Ketones and Human Performance

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ABSTRACT

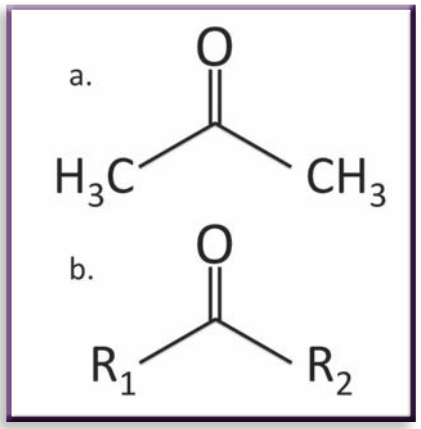
Everyone is seeking nutritional strategies that might benefit performance. One approach receiving much attention is ketones, or ketosis. Ketones are very simple compounds made of hydrogen, carbon, and oxygen, and ketosis is a metabolic state whereby the body uses predominantly ketones. Ketosis can be achieved by fasting for longer than 72 hours or by following a very low-carbohydrate, high-fat diet (ketogenic diet) for several days to weeks. Alternatively, ketone supplements purportedly induce ketosis rapidly and do not require strict adherence to any specific type of diet; however, much of the touted benefits are anecdotal. A potential role for ketosis as a performance enhancer was first introduced in 1983 with the idea that chronic ketosis without caloric restriction could preserve submaximal exercise capability by sparing glycogen or conserving the limited carbohydrate stores. Few human studies on the effects of a ketogenic diet on performance have yielded positive results, and most studies have yielded equivocal or null results, and a few negative results. Many questions about ketones relevant to Special Operations Forces (SOF) remain unanswered. At present, a ketogenic diet and/or a ketone supplement do not appear confer performance benefits for SOF. Instead, Operators should engage with their unit dietitian to develop individualized nutritional strategies based on unique mission requirements. The authors review the concept of a ketogenic diet, describe some potential benefits and risks of ketosis, review the performance literature and how to measure ketone status, and then summarize the landscape in 2017.

KEYWORDS: *ketosis; ketones; diet, ketogenic; ketone supplement; performance*

Introduction

We have discussed previously the concept of precision performance and how various nutritional strategies might benefit performance in some and not in others. Such appears to be the case for ketones or ketosis. Ketones are very simple compounds made of hydrogen, carbon, and oxygen. They are basically nonreactive and have a standard structure; they are made in the liver from fat. The word *ketone* comes from the German word *Aketon*, for "acetone," which is the simplest ketone. Figure 1 presents the structure of acetone and the general structure for ketones. Ketosis is a metabolic state whereby the body generates most of its energy requirements (in the form of adenosine triphosphate) from ketones rather than carbohydrate (in the form of glucose). It can be achieved through prolonged fasting (longer than 72 hours) or following a strict ketogenic diet (KD)—a very low-carbohydrate, moderate-protein, high-fat diet—for several days to weeks.[1] Skeletal muscles and the brain can use ketones for energy production under aerobic conditions. Given the greater propensity for humans to store fat than carbohydrate, some people are of the opinion that being in a state of ketosis provides an almost "endless" supply of energy.[2]

Figure 1 *The structure of* **(a)** *acetone, the simplest of ketones, and* **(b)** *the general structure of ketones, where R_1 and R_2 are groups with a carbon atom attached to the rest of the molecule.*



A potential role for ketosis as a performance enhancer was first introduced in 1983,[3] with the idea that chronic ketosis without caloric restriction could preserve submaximal exercise capability by sparing glycogen or conserving the limited carbohydrate stores; fat would be the predominant muscle substrate. The data were positive and studies by the military in the late 1980s reconsidered the possibility.[4,5] Success was limited and the idea faded away until the early 2000s.[6,7]

This report reviews the concept of a ketogenic diet, describes some potential benefits and risks of ketosis, reviews the performance literature and how to measure ketone status, and then summarizes the landscape in 2017. It is a topic related to precision performance.

Ketogenic Diet

A KD is an eating pattern that produces an increase in the level of ketones produced by and circulating in the body. A traditional KD consists of four parts fat to one part carbohydrate and protein combined.[8] Paoli et al.[9] suggest a KD should contain less than 20g of carbohydrate and 1.2g to 1.7g of protein per kilogram of body weight (0.55g to 0.77g of protein per pound of body weight), and the remaining calories must come from fat.[7] Note that a KD is not a high-protein diet and intake of protein in amounts greater than 2.5g of protein per kilogram of body weight (1.1g of protein per pound of body weight) may interfere with ketone production.[9] A "keto-adaptive" diet has been defined as 20g to 50g carbohydrate (by comparison, one medium banana has approximately 27g of carbohydrate), 15% calories from protein, and at least 70% of calories from fat. However, no standard definition exists because of individual variability in achieving ketosis.[10] It is very important to note that a KD is contrary to the current military dietary reference intakes[11] and sports nutrition recommendations for performance.[12] Despite this, the KD is still fashionable and heavily marketed.

The types of fat included in a KD are predominantly saturated (e.g., coconut oil, butter, heavy cream) and monounsaturated (e.g., olive oil, canola oil, avocados, macadamia nuts) and may include medium-chain triglyceride (MCT) oil and/or omega-3 supplementation (e.g., fish oil or flaxseed oil). High-dose MCT oil is not well tolerated and may cause upset stomach, diarrhea, and gastrointestinal distress. Table 1 provides an example of a ketogenic breakfast.

Reports indicate an individual must follow a strict KD for 4 to 6 weeks for the body to adapt to using ketones as its main fuel source, sometimes referred to as "keto-adapted"; however, this time frame remains controversial.[13] Importantly, several weeks may be required before the lethargy and general decrease in morale associated with consuming a KD lessens.[3]

Table 1 *Sample Ketogenic Breakfast*

Meal	Food	Calories	Carbs (g)	Fat (g)	Protein (g)
Breakfast	2 Tbsp. butter	200	0	24	0
	2 large eggs	150	0	10	12
	2 Tbsp. heavy cream	100	0	10	1
	½ cup white mushrooms	10	1	0	1
	3 sausage links	180	3	16	7
	½ cup blackberries	30	7	0	0
Meal Total		670	11	60	21

Ketone Supplements

Ketone supplements are now being marketed as an alternative to the KD (Table 2). Ketone supplements typically come in either a powder form (ketone salt), which is mixed with water, or a liquid form (ketone ester). Manufacturers claim that ketone supplements rapidly increase levels of blood ketones (typically in less than 1 hour) in lieu of eating a KD, and that this alone should subsequently improve performance. What makes ketone supplements interesting is that they preclude the need to consume a high-fat diet and restrict carbohydrates.

Table 2 *Ketone Supplements*

Commercially Available Ketone Supplements[a]	Servings per Container	Cost ($)	Cost per Serving ($)
Keto OS 2.0	15	85.00	5.67
Kegenix	30	147.00	4.90
KetoCaNa	16	59.99	3.75
KetoForce	16	59.99	3.75
InstaKetones	30	69.99	2.33
KGX Boost	30	29.99	1.00

[a]Information obtained from manufacturer's website.

Unfortunately, many of the performance-enhancing claims are anecdotal and not yet supported by studies published in the peer-reviewed literature. In fact, only one study examining the effect of a ketone supplement on human performance has been published.[14] The authors conclude that a ketone supplement may improve cycling performance by up to 2% in a group of elite (i.e., Olympic caliber) endurance cyclists. Importantly, not all study participants saw an improvement in performance when consuming the ketone supplement. Thus, the importance of precision performance. It remains to be seen whether similar results would be found in non–Olympic-level athletes across different athletic

disciplines. The relevance of the current finding to the Special Operations Forces (SOF) population is discussed in this article. Other considerations for ketone supplements include palatability, timing, dose, and price.[15] These issues are both important and relevant.

Potential Benefits and Risk of a Ketogenic Diet

Benefits

For nearly a century, a KD has successfully been used to reduce seizure frequency in children with epilepsy.[16] A KD may also be used to treat risk factors for metabolic syndrome—mainly obesity, hyperglycemia, and dyslipidemia.[17–23] Emerging evidence also suggests that ketones may improve cognitive function for those with neurological impairments, including Alzheimer disease and Parkinson disease.[24,25] But these are benefits for only those with health problems, not for those hoping to improve their performance.

Risks

Long-term data regarding any potential risks associated with consuming a KD are lacking for adults, and this applies to clinical and performance studies. Clinical studies of longer than 1 year to assess insulin sensitivity, cardiovascular disease risk factors, and/or skeletal health have not been conducted.[10,26,27] However, results from several studies are of concern: after a period of 6 weeks, a KD increased urinary calcium loss and decreased markers of bone formation.[26] Another study demonstrated increases in urinary calcium loss in participants who consumed a KD for 6 months.[27] Together, these results suggest a long-term KD may negatively affect skeletal health because of an increase in urinary calcium.

Following a KD may also place one at risk for a nutrient deficiency. A KD is typically low in several nutrients, including dietary fiber, calcium, potassium, magnesium, iron, zinc, selenium, and copper.[10,28] Without careful monitoring and varied food intake, a nutrient deficiency would likely occur.

KD and Human Performance

There has been a resurgence of interest in studying the effect of ketones or a KD on performance.[6,29–32] A 2014 editorial by Noakes and colleagues[33] summarized the findings of 11 studies published in the past 31 years on low-carbohydrate diets (not all were KD) and physical performance in humans. Many studies relied on self-reported carbohydrate intake and failed to measure ketone levels. The studies focused mainly on elite cyclists but included one study with gymnasts and one study with taekwondo athletes. Three studies found modest improvements in exercise performance after subjects adopted a low-carbohydrate diet; four showed equivocal results, two found no beneficial effect, and two reported an adverse outcome. The major finding was that fat was the major energy source rather than carbohydrate. Whether glycogen levels were spared remains unknown because low resting glycogen levels are known to reduce glycogen use during exercise.[34]

Since 2014, three additional studies have been published on KD and performance.[35–37] One study[35] found a small negative impact on physical performance in recreationally active adults, whereas two studies[36,37] concluded that consuming a KD increased the amount energy derived from fat during low- to moderate-activity levels. However, the change in fuel source has not yet translated into an improvement in performance overall, and some individuals experienced a decrease in performance. Taken together, neither a low-carbohydrate diet nor a KD appears to produce superior results in performance compared with current sports nutrition recommendations.[12,37]

Some argue the aerobic performance benefits of the KD are not the result of ketosis but rather just reflect reliance on fat for fuel due to an upregulation in fatty acid oxidation.[38] The ability of trained endurance athletes to use more fat as energy has been attributed to increased adaptation to or ability to use/metabolize fatty acids and spare plasma glucose and muscle glycogen.[2,14,34,36,39] Limiting the use of scarce glycogen over a long time should theoretically enhance endurance performance.[40] A meta-analysis comparing a high-fat diet (i.e., greater than 30% of calories from fat) to a high-carbohydrate diet (greater than 50% calories of from carbohydrate) found that endurance exercise performance was moderately prolonged after a high-carbohydrate diet compared with a high-fat diet. However, advocates of a KD would argue that many of the diets included in the meta-analysis were too high in carbohydrate and not high enough in fat to induce ketosis and/or the diets were not followed for a sufficient time to facilitate keto-adaptation. Also, training status (i.e., trained versus untrained) appears to significantly correlate with effect size—an indication that one's fitness level will affect how long endurance exercise can be performed after a modified diet. A stronger correlation was found with untrained versus trained individuals.[40] Overall, the only firm conclusion for endurance performance is that individual differences are marked and strategies to identify those who do respond are needed if this approach is even going to be considered. No blanket recommendation can be made.

In contrast to endurance exercise, reports of performance decrements and early onset of fatigue have been reported when the exercise is in short anaerobic bursts.[6,41–43] The preferred explanation for why ketosis may be detrimental to anaerobic work capacity relates to reduced muscle

glycogen stores and possibly a diminished ability to maintain glycolysis after being "told" to rely only on fat.[41–43] But this remains to be confirmed. Given the diverse nature of SOF missions and the requirement to always be able to respond, any intervention that could potentially compromise performance would be avoided.

To our knowledge, no studies exploring the effects of a KD on military performance (physical and/or cognitive) or under simulated mission scenarios have been published. Specific to SOF, more research is needed to explore the impact of ketones on recovery, immune system function, injury risk, hand–eye coordination, and cognitive capacity.[33] Also, additional research to understand how ketones are used under diverse environmental extremes (i.e., heat, cold, altitude, and/or depth) would be required prior to using them in deployed settings. Given, the relatively short deployment notification within Special Operations, a KD may not be feasible. Also, few military rations or ration components are available to support a KD while in the field. Last, appetite suppression may be an unforeseen consequence of a KD that could negatively impact performance, particularly at altitude or under conditions of hypoxia.[44]

Measuring Ketones

If one decides to try a KD, it is important to be able to assess metabolic status or measure the degree of ketosis. Ketosis or ketone status can be measured with either a blood or urine sample. Some argue that a blood sample should be used to confirm ketosis because urine ketone values lag behind those in blood.[9] Also, urine values may vary based on hydration status, urine volume, acid-base balance, renal hemodynamics, and excretion.[45] Additionally, false-negative results are more common with urine[9] compared with blood testing. Blood ketone levels can be measured with commercially available blood glucose meters by using metabolic test strips specific for ketones. Importantly, no consensus currently exists regarding what level of blood ketones is indicative of ketosis or keto-adaptation. Previous work indicates that ketones begin to be used by the central nervous system at fairly low blood concentrations (0.3mmol/L to 0.5mmol/L), whereas blood levels must be greater than 5mmol/L for ketones to use be as preferential (at least 60%) fuel source for the brain.[25,46] It is likely that the exact concentration required is highly individual.

Conclusion

Ketosis, achieved either through a high-fat diet or ketone supplementation, is of interest to many as a potential performance enhancer. To date, given the logistical constraints and unique demands and deployment cycles, a KD may not be feasible and requires research to address important unanswered questions. These include (1) how do environmental extremes impact ketone use? (2) Do ketones improve anaerobic performance (i.e., sprinting) and strength/power performance? (3) Do ketones enhance recovery and/or resilience? Until those questions are answered, insufficient evidence supports using a KD and/or a ketone supplement to enhance performance for the Special Operations community. Instead, SOF Operators should leverage the expertise of their unit dietitian to develop individualized nutritional strategies[47] and engage with the rest of their human performance team to optimize all aspects of total-force fitness.[48]

Disclaimer

The opinions or assertions contained herein are the private views of the authors and are not be construed as official or as reflecting the views of the Uniformed Services University or US Department of Defense.

Disclosure

The authors have nothing to disclose.

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