L-CARNITINE – A Cardiovascular Disease Factor

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Abstract: The metabolism of choline, phosphatidyl and l-carnitine by intestinal microbiota generate TMAO and accelerates cardiovascular disease and atherosclerosis. Omnivorous produce more TMAO as compared to vegans and vegetarians. Some bacterial taxa were found to be associated with plasma TMAO as well as dietary status. The high level of l-carnitine predicted high risk for CVD, but only among the subjects with high TMAO levels. Only statistical manipulations must have find an association of increased heart disease risk with increased levels of carnitine and TMAO combined.It can be speculated that carnitine and TMAO levels in humans are not causative agent in CVD rather marker of red meat intake.

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I. INTRODUCTION

Our body synthesize l-carnitine in the liver and kidneys after that stores it in the skeletal muscles, heart, brain, and sperms.The effects of L-carnitine supplementation on nutrition have been studied in past two decades. The combination of l-carnitine and lipoic acid, as well as carnitine alone, is suggested to increase fat burning and improve metabolism, especially in elderly people.Some results were found positive while others were contradicting. The reason for the conflict is not important to be elucidated here. This review summarizes the different studies and the attributes of l-carnitine. An attempt has been made to give a brief idea about its sources,synthesis, different properties, pharmacology and physiological role in vertebrates including human being. This review summarizes different research and clinical studies on supplementation of l-carnitine and various attributes. It will also help to understand the wonders of L-carnitine.

II. GENERAL DESCRIPTION

L-Carnitine is known as a non-essential organic nutrient, which is essential for the penetration of long- chain fatty acids into mitochondria. It is also known asa quasiamino acid. It's molecular weight is 161.2 and is hygroscopic in nature. It is easily soluble in water. The solubility in water is 2500mg/and at 20^{o} C. It is synthesized from lysine and methionine in the presence of vitamin C and some other compounds generated in body. 100 years ago it was isolated from red meat (*carnus*). In mealworm (*Tenebrio molitor*) it appeared to act as vitamin, that's why it was named vitamin B_T.The vitamin term for carnitine was found to be misleading when it has been discovered that human beings can synthesize l-carnitine. D-carnitine is either less active or biologically inactive [1].

The first evidence for the biosynthesis of carnitine was found from chick embryos, which contained carnitine but it was absent in eggs. The microorganism *Neurosporacrassa* also developed carnitine when grown in synthetic carnitine –free medium. It was found that the methyl group of carnitine was imported from methionine and γ-butyrobetaineconverted to carnitine. Similarly, lysine is also converted to carnitine through 6-N-trimethyllysine (an intermediate) [2]. The endogenous synthesis of carnitine occurs in the liver, kidney and brain. The process requires two amino acids, iron, vitamin C, vitamin $B_6$and niacin. Fatigue is one of the symptom of vitamin C deficiency, it is assumed to be related to less synthesis of l-carnitine [3].

III. PHARMACOLOGY

Carnitine acts as an antioxidant that is why it can be used for the treatment under different conditions. Antioxidants fight against free radicals generated in our body and neutralize them. Thus it can prevent damages in our body. It can be used for the treatment of :

i. Angina –Carnitine can be used for the treatment of angina along with the conventional one.angina. It is evident from several research studies and clinical trials that l-carnitine and propionyl-l-carnitine reduce symptoms of angina.

ii. Heart attack –There are contradictory views about the relation between heart attack and l-carnitine. A few studies suggested that it helps after heart attack when used along with conventional treatment. If l-carnitine is supplemented after heart attack it reduces the chances of another attack. Some studies are against this view.

iii. Heart failure –It is evident from few studies that propionyl-l-carnitine can reduce heart failure. Further research is still needed for assurance.

iv. Peripheral vascular disease - Propionyl-l-carnitine can reduce the symptoms of PVD (reduced blood flow to the legs). It is not confirmed about l-carnitine.

v. Diabetic neuropathy – When high sugar level disrupt nerves of legs, arms and feet, causes numbness. Acetyl-l-

carnitine reduces pain but further research is required for l-carnitine.

vi. Weight loss – It is supplemented for weight loss but there is no scientific evidence. According to some studies it reduces fat mass, increases muscle mass and reduces fatigue.

vii. Alzheimer's disease –It has been believed that acetyl-l-carnitine slows down the progression of it and improves the memory but latest studies are totally against this view.

viii. Kidney disease – It is synthesized by kidney; hence any kind of ailment in kidney reduces the level of carnitine. Sometimes doctors prescribe carnitine supplement but it should be taken under medical supervision.

ix. L-carnitine may increase sperm count and their mobility.
x. Erectile dysfunction – It has been found in men, who had erectile dysfunction after prostate surgery, improved the effectiveness of Viagra.

xi. Hyperthyroidism – l-carnitine can reduce the symptoms of hyperthyroidism, such as nervousness, insomnia and tremor. Carnitine may work by blocking the action of thyroid hormone which may be dangerous for people with low thyroid levels.

IV. PHYSIOLOGICAL ROLES OF CARNITINE

The roles of carnitine have been studied in details. Most of the studies have considered its significance in fatty acids oxidation. However, it plays some other important roles also:

1. From peroxisomes it transfers acetyl and other acyl groups to mitochondria [4.5]
2. Beta oxidation of long-chain fatty acids in mitochondria and very large chain fatty acids in peroxisomes [6].
3. Re-esterify triacylglycerol in endoplasmic reticulum before its secretion as very low –density lipo-protein [7]
4. Stimulate oxidative metabolism of branched-chain amino acid and pyruvate [6].
5. It act as scavenger system for acyl groups [8-10].
6. Synthesize and elongate fatty acids (polyunsaturated) [6, 11-13].
7. It act as partner In the pathway of triglyceride fatty acid and phospholipidturnover in neurons [14]
8. In erythrocyte membrane phospholipids it undergoes deacylation and reacylation for remodelling [15].
9. Stabilize protein and counteract the effect of denaturants [16-17].

V. CARNITINE AND CVD RISK

There are conflicts on risk of cardiovascular disease and origin from red meat. L-carnitine, choline and phophatidylcholine by gut microbiota generate TMA (Trimethylamine), which further churn down into TMAO (Trimethylamine-N-oxide). TMAO accelerates atherosclerosis in mice. Longer exposure to l-carnitine altered ceacalmicrobiota and high amount of TMAO resulted in atherosclerosis. With the use of antibiotic these effects were suppressed. This indicated that gut microbiota plays an important role in generating pro-atherogenic substance from red meat [18]. As compared to vegans and vegetarians omnivorous human are at risk for TMAO production. As a result there are possible risks of CVD adverse effects [19]. TMAO not only comes from carnitine but also from choline, choline phospholipids, acetyl choline, and even fish, which is known to lower the cardiovascular risk [20]. Moreover, the plasma levelsof immediate precursor of TMAO,trimethyllysine, are originally very high in human beings.It is hardly affected by the supplementation of carnitine. It is interesting to know that, while carnitine levels were associated with an increased risk of CVD, TMAO itself was not [21-23]. Only statistical manipulations must have find an association of increased heart disease risk with increased levels of carnitine and TMAO combined.It can be speculated that carnitine and TMAO levels in humans are not causative agent in CVD rather marker of red meat intake. Just because carnitine levels are related to increased heart disease risk does not mean carnitine (or TMAO) are causing factors. Much more research and thought process needs to be done to develop mechanisms and causality in humans. It is unjustified to declare carnitine as a culprit of heart disease.The main causative factorof atherosclerosis and CVD in red meat is saturated fat, carnitine or TMAO are not even close to that [24]. At present, a large data has been accumulated over decades that up to crtain extent acetyl-l-carnitine and lipoic acid are safe to use [23-26].Very high doses (as much as 8 grams per day) acetyl-l-carnitine alone has been given clinically without any side effects. It has already been concluded that acetyl-l-carnitine improves muscle function, mitochondrial activities and lowers lipid levels, which is responsible for lowering the cardiovascular risk. Before taking any decision it is necessary to take "risk-to-benefit ratio" into account. Right now, this new study is the only one that suggests there may also be an adverse effect in some individuals with the use of carnitine as a precursor of TMAO.

VI. CONCLUSION

Red meat can be taken three times a week, provided it should be organic. We should take l-carnitine supplement to withdraw its benefit. It is the only molecule in our cell which can transfer fatty acids to mitochondria and generate energy. Besides that l-carnitine removes waste from mitochondria, which is produced by ATP metabolism. We can include probiotics also in our routine. Probiotics are beneficial bacteria, acidophilus and bifida. It maintains a beneficial bacteria balance. If future research indicates the role of TMAO in atherosclerosis then better to take probiotic. In 2008 a study on animal model suggested that the production of TMAO can be managed by probiotics. It is evident that the increase in TMAO might be a biomarker of gut microbiome [27]. It can be hypothesized that a diseased subject have a different microbiome than non-diseased one. The specific microbiome can be marked by the level of TMAO in blood.Future research should concentrate on the role of microbiomes in CVD and try to bserve the benefits on the reduction of TMAO circulation.

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