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Estimation of L-carnitine levels in diabetic completely edentulous patients for implant diagnosis: A cross-sectional study

Rinki George, Subhabrata Maiti, Dhanraj M. Ganapathy

Departments of Prosthodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamil Nadu, India

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Address for correspondence:
Dr. Subhabrata Maiti, Department of Prosthodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai - 600 077, Tamil Nadu, India.
E-mail: drsubhoprostho@gmail.com

ABSTRACT

Background: Carnitine is effective in preventing the accumulation of end products related to lipid peroxidation due to its anti-inflammatory and antioxidant effects. Carnitine also exerts a significant anti-inflammatory role through the downregulation of the nuclear factor kappa beta pathway, which leads to a decrease in the expression of pro-inflammatory cytokines. The aim of the study was to estimate the L-carnitine (L-C) levels in diabetic completely edentulous patients.

Materials and Methods: A cross-sectional study was conducted after the selection of 60 samples based on the inclusion and exclusion criteria. The collected saliva samples were utilized to measure the levels of L-C using the sandwich enzyme-linked immunosorbent assay (ELISA) method. One hundred microliters of sample was applied to a particular row of wells and incubated for an hour as part of the sandwich ELISA procedure. After the wells had been cleaned, a second batch of monoclonal L-C was added, and they were once more incubated for an hour. The horseradish peroxidase substrate was then applied after washing the second batch as well. To allow the blue-to-yellow color transition, the wells were kept steady. Following the observation of the color shift, the OD was measured, and the concentration was determined using the sandwich ELISA kit's standard curve as an intercept. The data were statistically analyzed using the independent *t*-test (significant level $P < 0.05$) and were tabulated.

Results: The L-C levels have higher levels in nondiabetic patients than in diabetic patients. The difference in the baseline mean value between the groups was statistically significant ($P = 0.00$). Although it is statistically significant ($P = 0.00$), the mean value for diabetic individuals is 0.19 as opposed to 0.29 for nondiabetic patients.

Conclusion: Based on the findings, it can be concluded that L-C improves insulin sensitivity and glucose disposal in diabetic completely edentulous patients.

Key Words: Adult-onset diabetes mellitus, dental implant, edentulous jaw, enzyme-linked immunosorbent assay, levocarnitine

INTRODUCTION

Inflammation is a complex biological process where there are elevated levels of free radicals and reactive oxygen species (ROS), which may cause structural damage to the cells. Inflammation

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and oxidative stress are associated with numerous range of chronic diseases, including atherosclerosis, diabetes mellitus, neurological disorders, pulmonary diseases, cancer, and rheumatoid arthritis.[1] Carnitine is widely effective in preventing the accumulation of end products related to lipid peroxidation due to its anti-inflammatory and antioxidant effects. The major physiologic role of carnitine is transporting long-chain fatty acids through the mitochondrial membrane and contributing to the oxidative release of energy.[2] It not only helps with long-chain fatty acids but also helps to remove the short- and medium-chain fatty acids from mitochondria.[3] Any differences in carnitine homeostasis will have an impact on the metabolism and function of lipids, red blood cells, and cardiac muscle cells.[4]

L-carnitine (L-C) constant infusion improves insulin sensitivity in insulin-resistant diabetic patients; a significant effect on whole-body insulin-mediated glucose uptake is also observed in normal subjects. In diabetics, glucose, taken up by the tissues, appears to be promptly utilized as fuel since glucose oxidation is increased during L-C administration.[5] L-C, a shuttle for the acetyl groups through the mitochondrial membrane and a cofactor in the oxidation of fatty acids, has been shown to stimulate human osteoblast functions and intracellular calcium signaling. Increased mitochondrial performance, particularly from L-C, may have favorable effects on high-energy-demanding organs such as muscle and bone. It is noteworthy that L-C has a direct impact on human osteoblasts, causing them to proliferate and operate more actively, as well as express collagen Type I, bone sialoproteins (BSPs), and osteopontin (OPN).

L-C has recently demonstrated antioxidant action that prevents age-related mitochondrial dysfunction and maintains the equilibrium of ROS generation in several types of cells.[6] The development of myotubes and their hypertrophy were seen to speed the differentiation of C2C12 myoblasts,[7] counteract mitochondrial malfunction, and reduce oxidative stress. Glycemia depicts the level of sugar in the blood, which plays a vital role in the consequences of osseointegration,[8] as a correlation between glycemic control and the development of microvascular and macrovascular complications was observed specifically during implant placement.[9] Tight and intensive glycemic control in diabetic patients can delay the onset and the progression of many microvascular-related complications associated with the condition.[10]

Our team has extensive knowledge and research experience that have translated into high-quality publications.[11-26] The aim of the study was to estimate the L-C levels in diabetic completely edentulous patients, where the null hypothesis stated that there is no difference in the level of L-C patients completely edentulous patients when compared to healthy individuals.

MATERIALS AND METHODS

Study design

This was a cross-sectional study.

Sample size calculation

In the prosthodontics department of a well-known university hospital, a clinical trial was conducted. The G*Power software (Version 3.1.9.4) Mac OS X and windows XP/ vista/7/8 was used to estimate the sample size, and the sample included 60 patients (30 diabetics and 30 nondiabetics). All of the chosen patients were told of the study and provided with voluntarily informed written permission.

Method of sampling

Patients with chief complaints of the replacement of completely edentulous teeth participated in the study. The study was on patients who were undergoing implant-supported complete denture treatment which included 30 diabetic and 30 nondiabetic participants with ages ranging between 40 and 65 years. A simple random sampling method was followed [Figure 1].

Ethical approval

Ethical approval was obtained from the Institutional Ethics Committee. Number: IHEC/SDC/UG-1873/22/PROSTHO/625.

Selection criteria

Inclusion

Completely edentulous diabetic and nondiabetic patients, time of edentulism within 1 year, and patient not wearing any denture were considered inclusion criteria.

Exclusion

Partial edentulous patients, patients wearing dentures for more than a year, patients with systemic disease, and patients needing preprosthetic surgery were considered exclusion criteria.

Procedure

Patients at the dental hospital provided 1.5 ml of unstimulated saliva samples. 50–90 years old is the age range. In uricol containers, the samples were gathered,

and they were thereafter kept in the cold room. Following that, the samples were utilized to measure the levels of L-C using the sandwich enzyme-linked immunosorbent assay (ELISA) method. One hundred microliters of sample was applied to a particular row of wells and incubated for an hour as part of the sandwich ELISA procedure. After the wells had been cleaned, a second batch of monoclonal L-C was added, and they were once more incubated for an hour. The horseradish peroxidase substrate was then applied after washing the second batch as well. To allow the blue-to-yellow color transition, the wells were kept steady. Following the observation of the color shift, the Optical density (OD) was measured, and the concentration in ng/mL was determined using the sandwich ELISA kit's standard curve as an intercept.

Data collection

A total sample of 70 patients for 1 month with complete edentulism was taken; out of which only 60 patients met the inclusion criteria. Two diabetic patients were eliminated from the data collection sheet as they did not report back after selection. Data were reviewed by an external reviewer. The result from the laboratory testing was tabulated.

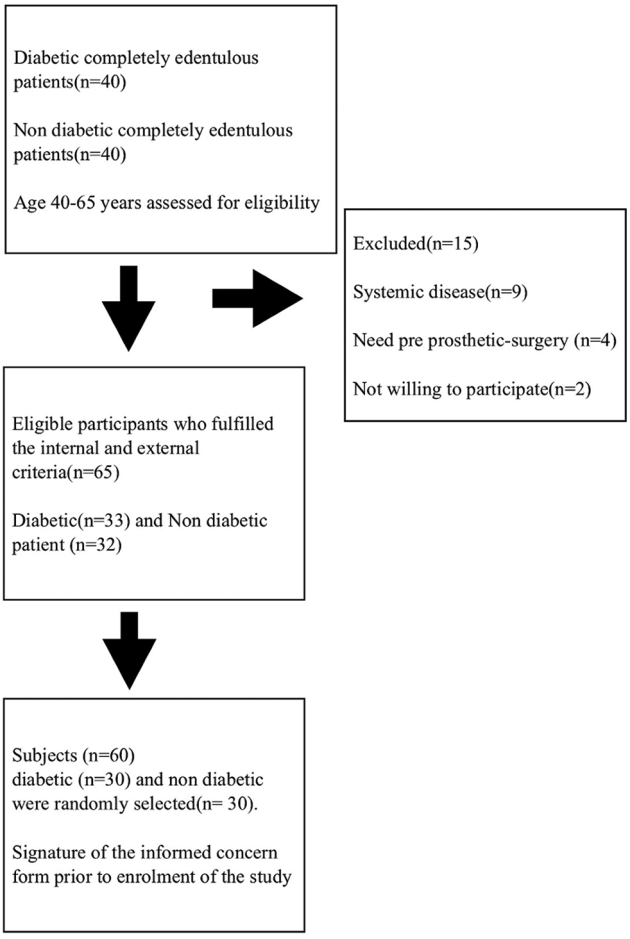

Figure 1: Flow chart of the study population selection including patient recruitment, exclusion criteria, and refusals. CD = Complete denture.

Statistical analysis

Data were recorded in Microsoft Excel 2016 (Microsoft Office 10) and later exported to SPSS (Statistical Package for the Social Sciences for Windows versions, 20.0), SPSS Inc., (Chicago, IL, USA), and subjected to statistical analysis. The data were statistically analyzed using the independent *t*-test ($P < 0.05$) and were tabulated.

RESULTS

The L-C levels have higher levels in nondiabetic patients than in diabetic patients [Table 1]. The difference in the mean value between the groups was statistically significant ($P = 0.00$).

DISCUSSION

The goal of the current study was to measure the L-C levels of diabetic patients with no remaining teeth. The current investigation demonstrated that there was a statistically significant difference between the groups in the mean value at the baseline ($P = 0.00$). Although it is statistically significant ($P = 0.00$), the mean value for diabetic individuals is 0.19 when compared to 0.29 for nondiabetic patients. Studies done in the past found that diabetic patients had dental implant chances of success that were similar to those of healthy individuals. The fact that diabetics under control are virtually always included in research could be the cause. The development of microvascular complications and subsequent early or late implant failure is brought on by continuous hyperglycemia.

Osseointegration is the process by which an alloplastic substance is rigidly fixed in bone and retained therein

Table 1: Comparison between the diabetic and nondiabetic groups based on L-carnitine concentration

Group	*n*	Mean±SD (ng/mL)	SE	95% CI		*t*	*P*
				Upper	Lower		
Diabetic	28	0.88±0.54	0.01	−0.37	0.42	33.20	0.00*
Nondiabetic	30	1.28±0.03	0.00	−0.37	0.42	32.77	

*A statistically significant value of $P<0.05$, the *P* value was derived from the independent *t*-test. SE: Standard error, SD: Standard deviation, CI: Confidence interval

under functional loads while exhibiting no clinical symptoms. Dental implants undergo osseointegration during the healing process, resulting in a functioning unit that may restore one or more lost teeth and support dental prostheses. The immune and nutritional state of the host should be considered in addition to important aspects that influence osseointegration, such as surgical technique, bone quality and quantity, postoperative inflammation or infection, smoking habits, and implant material and surface.[27]

L-C improves the mitochondria's overall functionality and guards against oxidative stress. In addition, L-C stimulates the CaMKII and ERK/AKT signaling pathways, favoring the activation of genes related to bone growth.[28] Reduced energy supply for altered mitochondrial biogenesis and activity could be blamed, at least in part, for the age-related structural degradation of bone caused by dysregulation of bone remodeling. Studies have shown that L-C improves the mitochondria's overall performance, which suggests that L-C might help meet the high metabolic demand of osteoblasts during bone production. L-C, a coenzyme in fatty acid oxidation, has been shown to promote the actions of human osteoblasts. The expression of collagen Type I, BSPs, and OPN are also all greatly increased, as are osteoblast activity and proliferation. L-C can prevent oxidative damage and support maintaining bone quality.[29]

A flaw in the regulation of mitochondrial ROS concentration leads to an imbalance between superoxide radical production and destruction, which is greater than the capacity of osteoblasts to detoxify them, and suppresses the expression of osteogenic genes and matrix mineralization. The ability of L-C to boost mitochondrial superoxide dismutase-2 production and lower osteoblast ROS concentration indicates that L-C therapy improves the mitochondrial-mediated equilibrium between ROS production and catabolism. Through the ERK pathway, L-C increases the expression of the RUNX2 and OSX genes, supporting a role for L-C in promoting osteogenic cell activities.[30]

Based on all these findings as well as the results from the present study, carnitine supplementation can be an effective intervention for the improvement of oxidative stress and promotes osteogenic activity when associated with implant placement; however, these findings need to be confirmed by more research and have to be performed for clinical significance. The null hypothesis was removed as there were increased levels of L-C in diabetically edentulous patients.

CONCLUSION

The present study demonstrated that L-C potentiates the anti-osteoporotic effect by suppressing the overexpressed inflammatory cytokines and ameliorates bone osteoporotic histopathological changes. L-C can be considered a new therapeutic regimen to maintain bone health and limit the worsening of osteoporotic bony changes in diabetic completely edentulous patients associated with implant placements.

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Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or non-financial in this article.

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