SHORT COMMUNICATION

L-carnitine in Beta Thalassemia

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This study was conducted to determine L-carnitine levels in regularly transfused and chelated beta thalassemia patients (*n*=40; mean age, 17.5±5.0 years).Ten age matched controls were also studied. The mean L-carnitine level in thalassemic patients was 23.71±7.3μM as compared to control 29.26±2.37μM (*P*<0.0001). Mean Carnitine was significantly lower (*P*=0.037) in those with ferritin greater than 2000ng/dL (22.80±6.97μM) in comparison to those with ferritin less than 2000ng/dL (30.1±7.77μM). Although Carnitine levels in non vegetarians was higher (26.91 ±8.4μM) than in vegetarians (22.34±6.55μM), this difference was not statistically significant (*P*=0.072). We conclude that L-carnitine levels were found to be lower in thalassemics as compared to age matched controls.

Key words: *Carnitine, Ferritin, Thalassemia.*

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Beta-thalassemia is characterized by an imbalance between the synthesis of α and β globin chains resulting in excess of free α chains, which form inclusion bodies leading to destruction of erythrocytes within the hemopoietic system(1). The exact mechanisms leading to red blood cell (RBC) destruction in thalassemia are still not clearly identified. In the treatment of thalassemia, newer approaches have been tried as alternative to standard therapy. Butyrate analogues such as L-carnitine have been found to increase HbF synthesis and hence used in treatment of β thalassemia(2,3). L-carnitine is made from the amino acids lysine and methionine and plays an essential role in fatty acid oxidation in mitochondria, and energy production(4). It also protects erythrocytes from oxidative stress, stabilizes the cell membrane, increasing the life span of red blood cells and is found to inhibit apoptosis in different diseases(5,6).

The aim of this study was to evaluate baseline levels of L-carnitine and to correlate these levels with clinical features, dietetic habits and serum ferritin in a group of thalassemics.

METHODS

Forty regularly transfused and chelated patients at the thalassemia center of Balabhai Nanavati Hospital Mumbai, India, were randomly selected for this study after obtaining written informed consent from patients or their relatives, and formal permission was obtained from the institutional ethical committee. There were 24 males and 16 females (8-28 years) with mean age of 17.5±5.03 years. Thirty six were thalassemia major and 4 thalassemia intermedia. Ten age matched controls were also studied. Detailed history regarding symptomatology with special reference to myalgia, chronic fatigue, muscle weakness, diet and splenectomy was obtained.

Total L-carnitine and ferritin levels were measured in all cases prior to transfusion. All measurements were performed within 2 hours of sample collection. Serum carnitine was measured

using enzymatic UV test method, and serum ferritin was determined by solid phase two site chemiluminescent immunometric assay on a fully automated immulite system. Means were compared using students *t*-test.

RESULTS

Mean L-carnitine levels of the thalassemics and controls is depicted in ***Table* I**. Thirty four studied cases had lower carnitine levels while 6 had values higher than the mean levels of control. Patients having low serum ferritin had high carnitine levels, and as ferritin increased carnitine levels decreased (***Fig.* 1**).

DISCUSSION

Primary carnitine deficiency is rare although secondary deficiency may occur due to either decreased biosynthesis, increased catabolism as in chronic diseases such as thalassemia(7,8), or non physiologic losses as seen in dialysis(9). In the present study, thalassemics had significantly lower mean serum total L-carnitine concentration as compared to controls. Although the precise mechanism of carnitine deficiency in β thalassemia is unknown, it is postulated that this may be related to reduced hepatic synthesis of carnitine in the liver(7).

In thalassemia, excess iron is deposited in the liver due to increased absorption and repeated blood transfusion, which could be responsible for decreased carnitine levels. This iron activates the respiratory burst and generates superoxide; peroxide and free hydroxyl radicals(10). L-carnitine is a free radical scavenger which prevents lipid peroxidation of cell membrane and apoptosis reducing serious tissue damage(8). Furthermore, it induces HbF synthesis by increased gamma chain production and decreased alpha chain precipitation, which is the triggering mechanism for apoptosis. This decrease in apoptosis on carnitine supplementation was more pronounced in well chelated patients as compared to those with improper chelation(6). Serum ferritin determines the chelation status of the patients and is an indirect method of measuring excess iron deposited in liver(11). Our observation also suggests that increased liver iron may be responsible for decreased carntitine levels.

In healthy individuals, carnitine homeostasis is maintained through endogenous biosynthesis, absorption from dietary sources, and elimination and reabsorption by the kidney. Nutritional carnitine deficiency has not been identified in healthy individuals without metabolic disorders, suggesting that most people can synthesize enough

TABLE I CARNITINE LEVELS IN STUDY POPULATION

Parameters	*n*	Mean (SD)	*P* value
Controls	10	29.3(2.4)	
Thalassemics	40	23.71(7.4)	<0.0001
Serum ferritin (ng)			
<2000	10	30.1(7.8)	0.04
>2000	30	22.8(7.0)	
Clinical features			
Present	12	22.9(9.0)	0.66
Absent	28	24.1(6.7)	
Diet			
Vegetarian	28	22.3(6.6)	0.07
Non-Vegetarian	12	26.9(8.5)	
Splenectomized			
Yes	17	25.2(5.5)	0.27
No	23	22.6(8.5)	

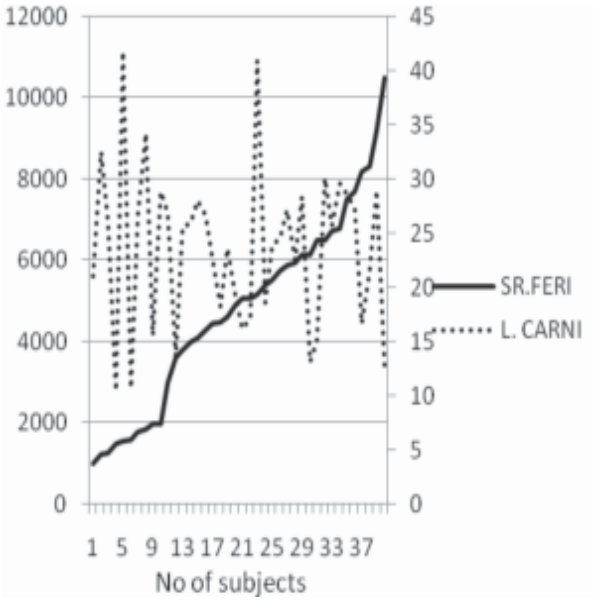

FIG.1 *Comparison of L-carnitine (μM) and ferritin (ng) levels.*

WHAT THIS STUDY ADDS?

- Carnitine levels are lower in thalassemics with ferritin>2000ng/dL and in vegetarians.

carnitine(12); even strict vegetarians (vegans) show no signs of carnitine deficiency despite the fact that most dietary carnitine is derived from animal sources (13). In this study, though the levels of carnitine in non vegetarians were higher than in the vegetarians, the difference was statistically not significant, suggesting that diet alone is not responsible for alteration in carnitine homeostasis.

As L-carnitine is an essential element for energy metabolism in mitochondrial fatty acid oxidation, it is most concentrated in tissues that use fatty acids as their fuel, such as skeletal and cardiac muscles. Supplementation with L-carnitine has shown not only to significantly improve cardiac function (14,15) but also general well being and exercise tolerance(6,7). In our study, no significant difference was noted between the mean carnitine levels of those who have any clinical evidence of myalgia, chronic fatigue or muscle weakness as compared to mean levels of those who were asymptomatic.

Studies are needed to document the role, if any, of carnitine supplementation in thalassemics.

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REFERENCES

1. Shiner E, Rachmilewitz EA. Oxidative denaturation of red blood cells in thalassemia. Semin Hematol 1990; 27: 70-76.
2. Stamatoyannopoulos JA, Nienhuis AW. Therapeutic approaches to hemoglobin switching in treatment of hemoglobinopathies. Annual Rev Med 1992; 43: 497-521.
3. Perrine SP, Miller BA, Faller DV, Cohen RA, Vichinsky EP, Hurst D, *et al.* Sodium butyrate enhances fetal globin expression in erythroid progenitors of patients with HbSS and beta thalassemia. Blood 1989; 74: 454-459.
4. Walter H. L-Carnitine. Arch Dis Child 1996; 74: 475-478.
5. Palmieri L, Ronca F, Malengo S, Bertelli A. Protection of β thalassemic erythrocytes from oxidative stress by propionyl carnitine. Int J Tissue React 1994; 16: 121-129.
6. El-beshiawy A, Seoud H, Ibharim A, Youssary I, Gabre H, Ismaeel H, *et al*. Apoptosis in thalassemia major reduced by a butyrate derivative. Acta Haematol 2005; 114: 155-159.
7. Tsagris V, Laipi-adamidou G. Serum carnitine levels in patients with homozygous beta thalassemia: a possible new role of carnitine? Eur J Pediatr 2005; 164: 131-134.
8. Toptas B, Baykal A, Yesilipek A, Isbir M, Kupesiz A, Yelcin O, *et al*. L-carnitine deficiency and red blood cell mechanical impairment in β thalassemia major. Clin Hemor Microcircu 2006; 35: 349-357.
9. Evangeliou A, Vassopoulous D. Carnitine metabolism and deficit- when supplementation is necessary? Curr Pharm Biotechnol 2003; 4: 211-219.
10. Gutteridge JM, Hallwell B. Iron toxicity and oxygen radicals. Clin Hematol 1989; 2: 195-256.
11. Maris TG**.** Myocardial and liver iron status using a fast T*2 quantitative MRI (T*2qMRI) technique. Magn Reson Med 2007; 57: 742-757.
12. Rebouche CJ. Carnitine. *In*: Shils ME, Shike M, Ross AC, Caballero B, Cousins RJ. Modern Nutrition in Health and Disease. 10th ed. Philadelphia: Lippincott, Williams & Wilkins; 2006.p.537-544.
13. Lombard KA, Olson AL, Nelson SE, Rebouche CJ. Carnitine status of lactoovovegetarians and strict vegetarian adults and children. Am J Clin Nutr 1989; 50; 301-306.
14. Ei-Beshlawy A, Ragab L, Fattah A, Ibrahim I, Hamdy M, Makhlouf A, *et al*. Improvement of cardiac function in thalassemia major treated with L- Carnitine. Acta Haematol 2004; 111:143-148.
15. El-Beshlawy A, El- Accaoui R, El- Sattar M, El-Deen M, Youssary I, Shaheen N, *et al*. Effect of L-Carnitine on physical fitness of thalassemic patients. Ann Hematol 2007; 86: 31-34.