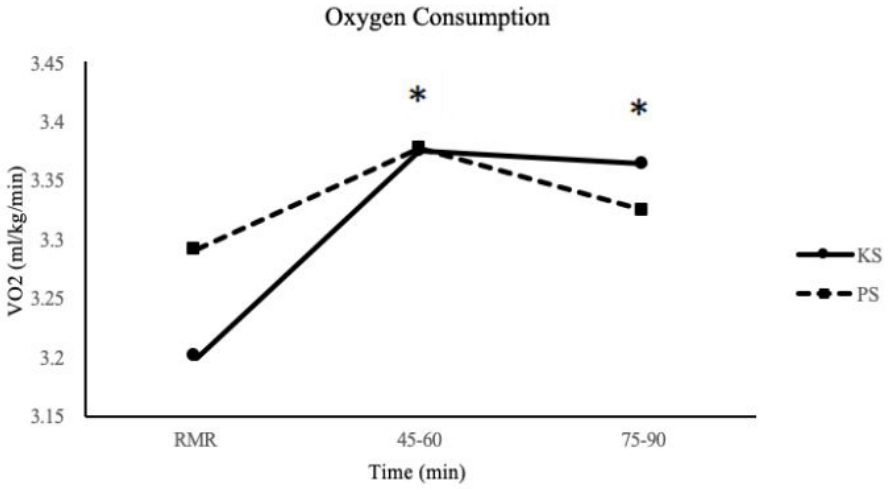

Figure 5: Effect of a liquid supplement on oxygen consumption over time.

** p<0.05 (time effect between pre-and post- supplement consumption)*

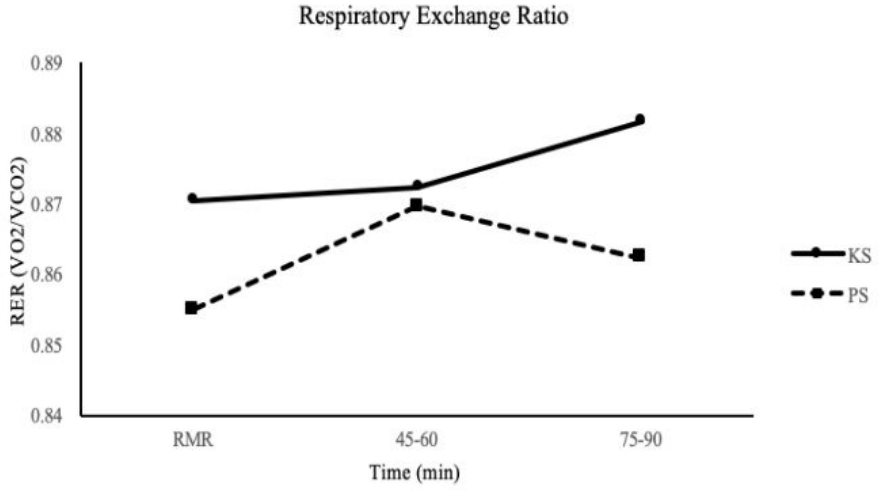

Figure 6: Effect of a liquid supplement on resting energy expenditure over time.

Discussion

The purpose of the present study was to investigate the acute effect of a beta-hydroxybutyrate (BHB) ketone salt supplement on blood glucose and ketone levels, appetite profile and food intake, energy metabolism, affect and cognitive function in healthy females. Higher blood ketone and lower blood glucose levels were observed following KS compared to PS. In addition, a significant time and supplement interaction was observed in oxygen consumption and overall lower levels of state anxiety in KS compared to PS. However, no significant difference in energy intake, appetite profile, arousal, sleepiness, or cognitive function was observed between KS and PS.

A significant difference in blood ketone and glucose levels was observed in the present study between KS and PS. Typically, a high-fat diet would be used to achieve nutritional ketosis, however, a high fat diet can be associated with an increase in plasma FFAs and reduced myocardial PCr/ATP [16]. In addition, high-fat ketogenic diet has shown to be associated with elevated levels of atherogenic containing lipoproteins, decreased anti-atherogenic HDL and an increased activity of peroxisome proliferator-activated receptors (PPARs) which may directly contribute to the development of chronic disease including atherosclerosis and diabetes [17]. Therefore, ketone supplements were suggested to be a practical way to achieve exogenous ketosis without elevating FFA and contributing to the reduced myocardial energy efficiency [3,16]. Previously, elevated ketone levels (0.8 - 3.3mM), increased fat oxidation, lower Free Fatty Acid (FFA) and triglyceride concentrations have been observed when comparing the effects of ketone ester and ketone salt beverages [3,5-7,9]. However, not all supplements elevated ketone levels required to achieve acute nutritional ketosis (0.5-3mM) [18]. Higher levels of ketone bodies have been observed following ketone ester supplementation (3-5mM) compared to ketone salts (<1mM) [3-7]. However, ketone ester supplements are not as readily available and are expensive, whereas more ketone salt supplements are on the market. In the present study, blood ketone levels peaked at 45 minutes post supplement consumption and reached beginning levels of acute nutritional ketosis (0.5 mM) while using commercially available KS compared to PS. In addition, lower blood glucose levels were observed in KS compared to PS. Similarly, other studies observed lower blood glucose levels following consumption of ketone salts and esters [3,6,19]. Limited liver gluconeogenesis and elevated peripheral blood glucose uptake may have contributed to the lower glucose levels following exogenous ketone supplementation [3,19]. Therefore, ketone salt supplements may have a modest effect on blood ketone and glucose levels which may deliver desired effect for individuals at increased risk for developing cardiovascular and metabolic disease without increasing the risk of heart failure or diabetic crisis.

In the present study, no significant difference in hunger, satiety, fullness, amount, desire to eat or energy intake at breakfast and over 24-hours was observed between KS and PS. Previously decreased energy intake, glucose production, and appetite via changes in hormone secretion and other metabolites were observed following ketone ester supplementation, however, very few studies in humans have been performed [6,20,21]. In rodents, ketone ester supplementation stimulated an increase in ketone levels and Malonyl Co-A, lower plasma glucose, insulin, and leptin, and decreased food intake [20]. Decreased food intake and increased energy expenditure would be expected with higher appetite regulating hormone leptin levels. However, it was suggested that leptin was not responsible for suppressed food intake and other factors such as increased levels of anorexigenic metabolite in the brain Malonyl-CoA may be responsible. In humans, suppressed hunger and desire to eat was observed following ketone ester supplementation compared to a matched placebo coinciding with reduced plasma insulin, ghrelin, Glucagon-Like Peptide-1 (GLP-1) and Peptide YY (PYY) levels [6]. It could be suggested that fast-acting appetite regulating hormone ghrelin was responsible for temporary appetite suppression via decreasing the activity of orexigenic Neuropeptide Y (NPY). Therefore, ketone supplementation could be an effective way of decreasing food intake, supporting weight loss and weight management. Due to the lack of consistent findings and limited research, the effects of exogenous ketone supplements on appetite profile and energy intake needs to be further evaluated. In addition, lack of observed difference in the present study could be due to the type of exogenous ketone salt supplement used and its inability to elevate blood ketones to the optimal levels to have a significant impact on appetite profile and energy intake compared to other forms of ketone supplements and high-fat ketogenic diets. Furthermore, although both drinks were the same volume, it may have altered gastric fill and emptying affecting levels of satiety, fullness, and desire to eat.

A significant interaction of time and supplement in oxygen consumption but not RER was observed in KS compared to PS. Oxygen consumption increased from pre- to post-supplementation in KS between 45-60 minutes and then remained elevated between 75-90 minutes. In addition, although a non-significant RER of 0.88 in KS compared to 0.86 in PS between 75-90 minutes could potentially suggest an increase in BHB oxidation. BHB has been shown to have an RQ of 0.89 when completely oxidized [22] and an increased oxygen supply is needed to generate energy from BHB [23]. Decreased glycolysis and increased use of alternative substrates during exercise has been observed with ketone ester ingestion, proposing that ketones may be a more favorable energy source when in surplus [7]. It can be argued that ketones may limit carbohydrate and skeletal muscle protein catabolism, as seen in cases of starvation [7]. In addition, it has been shown that ketone

supplement reduced lipid oxidation in the hypothalamus, causing the chemical inhibition of hypothalamic carnitine palmitoyl transferase I (CPT-1) activity, ultimately altering exogenous and endogenous inputs of nutrients in the body [24]. Previously, lower RER, higher total fat oxidation and lower total carbohydrate oxidation was observed during exercise at 30% and 60% of ventilatory threshold following acute ketone salt supplementation compared to a placebo [5]. Therefore, higher RER could help explain an increase in oxygen consumption in KS compared to PS. However, due to the limited number of studies it is difficult to draw concrete conclusions of ketone supplementation on energy metabolism, substrate utilization and oxygen consumption when at rest.

KS condition was without benefits to levels of arousal, sleepiness, or cognitive function. However, as would be expected participants performed better on each test over time which could be attributed to individuals feeling more awake or due to increased practice. State anxiety was increased during PS trials which could have been due to personal reasons, anticipation of testing or other factors. Detrimental effects of high fat diets on attention, speed and mood have been previously observed in some studies [16]. However, cognitive performance benefits and neuroprotective effects of ketogenic diets have been established in other human and rat studies [8,9,25,26]. Increased uptake of ketone bodies and cerebral blood flow following an intravenous infusion of ketone bodies suggests that ketone bodies could be used as an alternative energy substrate for the brain [27]. Thus, researchers have argued for its efficiency in energy use for the mind and body during times of stress [8]. Further studies are needed to determine the benefits of various supplement forms on cognitive function and performance.

A few limitations should be considered when interpreting the findings of the present study including underreporting of dietary intake. Some participants reported consuming ~1000 calories per day, which we believe is underestimating the actual amount of energy and nutrients consumed. Although participants were provided with detailed instructions on how to complete 24-hour dietary recall, underreporting of energy intake using 24-hour dietary recall is not uncommon [28] which makes it difficult to assess energy intake in free-living conditions. Moreover, breakfast consumption during the testing session may have been limited due to close observation of investigators, the type of breakfast offered, food preferences and familiarity with food. Not all participants may have been consuming cereal and milk for breakfast on a regular basis, thus may have affected the likeness and amount of food consumed.

In conclusion, an acute oral ingestion of commercially available ketone salt supplement has shown a modest effect on blood glucose and ketones levels; however, had no effect on appetite profile, energy intake or cognitive function. Future studies should be used to continue to investigate the long-term effect of ketone salt supplement compared to ketogenic diet and ketone ester and its benefits for substrate utilization, appetite, and energy intake for chronic disease management.

Authors Contributions

SN and MT designed and conducted the study, performed data analysis, wrote and edited the manuscript. EH assisted in study design, data analysis and manuscript preparation.

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