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Does Carnitine Supplementation Enhance Exercise Performance in Healthy Adults?

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DOES CARNITINE SUPPLEMENTATION ENHANCE EXERCISE PERFORMANCE IN HEALTHY ADULTS?

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Introduction

The desire to excel in competition is an impetus for many athletes to turn to nutritional supplements to manipulate energy production and enhance performance. To sustain physical activity the onset of fatigue must be delayed. Wilmore & Costill (1994) describe fatigue as simply "an inability to continue work" (p. 536). McArdle, Katch, & Katch (1996) define fatigue as "the decline in muscle tension capacity with repeated stimulation" (p. 351). The near depletion of muscle glycogen leads to fatigue resulting in the decline of athletic performance, as presented in the textbook Nutrition for health, fitness & sport (1999), written by Melvin H. Williams. Research on animals suggests carnitine supplementation increases fatty acid oxidation thus exerting a muscle glycogen sparing effect and delaying the onset of fatigue (Brass, Scarrow, Ruff, Masterson, & Van Lunteren, 1993; Cooper et al., 1986).

It has become common practice for athletes to utilize ergogenic aids in an attempt to enhance athletic performance during competition by altering energy generating metabolic processes. The utilization of carbohydrates as an energy source increases, and the use of fatty acids decreases as exercise intensity exceeds 65% of VO_2 max (Kanter & Williams, 1995). As L-carnitine is used to transport fatty acids across the mitochondrial membrane, it is suggested that L-carnitine supplementation could increase fatty acid oxidation (Colombani et al., 1996; Vukovich, Costill, & Fink, 1994) and prevent a deficiency of carnitine, possibly sparing muscle glycogen, delaying fatigue, and enhancing performance (Gorostiaga, Maurer, & Eclache, 1989). Another proposed mechanism and possible benefit of L-carnitine supplementation is the buffering effect it has on

acetyl-CoA. This buffering action would decrease the acetyl-CoA/CoA ratio, decrease the inhibition of pyruvate dehydrogenase complex (PDC), and reduce lactic acid accumulation. The buffering action would then allow for enhanced oxidation of pyruvate, resulting in improved performance (Barnett et al., 1994; Trappe, Costill, Goodpaster, Vukovich, & Fink, 1994). The major source of energy for the synthesis of adenosine triphosphate (ATP) during sustained exercise is mitochondrial oxidation of long-chain fatty acids, which is dependent upon the availability of adequate carnitine (Oyono-Enguelle et al., 1988).

Ninety-five percent of endogenous L-carnitine is located within the muscle system, theoretically impacting both aerobic and anaerobic energy production during exercise (Kanter & Williams, 1995). The intention of many investigations is to determine whether ingestion of L-carnitine enhances the transport of fatty acids into the mitochondria for oxidation, increasing the use of lipids for energy production.

Carnitine is required for the transport of free fatty acids into the mitochondria. It has been reported that 40 minutes of moderate exercise produced a large reduction in the amount of carnitine in active skeletal muscle tissue (Carlin, Reddan, Sanjak, & Hodach, 1986). It is speculated that the inherent concentration of carnitine in human muscle is at a level that could potentially limit the capacity for fatty acid oxidation thus restricting physical performance (Decombaz, Gmuender, Sierro, & Cerretelli, 1992). Considering carnitine deficiency will interfere with normal muscle function, and muscle fat oxidation corresponds with the level of carnitine in the muscle, there is the possibility that carnitine supplementation may affect muscle metabolism (Heinonen, 1996). Evidence is

inconclusive, but it may be that L-carnitine supplementation could be a beneficial effect on physical performance, allowing the athlete to perform for a longer duration before the onset of fatigue. If true, this would be especially beneficial to the endurance athlete in addition to individuals desiring to increase their lean body mass by reducing fat tissue. This literature research will aid in answering the hypothesis that there is a positive relationship between L-carnitine supplementation and physical performance.

The use of L-carnitine to enhance exercise performance is controversial and has evidence both for and against its efficacy. The ability of the athlete to delay the onset of fatigue and enhance performance through the ergogenic effect of orally ingested L-carnitine is the focus of this literature review.

History of Carnitine

In 1905 L-carnitine (3-OH, 4-N-trimethylamine butyrate) was discovered in bovine muscle, with its structure established in 1927 (Canale et al., 1988). A short-chain carboxylic acid, carnitine contains nitrogen, is water soluble, and was once considered a vitamin (Kanter & Williams, 1995). In 1955 Fritz first discovered the role of carnitine to be fatty acid oxidation. Experiments he performed with liver slices confirmed carnitine stimulated fatty acid oxidation (Heinonen, 1996). In 1958 experimenters discovered the role of carnitine in mammals when it was demonstrated carnitine enhanced stimulation of oxidation of fatty acids in the mitochondria (Canale et al., 1988). In 1962 it was reported that the natural, physiologically active form of carnitine was in the L-configuration (Heinonen, 1996). L-carnitine transports fatty acids from the cytoplasm into the mitochondria, facilitating oxidation of long-chain fatty acids (Vukovich et al., 1994).

Carnitine is synthesized in the liver and kidney (Armsey & Green, 1997; Brass & Hiatt, 1994) from two essential amino acids, lysine and methionine (Barnett et al., 1994; Kanter & Williams, 1995), and it is believed that the body is limited in its ability to synthesize carnitine in adequate amounts to maintain tissue and fluid levels in adults (Decombaz, Gmuender, et al., 1992). Specific requirements for carnitine in humans are unknown because the amount needed is dependent upon diet and utilization (Gorostiaga et al., 1989). L-carnitine is found primarily in beef and lamb, with milk, cheese, poultry, fruits, vegetables, and grains providing lesser amounts (Kanter & Williams, 1995). However, the availability of carnitine in cooked foods is not known (Gorostiaga et al., 1989).

Function of Carnitine

Mitochondria need carnitine for energy production. The primary role of carnitine is the transportation of long chain fatty acids into the mitochondria for fatty acid oxidation (Brass & Hiatt, 1998; Cerretelli & Marconi, 1990; Kanter & Williams, 1995), a principal source of energy during exercise (Armsey & Green, 1997; Brass & Hiatt, 1998). Once activated, fatty acids are esterified to acylcarnitines (Heinonen, 1996). Acylcarnitine is a metabolic by-product of long chain acyl-CoA and the enzyme carnitine palmitoyl transferase I (CAT I), which is located on the outer surface of the inner mitochondrial membrane (Cerretelli & Marconi, 1990). This reaction allows acylcarnitine to pass through the inner mitochondrial membrane into the mitochondrial matrix and then react with CoA, catalyzed by carnitine palmitoyl transferase II (CAT II), which was affixed to the inner lining of the mitochondrial membrane. Through this process, acylcarnitine is

reconverted to acyl-CoA and carnitine in the mitochondrial matrix (Cerretelli & Marconi, 1990; Heinonen, 1996).

The enzyme carnitine-CoA acetyltransferase, located on the inner surface of the inner mitochondrial membrane, may be associated with buffering the mitochondrial pool of acetyls by liberating CoA and restoring the metabolic flux in the TCA (tricarboxylic acid) cycle (Carlin et al., 1986; Cerretelli & Marconi, 1990).

Fuel for Exercise

Glucose and fatty acids are the major source of energy during exercise. Fat has a few advantages over carbohydrates as a source of energy. The energy density of fat is higher (37.5 vs. 16.9 kJ/g) plus the relative weight as stored energy is lower (Hawley, Brouns, & Jeukendrup, 1998). Approximately 2g of water are stored for every gram of carbohydrate stored as glycogen limiting the amount of stored glycogen in muscle and liver to about 450g (Hawley et al., 1998). "The amount and type of fuel used and the proportion of aerobic to anaerobic metabolism called into play depend on three main factors: intensity and duration of the exercise, condition of the athlete, and diet." (Berning, McKibben, Benardot, & Fike, 1993, p. 7) With higher temperatures there is greater muscle glycogen breakdown which also affects fuel use in exercise. During all types of exercise both anaerobic and aerobic metabolism are required to provide energy to the working body. Anaerobic metabolism provides the largest portion of energy during the first few minutes of exercise or activity. As the duration of exercise or activity increases, and the intensity remains low, aerobic metabolism takes over and provides most of the energy required by the body. During high intensity anaerobic exercise,

carbohydrates are the preferred fuel source because catabolism is immediate and the ATP produced goes directly to the working muscle. Carbohydrates have the potential to produce ATP for muscle contractions up to three times faster than fats.

Forty percent of the body's energy needs at rest are provided by carbohydrates. During moderate exercise carbohydrate use increases to at least 50% and carbohydrates become the preferred and primary source of energy when exercise intensity reaches 70-80 percent of capacity (Williams, M. H., 1999; Hawley et al., 1998). For sports and activities with intensity greater than 65% VO_2 max and lasting more than 90-120 minutes, muscle glycogen is the preferred carbohydrate source for energy, particularly the glycogen in the muscles that are active (Bortz, Schoonen, Kanter, Kosharek, & Benardot, 1993; Williams, M. H., 1999). The stored glycogen provides enough energy for approximately two hours of exercise, after which the energy source has been depleted and fatigue sets in. Carbohydrates are especially important for prolonged sports involving multiple bouts of high-intensity exercise such as ice hockey, football, soccer, and basketball (Bortz et al., 1993; Williams, M. H., 1999).

"High exercise intensity (high percentage of VO_2 max) relies more heavily on glucose as a fuel while low exercise intensity (low percentage of VO_2 max), with adequate oxygen and oxidative enzymes, relies on a mixture of fat and carbohydrates as a fuel." (Bortz et al., 1993, p. 8) Fat becomes a more important source of fuel as exercise intensity decreases and exercise duration increases. Athletes experience an increased fat utilization from muscle and adipose tissue, thus sparing glucose and glycogen fuel sources, whereby the duration of the activity may be extended. The increase of fatty acid

utilization for fuel and sparing glycogen would be beneficial for those participating in marathons or runs exceeding a marathon distance.

Endurance training increases the number of mitochondria per cell and also increases the enzymes required for fatty-acid oxidation. One effect of improved enzyme function is carnitine activity is enhanced, allowing for more efficient processing of fatty acids as a source of energy (Williams, M. H., 1999). A major effect of training for the endurance athlete is increased utilization of fat during exercise. This increased utilization of fat for energy is evidenced by:

1. Lower respiratory ratio at the same exercise intensity, indicating a more efficient use of oxygen
2. Lower respiratory quotient, indicating more oxygen able to be used at a given workload
3. Decreased rate of glycogen utilization, indicating more fat used to meet energy needs
4. Lower lactate production, indicating more complete oxidation of energy substrates (Berning et al., 1993, p. 15)

The endurance athlete must become better at utilizing fat as a source of energy. This enables the athlete to spare glycogen and prevent early fatigue during an extended event such as a marathon. Using fat as a source of energy does not benefit the athlete who participates in high-intensity exercise (65-70 percent of VO_2 max) because carbohydrate is the preferred source of energy for this type of exercise.

The Effect of Exercise on Carnitine Levels

Exercise has been associated with an increase in plasma acylcarnitine concentration (Bordin, Bottecchia, Bettini, Aragno, & Sartorelli, 1992; Brass & Hiatt, 1994). Some have suggested that the increase in plasma esterified carnitine comes as a result of a

decrease in muscle carnitine during exercise and recovery (Carlin et al., 1986; Constantin-Teodosiu, Howell, & Greenhaff, 1996). Several studies are presented here showing the effect of exercise on endogenous carnitine levels in both well-trained and moderately-trained individuals.

Endurance Exercise

Mitochondrial enzymes utilized in the oxidation of carbohydrates and fatty acids in muscle tissue exhibit an adaptive response by increasing with regularly performed endurance exercises (Heinonen, 1996; Lennon et al., 1983; Spina et al., 1996). This adaptation results in an increase in both the size and number of mitochondria, and leads to a greater dependence on fat oxidation for energy in the trained muscles (Spina et al., 1996). An additional adaptation to endurance training is the increase of carnitine and carnitine transferase within the muscle fibers for transport of fatty acids (Saltin & Astrand, 1993). Theoretically, an increase in the concentration of carnitine that is available to the working muscle could increase fatty acid oxidation and preserve glycogen (Clarkson, 1996, Spina et al, 1996). An individual's training status and intensity and duration of exercise activity are primary determinants of the proportion of carbohydrate and fat supplying energy to the working muscles. Additionally, carnitine may transform acetyl-coenzyme A (CoA) into acetylcarnitine and CoA, increasing the availability of CoA, which is critical for maximum functioning of the Krebs cycle (Clarkson, 1996). The availability of free coenzyme A (CoA) is increased by carnitine thus enabling increased beta-oxidation to acetyl-CoA (Bordin et al., 1992; Hiatt, Regensteiner, Wolfel, Ruff, & Brass, 1989). Lactic acid production and accumulation

may be lessened by the decrease in the ratio of acetyl-CoA:CoA, which stimulates pyruvate dehydrogenase to increase glucose oxidation (Clarkson, 1996; Kanter & Williams, 1995). This could potentially enhance performance that would ordinarily be limited by excess lactic acid production and accumulation. Endurance exercise at moderate intensity has been reported to decrease the level of muscular carnitine and at the same time increase the level of plasma carnitine (Bordin et al., 1992). The balance between carnitine synthesis, tissue uptake, and carnitine excretion is denoted in the plasma carnitine levels (Lennon et al., 1983).

As changes in carnitine levels and different carnitine enzymes are indicative of adaptations to endurance exercise training, an investigation was conducted by Lennon et al., 1983, to "quantify and evaluate carnitine dynamics and carnitine palmitoyl transferase (CPT) activity at rest and during exercise in well-trained and moderately-trained men and women" (p. 489). Primarily, the investigation focused on the possibility of differences in plasma and skeletal muscle carnitine concentration and CPT activity between well-trained and moderately-trained participants. The effect of intense exercise on carnitine levels in plasma and working skeletal muscles and on muscle CPT activity was also of principal interest.

Twenty-eight subjects volunteered to participate in the experiment. A bicycle ergometer was used to determine maximal aerobic power (VO_2 max), after which the subjects were divided into four groups based on measured VO_2 max and previous exercise history. The groups consisted of seven well-trained males (WTM), seven well-trained females (WTF), seven moderately-trained males (MTM), and seven

moderately- trained females (MTF). After an eight hour fast, subjects performed on an exercise bicycle at a workload of 55% of their individual VO_2 max for 40 minutes. Muscle biopsies from the vastus lateralis were obtained immediately prior to the session and upon completion of the exercise.

Results indicate there were no significant differences between groups in plasma carnitine levels at rest, after 40 minutes of exercise, or after 15 minutes of recovery. As a group, acid-soluble plasma carnitine tended to increase from 41.4 ± 12.0 μM at rest to 43.6 ± 13.9 μM following 40 minutes of exercise. Individually, only the MTM group showed a significant increase in acid-soluble plasma carnitine from 43.2 ± 14.8 μM at rest to 48.8 ± 16.3 μM at 40 minutes of exercise ($p<0.05$) and no change in free carnitine levels from 36.3 ± 9.70 μM at rest, through exercise 36.2±10.2 μM to 36.2 ± 11.0 μM during the recovery period. A significant decline ($p<0.001$) in free carnitine levels in plasma was observed in the group from 33.4 ± 7.77 μM at rest to 31.4 ± 8.25 μM following 15 minutes of recovery.

Muscle carnitine content showed no significant differences at the resting stage between any of the groups for acid-soluble carnitine or free carnitine. Muscle carnitine levels are decreased under conditions of physiological stress such as exercise, which is associated with increased fat oxidation. Acute exercise at a moderate intensity increases fatty acid oxidation and significantly reduces muscle carnitine concentration. All subjects experienced a significant ($p<0.001$) drop in acid-soluble carnitine levels from 4.21 ± 1.27 at rest to 3.29 ± 1.27 μmol/g wet weight in recovery. A significant ($p<0.01$) decrease was also observed in free carnitine levels from 2.98 ± 1.02 at rest to 2.16 ± 0.77

μmol/g wet weight in recovery. The well-trained ($p<0.05$) and moderately-trained ($p<0.01$) groups exhibited a significant decline in muscle acid-soluble and free carnitine levels from resting to recovery. No differences were detected in CPT activity among the groups at rest to recovery. However, CPT activity decreased significantly after the exercise session ($p<0.05$) in WT subjects. The decrease in CPT activity may be explained by changes in carnitine levels and enzyme activity associated with biochemical adaptations to intense exercise training that have not yet been considered in a study.

Supporting the concept that physical exercise does not cause a decline in carnitine levels in the body is presented in a study by Janssen, Scholte, Vaandrager-Verduin, & Ross (1989) which examined the concentration of total muscle carnitine during a marathon training period and subsequent marathon run, and explored the possible relationship of muscle carnitine levels with the levels of muscle ATP, creatine phosphate, and glycogen, and relative velocity. Twenty sedentary volunteers participated in an 18-20 month training program. Maximal aerobic power was assessed on a bicycle ergometer with an increase in workload until exhaustion was reached both at the beginning of the training program and again 2-3 weeks following the marathon run. In addition, three days prior to the marathon the participants ran on a treadmill to exhaustion to determine maximal running velocity. The percentage of average velocity during the marathon and maximal possible velocity on the treadmill test was calculated to provide the relative velocity during the marathon run. Needle biopsies were collected from the m. vastus lateralis 5-6 days prior to and 4-5 hours after the marathon. All subjects consumed water that contained dextrose during the marathon. Results indicate the

marathon-training program did not significantly alter carnitine concentration in muscle tissue [all subjects: pre: 4.47 ± 0.74 μmol · g^{-1} dry weight; post: 4.14 ± 0.98 μmol · g^{-1} dry weight]. However, there was an observed decrease in muscle glycogen in all runners after the marathon [males: pre 287 ± 52 μmol · g^{-1} dry weight; post 168 ± 51] [females: pre 292 ± 59 μmol · g^{-1} dry weight; post 194 ± 47] (p. S154). The decrease in muscle glycogen was not found to have a statistically significant correlation to muscle carnitine.

The authors concluded that running a marathon did not result in a decreased concentration of muscle carnitine. There was no statistically significant relationship found between muscle carnitine and muscle ATP and creatine phosphate. The study did show there was a correlation between muscle carnitine concentration and relative velocity [men 67.8 ± 5.6% & women 74.3 ± 4.7%], suggesting muscle carnitine may be a "positive conditioning factor" (Janssen et al., 1989, p. S155). It was concluded the amount of carnitine in the muscle is not a limiting factor in energy metabolism, as evidenced by the insignificant decrease in muscle carnitine post-marathon. It has been found that much less carnitine is needed for optimal fatty acid oxidation in the muscle than is present in the tissue. This investigation supports the position that the body has an ample supply of endogenous carnitine to maintain fatty acid oxidation for exercise performance.

In opposition to the previous study, Bordin et al. (1992) suggested that the level of muscular carnitine is reduced following 40 minutes of moderate-intensity exercise and simultaneously the concentration of plasma carnitine is increased. This group of authors conducted a study to confirm the influence of moderate-intensity exercise on the levels of

total carnitine (TASC), free carnitine (FC), and short chain acylcarnitine (SCAC) in the plasma. Twenty-two healthy untrained (no regularly practiced sport) subjects (11 males, 11 females) participated in the experiment. The participants avoided exercise and sport activities the week prior to experimentation. Prior to testing, the VO_2 max was estimated following the indirect method of Astrand and Rhyming. For the study, each subject then performed on a motor-driven treadmill at 50-60% VO_2 max, maintaining constant speed for ninety minutes.

Results of the study indicate the carnitine concentration was not significantly modified by exercise. The plasma concentration of SCAC indicated a statistically significant increase following 90 minutes of exercise at 50 – 60% VO_2 max in both males [at rest: 5.51 ± 1.91 nM · ml^{-1}; post exercise: 14.21 ± 5.4 nM · ml^{-1}] and females [at rest 6.14 ± 1.01 nM · ml^{-1}; post exercise: 11.09 ± 3.91 nM · ml^{-1}]. The plasma concentration of FC showed less significant changes [males: at rest, 45.21 ± 11.5 nM · ml^{-1} / post exercise, 40.83 ± 8.9 nM ·ml^{-1} and females: at rest 33.9 ± 11.1 nM · ml^{-1} / post exercise, 28.2 ± 8.2 nM · ml^{-1}]. Throughout the duration of the exercise performance until recovery, the TASC remains relatively unchanged from its resting level [rest: males 50.72 ± 12.34 nM · ml^{-1} / females 40.05 ± 11.44 ($p<0.05$); recovery: males 51.54 ± 8.72 / females 38.91 ± 6.00 ($p<0.001$)]. During exercise performance it is evident there was an increase in the concentration of plasma acylcarnitine with a concurrent decrease of free carnitine. It appears plasma levels of carnitine and carnitine turnover are affected by factors that influence fat metabolism. Concentrations of muscle carnitine are lowered by situations that utilize a high degree of fat oxidation, such as the moderate intensity

endurance exercise performed by the untrained subjects of this study. The results of the study suggest moderate-intensity exercise in untrained subjects generates a physiological stress that alters carnitine metabolism by simultaneously increasing the plasma concentration of acylcarnitine and decreasing the free carnitine concentration.

High Intensity Exercise

Exercise induces a change in metabolic conditions including the concentration and distribution of carnitine and acylcarnitine. Minkler, Brass, Hiatt, Ingalls, & Hoppel, (1995) conducted a study to measure carnitine, total carnitine and acetylcarnitine in the skeletal muscle of subjects participating in high-intensity (high workload) exercise. Previous studies have indicated exercise performance exceeding the lactate threshold "was associated with a large redistribution of the muscle carnitine pool from carnitine to short-chain acylcarnitines" (Minkler et al., p. 316). Data was collected from six subjects who completed the experiment. Precise methods were not included in the report; but muscle biopsy samples from the vastus lateralis were obtained from each subject at rest, following 30 minutes of bicycle exercise exceeding individual lactate thresholds, and after 30 minutes of recovery. The muscle biopsies are analyzed using two different procedures, high-performance liquid chromatography (HPLC) and radioenzymatic assay (REA). Carnitine dominated the muscle carnitine pool at rest with acetylcarnitine and non-acetyl acylcarnitine at a minimum level. HPLC analysis shows a shift in the carnitine pool from carnitine [at rest: 4.93 ± 2.36 nmol/mg wet weight] to acylcarnitine [at rest: 0.96 ± 0.60 nmol/mg wet weight] occurred following 30 minutes of high intensity exercise. Acylcarnitine [3.51 ± 1.89 nmol/mg wet weight] was predominate in

the muscle carnitine pool following 30 minutes of high-intensity exercise and remained elevated after 30 minutes of recovery [2.51 ± 1.13 nmol/mg wet weight].

From the results of this study, it is clear that with exercise total carnitine [at rest: 6.38 ± 2.97 nmol/mg wet weight; during exercise: 6.98 ± 2.35 nmol/mg wet weight] is not altered, rather it is redistributed from carnitine to acylcarnitine. In this particular study of high-intensity exercise the increase in acylcarnitine concentration is mainly acetylcarnitine, while the non-acetyl acylcarnitine was unaffected by exercise.

Summary

The results of the studies thus far indicate there is no significant change in total carnitine levels following exercise. Two of the studies had participants that were well to moderately trained prior to testing. These subjects may not have produced any significant changes in total carnitine levels because it is possible the body may have adapted to training, resulting in an adjustment in carnitine metabolism. The untrained subjects may not have shown changes in carnitine levels because of the short time involved in the testing procedures. One would speculate that if significant changes in carnitine levels would occur, it would be in the subjects without exercise experience. All of the participants of the endurance trials performed within 50-60% VO_2 max. It was unclear how intense the high intensity workouts were for the participants. Results could also be affected by the length of the test performed. There was no consistency in the amount of time the subjects performed for any of the trials. There was also no control on any of the participants' diets. A diet high in carnitine may have played a role in the

carnitine levels during testing. To have reliable results from testing, controls must be in place to account for any differences the testing produces.

As L-carnitine plays a primary role in transporting fatty acids into the mitochondria for oxidation, it has been hypothesized that increased fatty acid oxidation and carnitine turnover linked with endurance training could produce a carnitine deficiency. A dietary supplement of L-carnitine could increase the potential for fatty acid oxidation and turnover during submaximal exercise, potentially resulting in muscle glycogen sparing and improved performance (Armsey & Green, 1997; Gorostiaga et al., 1989). Several studies are presented here that explore the relationship of carnitine supplementation and exercise performance.

The Effect of Carnitine Supplementation on Exercise

There are challenges that must be recognized when attempting to study the effects of carnitine supplementation on exercise in humans. It is estimated that there is approximately 128 mmol or 20g of total body carnitine in a 70 kg man (Brass & Hiatt, 1998). The bioavailability of carnitine taken orally is in the range of 5-15% (Brass & Hiatt, 1998). As only a percentage of ingested carnitine will reach the systemic circulation, large amounts of orally administered carnitine are required to disturb the body's endogenous pools of carnitine. The dosage of carnitine administered is complicated by the variations of over-the-counter formulas with low carnitine content and the inability of the formulas to completely dissolve. As an example, if a study participant received an oral dose of 2g per day of carnitine for two weeks, an estimated 10% of the dose reaches systemic circulation and about 4% of the dose is excreted in

urine. The net increase in the body pool of carnitine is only 0.12g per day meaning the two week supplementation would increase the body pool by only 8% (Brass & Hiatt, 1998).

Another factor that must be considered when studying healthy subjects is the biochemistry and physiology of the different populations studied. Different responses or results may be obtained when studying sedentary adults, recreational athletes and highly trained elite athletes. Additionally, appropriate controls must be utilized to show, with confidence, any effect the supplementation may produce.

Endurance Exercise

Gorostiaga et al. (1989) conducted a study to determine the effects of L-carnitine supplementation, examining a group of endurance-trained athletes during submaximal exercise following L-carnitine addition to the diet. This study was done to determine whether energy metabolism (specifically, increased lipid utilization in muscle tissue) during submaximal exercise is altered by carnitine supplementation.

This was a double blind crossover study of endurance-trained, healthy subjects, nine males and one female. Following a four-hour fast on the day of submaximal testing, each subject performed a control test of 45 minutes of cycling at 66% of VO2 max followed by 60 minutes of recovery in a sitting position. After 28 days of 2g/day of L-carnitine supplementation or placebo treatment, the trial was repeated. Each subject had oxygen uptake (VO2), respiratory quotient (RQ) and heart rate (HR) measured at rest, prior to exercise and each minute during the cycling session.

The results of the study indicate the L-carnitine treated group (0.95 ± 0.01) displayed a significantly lower respiratory quotient during exercise when compared with the placebo group (0.98 ± 0.02) during the last minute of exercise. Heart rate between treatments showed no differences. However, during exercise the L-carnitine supplemented group (178.8 ± 2.8) did display an insignificant tendency toward higher heart rate values than the placebo group (176.3 ± 3.2). The L-carnitine supplemented group (2.82 ± 0.11 $L \cdot min^{-1}$) exhibited a nonsignificant trend toward higher VO_2 levels than the placebo treated group (2.80 ± 0.13 $L \cdot min^{-1}$) during the last minute of exercise. Free fatty acids showed no detectable treatment effects during exercise or recovery. Although not significant, the L-carnitine group displayed higher resting levels of free fatty acids (0.284 ± 0.05 mM) than the placebo group (0.143 ± 0.03 mM). There were no observed differences between treatments in blood concentrations of free carnitine [Placebo: rest 31.4 ± 1.7 mM, exercise 35.5 ± 4.4 mM; L-Carnitine: rest 39.2 ± 3.3 mM, exercise 38.9 ± 2.8 mM] or total carnitine [Placebo: rest 41.4 ± 4.7 mM, exercise 47.4 ± 5.9 mM; L-Carnitine rest 46.1 ± 4.0 mM, exercise 49.1 ± 4.9 mM].

The major result of this study was that the respiratory quotient decreased during submaximal exercise following 28 days of supplementing the diet with 2g of L-carnitine. A decreased respiratory quotient implies increased utilization of lipids by working muscles and a sparing of muscle glycogen during exercise. It is unclear whether L-carnitine actually enhanced performance, or it was the physiological effects of exercise that decreased the respiratory quotient.

There were no differences noted in the levels of circulating carnitine between treatment groups. Gorostiaga et al. (1989) make reference to other studies that have found that carnitine levels in the blood during exercise and at rest are not related to the carnitine concentration in muscle tissue. Nonetheless, a lack of difference in carnitine levels between treatments does not exclude possible effects of L-carnitine supplementation on the concentration of carnitine in muscle tissue.

The subjects were asked to keep dietary patterns and habits and training status constant throughout the study. There is no evidence the subjects were compliant with this request. Either an improvement in endurance capacity or a diet low in carbohydrates can result in a decreased respiratory quotient. It follows that the decreased respiratory quotient during exercise in the group supplemented with L-carnitine could be associated with dietary changes and/or training status during the term of the study. There were no differences observed between the control group and the placebo treated group during the study, strongly suggesting that dietary habits and training status remained constant throughout the study.

There is the possibility the participants of this study may have been carnitine deficient and the observed increase in lipid utilization during exercise was positively associated with L-carnitine supplementation. Three options may have contributed to the carnitine deficiency (Gorostiaga et al., 1989, p. 172-173):

1. Endurance-trained subjects experience increased carnitine utilization
2. Diet provides an insufficient amount of carnitine
3. Endurance-trained subjects may have an insufficient capacity for carnitine synthesis despite sufficient precursors.

It was concluded that L-carnitine supplementation in endurance-trained subjects during submaximal exercise resulted in a decreased respiratory quotient, suggesting increased lipid utilization and a likely carbohydrate-sparing effect.

It has been suggested that carnitine availability may be a limiting factor in fatty acid oxidation. During exercise there is a potential loss of carnitine from muscle to plasma; consequently, sustained exercise may further decrease muscle carnitine, affecting transport of fatty acids into the mitochondria. Soop, Bjorkman, Cederblad, Hagenfeldt, & Wahren (1988) investigated the effect of L-carnitine supplementation on plasma levels and leg muscle exchange of free fatty acid and carnitine during endurance exercise.

Seven moderately-trained male subjects participated in two bicycle exercise sessions and served as their own controls. Each subject performed a submaximal bicycle session continuing 120 minutes at 50% of individual VO_2 max. A second submaximal bicycle session was conducted 1-2 months later, immediately preceded by five days of 5g/day of L-carnitine and an additional 1g L-carnitine the morning of the second bicycle exercise session. Only one subject reported a sensation of warmth with the supplementation. Femoral artery and vein blood samples were collected at rest, after 40 minutes and 120 minutes of exercise, and 40 minutes post-exercise and analyzed for hormones, glucose, substrates, amino acids, and carnitine. Each subject received an infusion of oleic acid bound to human albumin during 30 minutes pre-exercise and during the final 20 minutes of exercise. Heart rate was monitored and VO_2 was computed.

Heart rate after L-carnitine supplementation was significantly lower ($P<0.05$) (Soop et al., 1988) at 40 and 120 minutes of exercise as compared to the heart rate prior to

supplementation. Glucose levels at rest were slightly lower with L-carnitine supplementation ($P< 0.05$), but carnitine did not influence the decline in glucose levels associated with exercise. Arterial hormone levels during exercise were not significantly affected by supplementation. L-carnitine supplementation had no influence on arterial oleic acid concentration and leg uptake. Prior to carnitine supplementation there was no observed net exchange of total carnitine during exercise. Following supplementation with L-carnitine, free carnitine levels increased ($P<0.01$) during exercise.

Findings in this study indicate carnitine supplementation resulted in a doubling of circulating carnitine levels. However, leg muscle exchange of substrates and changes in concentration of substrates during exercise were not influenced by L-carnitine supplementation. Post-supplementation, an increase in acylated plasma carnitine levels during and after exercise was observed. There was a release of free carnitine from muscle tissue during exercise, along with a decrease in plasma-free carnitine. There are indications that during exercise free carnitine is released from muscle and acylated most likely in the liver. Findings of the study do not support implication of a potential loss of acylated carnitine from muscle tissue during exercise.

Results of this study suggest muscle carnitine levels are adequately maintained in healthy subjects during exercise and L-carnitine supplementation has no significant effect on skeletal muscle metabolism or substrate utilization.

Hypothetically, an increased availability of L-carnitine during exercise may facilitate increased lipid oxidation. Supporting evidence indicates a significantly reduced respiratory exchange ratio (RER) during exercise following ingestion of L-carnitine

(Vukovich et al., 1994). To further address the implication of increased muscle L-carnitine content following supplementation and the possibility of enhanced lipid oxidation Vukovich et al. conducted an investigation on the influence of L-carnitine ingestion on muscle carnitine and glycogen concentration during submaximal exercise.

Eight male volunteers consumed 90g of fat and three hours later cycled for 60 minutes at 70% of VO_2 max. This first trial was used as a control (CON). Two subsequent trials followed the same bicycle ergometer testing protocol after seven and fourteen days. During the second trial (CN) all of the subjects received 6g of L-carnitine per day; however, four also received 2000 units of heparin 15 minutes prior to the start of the cycling to increase the circulating free fatty acids. For the third trial (CNhep) the same exercise protocol was again followed, but the two groups were treated oppositely as compared with the second trail.

There was a significant reduction of free carnitine concentration in the muscle following all three cycling trials [CON (65%), CN (53%) and CNhep (48%)]. During 60 minutes of exercise, the total muscle glycogen utilized did not differ significantly among the three trials [CON 73.5 ± 4.7; CN 70.6 ± 3.3; and CNhep 73.0 ± 7.4 mmol/kg wet weight]. Contrary to evidence from previous experimentation presented in Vukovich et al. (1994), substrate utilization was relatively uninfluenced by L-carnitine ingestion. Results indicate lipid oxidation did not increase nor was there evidence that muscle glycogen was spared during exercise at 70% of VO2 max following L-carnitine supplementation [RER = CON 0.88 ± 0.01; CN 0.87 ± 0.02; CNhep 0.89 ± 0.01]. The study concluded that L-carnitine supplementation did not increase muscle carnitine

concentration nor modify lipid oxidation. Apparently, there is adequate L-carnitine in the mitochondria for lipid oxidation to proceed.

The effects of L-carnitine supplementation on submaximal exercise require exploration. As carnitine is required for rapid transport of fatty acids into the mitochondria for oxidation, Decombaz, Deriaz, Acheson, Gmuender, & Jequier (1993) examined the effects of L-carnitine supplementation in nine active males on submaximal exercise metabolism following muscle glycogen depletion. Each subject performed two identical bicycle ergometer exercise tests; one following seven days of 3g per day of L-carnitine ingestion (CARN) and one as a control (CONT). An elapsed time of 3-5 weeks separated the two trials. For each testing session, the first half of the test was conducted with each subject having normal glycogen stores. After a muscle glycogen depletion routine, the second half of the exercise test was conducted.

Fuel for exercise is supplied by a mixture of carbohydrates and fat substrates, and reliance on lipids for energy will occur only when carbohydrate stores are depleted. Results of the study indicate energy expenditure was not significantly altered following glycogen depletion, at rest, or during the lower exercise levels. However, fat utilization following glycogen depletion increased during rest and exercise, as evidenced by a substantially decreased respiratory quotient (RQ). There was no significant effect observed of L-carnitine supplementation on lipid utilization prior to glycogen depletion (CONT 0.95 ± 0.04; CARN 0.90 ± 0.01). The study concluded that during exercise, energy metabolism and the rate of lipid utilization in the glycogen depleted state, double the rate under normal conditions, was not altered by L- carnitine ingestion. A probable

explanation for L-carnitine ingestion not producing a significant effect on lipid utilization prior to glycogen depletion may be supported by the research of Vukovich et al. (1994) indicating there is a sufficient supply of endogenous carnitine to support increased lipid oxidation during physical performance.

Additional evidence that carnitine supplementation does not affect exercise performance is provided in a study where Colombani et al. (1996) examined the effect of L-carnitine supplementation on physical performance and energy metabolism in an endurance affiliated field study. L-carnitine transports fatty acids into the mitochondria for oxidation and it is possible that supplementation may enhance that process. Carnitine in skeletal muscle buffers coenzyme A (CoA), which is essential in maintaining normal energy metabolism. Exercise performance could potentially be enhanced if adequate L-carnitine were made available to enter skeletal muscle. Consequently, this study was done to evaluate whether a bolus of L-carnitine prior to and during a marathon run affected running performance and energy metabolism during the event and after completion of the run.

This was a double-blind crossover study of seven male endurance-trained athletes who participated in two marathons, separated by four weeks. The athletes received either 2g of L-carnitine or placebo treatment two hours prior to the marathon run [42.8 kilometers (Km)] and again after 20 Km. They were forced to drink 125 ml of sweetened tea every 5 Km during the run and 500 ml during the one hour recovery period. Before the start of the marathon and after completion, the respiratory exchange ratio (RER) was determined using a treadmill. After a four-week washout period, the entire procedure was repeated.

Blood samples were collected at one hour prior to the run, immediately following the run, one hour later, and the morning after the marathon for analysis of at least carnitine, glucose, pyruvate, free fatty acid, and glycerol concentration. The morning after the marathon, a submaximal treadmill test was done to determine the aerobic-anaerobic threshold. Lactate concentration was determined from a blood sample taken from the earlobe, and heart rate was recorded.

Results indicate there was not a significant difference in running times between the L-carnitine supplemented group (197 ± 9 min) and the placebo treated group (198 ± 8 min). Furthermore, the mean RER between the two groups did not significantly differ before [placebo 1.00 ± 0.01; carnitine 1.00 ± 0.00] or after [placebo 0.86 ± 0.01; carnitine 0.85 ± 0.01] the run. All carnitine fractions were significantly ($P<0.000$) elevated in the supplemented group when compared to the placebo group. The carnitine was significantly elevated within the supplemented group immediately following the marathon [122.4 ± 8.3 $\mu mol \cdot l^{-1}$] and one hour after the run [123.2 ± 11.5 $\mu mol \cdot l^{-1}$] compared to values at the beginning of the run [57.9 ± 1.6 $\mu mol \cdot l^{-1}$]. The morning after the event, concentrations of total carnitine and free carnitine remained elevated in both groups.

No significant differences were observed in concentrations of glucose ($P = 0.83$), lactate ($P = 0.83$), pyruvate ($P = 0.18$), free fatty acid ($P = 0.51$), or glycerol ($P = 0.83$) between the two groups.

The major implication in the lack of significant difference in concentrations of metabolites and in RER between the L-carnitine supplemented group and the placebo

treated group is that carnitine did not alter substrate utilization. It is concluded in this study that L-carnitine supplementation did not improve running performance and no recovery effect was observed in performance of the aerobic-anaerobic threshold testing the morning following the marathon.

High Intensity Exercise

The data regarding L-carnitine supplementation and its beneficial effects on athletic performance is controversial. It has been suggested that a possible result of L-carnitine supplementation is a decrease in lactate accumulation from short bouts of exhaustive exercise due to maintenance of the acetyl CoA/CoA ratio which ultimately enhances pyruvate's conversion to acetyl CoA, resulting in delayed fatigue and enhanced performance. In a study examining the effects of L-carnitine supplementation on high-intensity exercise, Trappe et al. (1994) tested highly-trained male athletes. The purpose of this study was to investigate the effect of L-carnitine supplementation on repeated bouts of high-intensity anaerobic exercise.

Twenty male varsity collegiate swimmers participated in this investigation. Each subject first completed a control trial of five 100-yard swims at maximal effort, with a two-minute rest between each bout. Following the trial swims, each subject received a citrus drink with either 4g of L-carnitine supplement (LC) or a placebo treatment (PL) two times per day for seven days totaling 14 drinks. A second trial of five swims was repeated after the seven days of L-carnitine or placebo treatment. Blood samples were taken and analyzed for lactate and L-carnitine concentration for all trials. In addition, blood gas was analyzed for pH, PO_2, and PCO_2.

The results of this trial indicate that although serum L-carnitine levels were elevated in the supplemented group [LC 75.9 ± 2.0 vs. 106.4 ± 3.5 μmol·L^{-1}; PL 79.5 ± 2.8 vs. 77.6 ± 5.3 μmol·L^{-1}], there were no observed differences in performance times between treatment groups or between control and treatment trials. There were no observable differences between groups or between trials post-exercise in serum lactate or pH levels. It was postulated that perhaps the exercise intensity was too extreme for the L-carnitine to enhance performance. The subjects were previously involved with intense training programs for a long period of time possibly creating an already achieved maximal capacity of their aerobic and anaerobic physiological limits. It has been shown that after only 6 to 8 weeks of intense exercise the aerobic capacity is near physiological limits and further gains are minimal. In addition, muscle adaptations such as mitochondrial density and enzyme concentrations may have been maximally developed. Conditions such as these could possibly nullify the benefits of L-carnitine supplementation.

In this study there was no evidence of decreased lactate concentrations suggesting "...a possible reduction in the inhibition of the pyruvate dehydrogenase (PDH) complex may not be apparent at the given dosage (4 grams)..." (Trappe et al., 1994, p. 183) nor during high-intensity exercise as in the trials. It was concluded that supplementation with 4g L-carnitine did not enhance performance on repeated bouts of high-intensity exercise in highly trained athletes. It is recommended that additional controlled investigations of varying intensities be performed to determine possible benefits of L-carnitine supplementation on an athlete's performance.

Supporting evidence negating the benefits of carnitine supplementation on athletic performance is provided in a study by Barnett et al. (1994) who studied the effects of L-carnitine supplementation on muscle and blood carnitine fractions and muscle and blood lactate concentration during high-intensity sprint cycling. Eight males performed three cycling trials; two control trials (CON I & CON II), separated by 14 days, and the third trial, (L-CN) 14 days following the second control trial. For the third trial, each subject ingested 4g per day of L-carnitine for 14 days prior to testing. The two control trials were conducted to minimize possible training effects. Each trial consisted of a 4-minute ride at 90% of VO_2 max followed by a 20-minute rest period. Each subject then began five 1-mile rides at 115% of VO_2 max with 2-minute rest intervals between each ride.

Data collected indicated blood concentrations of total and free carnitine were significantly higher following supplementation with L-carnitine (1-min post 115%, total and free, respectively: CON I 80.0 ± 4.8, 41.2 ± 3.2; CON II 78.7 ± 3.4, 42.8 ± 2.1; L-CN 100.2 ± 6.2, 58.7 ± 5.4 in μmol/L).

Concentrations of blood lactate during CON I were significantly higher ($P<.05$) than during both CON II and L-CN. There were no significant differences observed in blood lactate concentrations between CON II and L-CN.

The results provide evidence that supplementation with L-carnitine had no significant effect on muscle carnitine concentration or muscle lactate concentration. The investigation concluded that L-carnitine supplementation does not increase L-carnitine concentration within the muscle and therefore could not modify skeletal muscle lactate

accumulation during high-intensity sprint cycling. This conclusion supports previous studies claiming L-carnitine ingestion will not enhance physical performance during exercise.

Evidence suggesting the positive benefits of carnitine supplementation is provided by Vecchiet et al. (1990) who examined male volunteers during three maximal exercise tests to study the effects of L-carnitine supplementation on maximal exercise capacity. Mitochondrial enzymes are increased in skeletal muscle tissue with an increase in exercise, enhancing fatty acid utilization. This implies more muscle carnitine is extracted from the blood and recycled through muscle tissue. With prolonged exercise it is possible there may be insufficient endogenous free carnitine to meet increased muscle demand, affecting physical performance. It is believed that L-carnitine, when administered orally, reaches maximal potential in the plasma within two hours of administration, a point at which obvious effects of supplementation should be anticipated. This investigation attempts to establish a relationship between L-carnitine supplementation and physical performance

This was a double-blind cross-over study of 10 moderately-trained male volunteers. Three tests of maximal exercise intensity on a cycle ergometer were performed. The first test, considered a baseline, was used as a control. The second and third tests began 90 minutes after 2g of L-carnitine supplementation or placebo treatment, using random administration. Each test was separated by a 72-hour interval. The subjects began exercising on a cycle ergometer as intensities increased by 50-W increments every three

minutes until the subject reached muscular exhaustion or the theoretical maximal heart rate was reached (220-age). During testing EKG, VO_2 and VCO_2 were monitored.

The results indicate that after L-carnitine supplementation, nine of ten subjects ($P<0.001$) were able to substantially increase the amount of work performed during the cycling exercise. All ten subjects experienced a reduction of VO_2 following L-carnitine supplementation ($P<0.02$). In addition, there was a significant decrease in blood lactate levels subsequent to L-carnitine supplementation ($P<0.01$). Ingestion of L-carnitine significantly increased the VO_2 max ($P<0.05$) while only slightly changing VCO_2. Taking into account the increased work output, together these results indicate more work can be done without an increase in metabolic energy output following supplementation with L-carnitine. The study concluded that, considering present experimental conditions, aerobic processes were enhanced following L-carnitine supplementation, resulting in more effective physical performance.

Studies have shown that as a result of physical performance, the acetylcarnitine/carnitine ratio in muscles and blood is increased (Siliprandi et al. 1990). The increase is directed at maintaining the highest possible level of free coenzyme A in the tissue and at the same time the lowest possible level of acetyl-CoA. "In high-intensity exercise the simultaneous formation of lactate and acetylcarnitine reflects the necessity of the concurrent disposal of both pyruvate and acetyl-CoA in order to allow the optimum energy supply by glycolysis...and compatibly with oxygen availability by pyruvate oxidation..." (Siliprandi et al., p.17). Because pyruvate dehydrogenase activity is strongly stimulated by carnitine in skeletal muscle, Siliprandi et

al. studied the effect of carnitine on subjects who performed to maximal exercise intensity.

Ten moderately-trained males participated in the study. They were instructed to maintain their current level of physical activity and dietary intake for the duration of the study. Following an overnight fast, the participants performed a maximal exercise test on a bicycle ergometer. They began testing with a warm-up then progressively increased the workout load in increments of 50 watts every 3 minutes. Testing was stopped when at least one of the following requirements was met: "(a.) achievement of the theoretical maximal HR; (b.) muscular exhaustion; (c.) onset of severe dyspnea." (Siliprandi et al., 1990, p. 18) The bicycle ergometer testing was repeated following the same protocol after a 3-day interval. Each subject was randomly chosen to receive an oral dose of either 2g of L-carnitine or placebo treatment. As the study was conducted as a double-blind cross-over trial, all participants performed in both exercise sessions and served as their own controls.

Results of the study demonstrate that supplementation with L-carnitine significantly decreased lactate and pyruvate levels in plasma following exercise, and at the same time the levels of acetylcarnitine were increased. Prior to L-carnitine supplementation, maximal exercise caused plasma lactate levels to experience a 15-fold increase and plasma levels of pyruvate to gain a 3.5-fold increase (Siliprandi et al., 1990, p. 18). Following L-carnitine supplementation each subject experienced a significantly lesser increase in plasma levels of both lactate ($P < 0.001$) and pyruvate ($P < 0.01$) after performing maximal exercise.

An improved working capability was associated with the decrease of both lactate and pyruvate following L-carnitine supplementation suggesting carnitine has the potential to increase working efficiency. The reasoning is pyruvate may be utilized more efficiently thus providing more energy and possibly more efficient use of fatty acids. The decrease in plasma lactate corresponds to the simultaneous increase in short-chain acetylcarnitine. The decrease of lactate and pyruvate levels in plasma and the concurrent increase of acetylcarnitine is a common result of increased pyruvate dehydrogenase activity caused by an increased amount of carnitine available due to L-carnitine supplementation (Siliprandi et al., 1990, p. 20).

Summary

Of the nine studies reviewed that utilized carnitine supplementation, the results from six studies did not support the theory that supplementation produced enhanced performance in the participants. Some of the subjects experienced a lower RQ following exercise after using the carnitine supplement, implying an increased use of lipids thus sparing glycogen use during exercise. The decreased RQ could, however, be related to changes in diet or training status of the subjects. A controlled diet of all the participants in the study could have eliminated the possibility of carnitine deficiency or excess as a factor in the results. If the rate of lipid utilization was unchanged by supplementation with carnitine, as shown in some of the studies reviewed, then it could be that there is adequate carnitine available in the mitochondria to support lipid oxidation during physical performance. As no significant changes in muscle carnitine concentrations were noted after ingesting carnitine before exercising, it appears carnitine is adequately

maintained. The need for additional carnitine for enhanced performance is not supported. A lack of evidence of increased carnitine in working muscles suggests no modification in muscle lactate accumulation; thus, enhanced performance was not possible.

Reasons for no evidence supporting claims that carnitine enhances performance during high intensity workouts could include the fact that following intense training, physiological limits had been reached and muscle adaptation had maximally developed. Another possibility is the intensity of the testing may have been too extreme and the maximal capacity of the mitochondria and its enzymes had been reached. More controlled studies using a variety of exercise intensities and dosages of carnitine during testing are necessary to provide more complete evidence to provide support of carnitine supplementation for enhanced physical performance before regular supplementation is recommended.

In contrast to the support that carnitine supplementation does not enhance performance during exercise, three studies indicated that following supplementation lactate decreased and acetylcarnitine increased, substantially increasing working capability. The aerobic process was enhanced suggesting carnitine does have the potential to increase physical performance and work efficiency.

Reasons for improved performance following carnitine supplementation vary with the testing of the participants. As previously noted, a lower RQ suggests increased lipid utilization. Twenty eight days of carnitine supplementation may play a role in altering lipid utilization in the subjects as shown in one study. Although the authors concluded the study was somewhat unclear whether carnitine had a significant effect on

performance, they could not exclude the possibility of the positive effects of carnitine supplementation. The interval between initial testing and testing after supplementation may be significant with regard to excess carnitine clearance from the body. It is believed carnitine reaches its maximal level in plasma within approximately two hours of ingestion (Vecchiet et al., 1990). If carnitine were ingested shortly before exercise, it may provide a higher level available to effect lipid utilization. The differences of imposed exercise or training status of the participants may affect the outcomes of the studies. Time of day, temperature and humidity all affect athletic performance. Each or a combination of the three variables could alter testing results. If controlled to provide a more comfortable environment for testing, results may prove to be more favorable for carnitine supplementation as was the case in one of the studies. All three of the studies recommend further research to learn of the effects of carnitine supplementation on performance. Dietary habits, training status, and initial physical fitness levels are all factors that should be considered when testing.

Conclusion

It is hypothesized that supplementation of L-carnitine could increase the capacity to transport fatty acids into the mitochondria thus increasing fatty acid oxidation and providing increased energy to endurance athletes. Since L-carnitine is naturally present in the muscles, excessive intake may not be harmful, although in some individuals large doses of L-carnitine may cause diarrhea (Kanter & Williams, 1995). However, individuals exposed to prolonged exercise bouts may experience increased urinary excretion of carnitine, possibly followed by a decrease in carnitine concentration in

working muscles (Cerretelli & Marconi, 1990). These individuals might benefit from carnitine supplementation. The typical dosage for carnitine supplementation during exercise trials is 2g/day with some studies providing doses ranging from 500mg/day to 6g/day for from one day to four weeks (Kanter & Williams, 1995). There were no reported adverse effects from these doses.

The effect of carnitine supplementation on endurance performance has not been thoroughly studied. Different workloads produce different metabolic states of the exercising muscle. These differences must be considered when designing the study to examine carnitine metabolism during exercise in order to prevent unexplained discrepancies.

In healthy persons, additional carnitine may not improve muscle metabolism and enhance physical performance. There is no definitive conclusion that supplementation with L-carnitine will enhance exercise or physical performance in normal, healthy subjects. The trials presented in this review are inconclusive and data do not support the use of carnitine supplementation to enhance performance for healthy adults.

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APPENDIX

DEFINITON OF TERMS

Acetyl Coenzyme A (acetyl CoA): The compound that forms the common entry point into the Krebs cycle for the oxidation of carbohydrate and fat (Wilmore & Costill, 1994).

Adenosine Triphosphate (ATP): High-energy phosphate compound found in the body that is a major source of energy for the body (Williams, M. H., 1999).

Anaerobic Threshold: The point at which the metabolic demands of exercise can no longer be met by available aerobic sources and at which an increase in anaerobic metabolism occurs, reflected by an increase in blood lactate concentration (Wilmore & Costill, 1994).

Carnitine: Quarternary amine which performs a crucial role in the catabolism of lipids and the production of energy (Lennon et al., 1983).

Ergogenic Aids: Work enhancing agents that are used in attempts to increase athletic or physical performance capacity (Williams, M. H., 1999).

Ergometer: An exercise device that allows the amount and rate of a person's physical work to be controlled (standardized) and measured (Wilmore & Costill, 1994).

Fatigue: The decline in muscle tension capacity with repeated stimulation (McArdle et al., 1996).

Lactic Acid: The anaerobic end product of glycolysis; it has been implicated as a causative factor in the etiology of fatigue (Williams, M. H., 1999).

NAD^+: Hydrogen-accepting, vitamin B (niacin)-containing coenzyme, nicotinamide adenine dinucleotide (McArdle et al., 1996).

Pyruvate Dehydrogenase Complex (PDC): A multienzyme complex that catalyzes the formation of acetyl coenzyme A from pyruvate and coenzyme A, using NAD^+ as an electron acceptor (Anderson et al., 1994).

Respiratory Exchange Ratio (RER)/Respiratory Quotient (RQ): The ratio of carbon dioxide expired to oxygen consumed at the level of the lungs (Wilmore & Costill, 1994).