L-Carnitine in Children with Idiopathic Dilated Cardiomyopathy

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Summary

L-carnitine has been used in dilated cardiomyopathy secondary to carnitine deficiency in children, with favourable results. There are no reports on the effects of L-carnitine in children with idiopathic dilated cardiomyopathy. We undertook a prospective study to evaluate the effects of L-carnitine in children with idiopathic dilated cardiomyopathy. Thirteen children, mean age 3.29±1.44 years, with idiopathic dilated cardiomyopathy underwent echocardiographic evaluation while on conventional treatment alone, and with additional L-carnitine (50 mg/kg/day). To obviate the effects of spontaneous improvement, eight patients (Group 1) were restudied three weeks after stopping the drug, and five (Group 2) were restudied three weeks after addition of carnitine. Conventional treatment was continued throughout. After repeat echocardiographic examination, the parameters were compared statistically. With addition of carnitine, besides symptomatic improvement, the mean left ventricular ejection fraction improved from 36.9±16.1 percent to 46.9 ± 14.5 percent ($p<0.001$) and the mean pre-ejection period/left ventricular ejection time ratio from 39.07±14.8 to 43.2±8.1 ($p<0.01$) in the entire group. These changes were concordant in both the subgroups. It was concluded that L-carnitine therapy in children with idiopathic dilated cardiomyopathy led to modest improvement in left ventricular function (*Indian Heart J 1998; 50: 59–61*).

Introduction

Carnitine has been used in patients with ischaemic heart disease with favourable results[1-3]. Carnitine, a low molecular weight amino acid derivative is essential for oxidation of fatty acids which are the preferred source of energy for the heart. This mechanism of action and the evidence of reduced carnitine levels in the endomyocardial biopsy specimens from patients with dilated cardiomyopathy (DCM)[4] makes L-carnitine an attractive drug to be administered in these patients.

The utility of L-carnitine in the rare disorder of DCM secondary to carnitine deficiency in children has been reported[5-7]; however, no systematic studies have been conducted on the effects of L-carnitine in idiopathic DCM in children. Hence, we undertook a study to analyse the same.

Material and Methods

Thirteen consecutive children (8 males, 5 females) with a mean age of 3.29 (SD 1.44; range 2-7) years, diagnosed to have idiopathic dilated cardiomyopathy with left ventricular dysfunction of more than six months duration, seen at this institute in the last one year, were the subjects of this study. All these children underwent a detailed clinical evaluation. Their symptoms, as described by the parents, were graded according to the NYHA class. An EKG and chest X-ray was followed in all by an echocardiographic evaluation. Patients in whom coronary artery anatomy was difficult to assess were subjected to an aortic root angiogram, and an endomyocardial biopsy done in those suspected to have viral myocarditis. All children were on conventional treatment including ACE inhibitors at least for a month before enrolling in the study which was continued throughout the treatment. Since improvement or deterioration in DCM could occur spontaneously as well, we chose to assess the effect of the drug in two groups. In Group 1 (n=8) the basal study was done on the children after they had been on carnitine in a dose of 50 mg/kg/day for three weeks. They were restudied after stopping carnitine for a further period of three consecutive weeks; the rest of the treatment being continued. In Group 2 (n=5) the basal study was done while the children were on conventional therapy alone and were studied after they had been on carnitine therapy for three weeks.

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In all patients an unbiased observer analysed the video records of the echocardiogram. The parameters recorded on and off carnitine which were compared statistically were: the ejection fraction (EF) and the pre-ejection period/left ventricular ejection time (PEP/LVET) ratio.

The results were analysed as 'with' and 'without' carnitine in both the groups using the Wilcoxon's signed rank test. The grouping was not systematically randomised; however we believe that any bias is unlikely to influence the outcome as each patient served as one's own control and the duration, severity of illness, and left ventricular ejection fraction were similar in both the groups.

Results

All children were markedly symptomatic (NYHA class III/IV), in congestive heart failure at the time of presentation. The mean age, duration of symptoms before diagnosis and the mean ejection fraction were similar in both the groups (Table 1). The mean EF of the whole group was 36.9±16.1 percent and PEP/LVET ratio was 39.07±14.8. Three patients underwent aortic root angiography to exclude an anomalous origin of left coronary artery from pulmonary artery, and in another two, endomyocardial biopsy excluded myocarditis.

There was a subjective improvement noticed by the parents in the patient's appetite, general wellbeing, interest in play and social interaction while the child was on L-carnitine. The NYHA class improved overall in both groups while on carnitine.

The two objective parameters that improved following administration of L-carnitine in the whole group were, the left ventricular EF and the PEP/LVET ratio. The mean EF improved from 36.9±16.1 to 46.9±14.5 percent ($p<0.001$) and the mean PEP/LVET ratio improved from 39.07±14.8 to 43.2±8.1 ($p<0.01$). Also, these changes were concordant in both the groups, in that the EF and the PEP/LVET ratio improved significantly while on carnitine, than when not receiving the drug (Tables 2 and 3).

TABLE 1

Baseline Parameters in Children with Dilated Cardiomyopathy

Parameter	Group 1 (n=8)	Group 2 (n=5)	'p' Value
Mean age (years)±SD	2.75±0.89	3.40±1.14	NS
Duration of symptoms (months)±SD	9.6±2.23	9.8±1.15	NS
Mean ejection fraction (%)	42.25±14.72	48.40±8.47	NS

SD - Standard deviation, NS - Not significant.

TABLE 2

Echocardiographic Parameters in Children with Dilated Cardiomyopathy Before and After Stopping L-Carnitine (Group 1)

Patient No.	Without Carnitine		With Carnitine		'p' Value*
	EF	PEP/LVET	EF	PEP/LVET	
1.	24	47	19	47	–
2.	65	56	43	45	–
3.	53	33	43	30	–
4.	31	41	31	36	–
5.	49	44	45	43	–
6.	24	41	15	41	–
7.	43	41	33	38	–
8.	49	35	46	33	
Mean EF	42.25±14.72		34.37±12.02		<0.001
Mean PEP/LVET ratio	42.25±7.15		39.13±5.94		<0.050

* p value calculated by Wilcoxon's signed rank test.

Discussion

A reduced carnitine concentration has been reported in explanted hearts and endomyocardial biopsies from patients with congestive heart failure secondary to DCM, suggesting the possibility that such patients might benefit from carnitine supplementation[4]. We administered L-carnitine to children with DCM in addition to conventional therapy and found symptomatic relief, an improvement in the NYHA class, and statistically significant increase in the mean ejection fraction and the mean PEP/LVET ratio in the children

TABLE 3

Echocardiographic Parameters in Children with Dilated Cardiomyopathy After Adding L-Carnitine (Group 2)

Patient No.	Without Carnitine		With Carnitine		'p' Value*
	EF	PEP/LVET	EF	PEP/LVET	
9.	63	70	70	61	–
10.	43	38	63	43	–
11.	47	42	57	47	–
12.	47	47	51	43	–
13.	42	36	42	44	–
Mean EF	48.40±8.47		56.60±10.78		<0.05
Mean PEP/LVET ratio	46.80±14.17		47.60±7.67		<0.05

* p value calculated by Wilcoxon's signed rank test.

while they were on the drug and a comparative deterioration of all the parameters without the drug. The concordant results in both the groups suggest that carnitine was indeed useful and the changes were not secondary to spontaneous improvement or deterioration.

Fatty acid oxidation is the preferred energy source for the heart. L-carnitine, another "metavitamin"[8] is a cofactor of several enzymes necessary for the transformation of free long chain fatty acids to acylcarnitines and their transport into the mitochondrial matrix. In the absence of L-carnitine the accumulation of free acids in the cytoplasm produces a toxic effect on the cell and an energy deficit arises from the unavailability of fatty acids within the mitochondria[9]. Recent experimental work however, suggests that L-carnitine therapy benefits cardiac function in rats with secondary carnitine deficiency by improving glucose utilisation, rather than normalising fatty acid metabolism[10].

Myocardial fatty acid oxidation has been shown to be inhibited in patients with systemic carnitine deficiency. Some of these patients present with reduced plasma and tissue carnitine levels with features of DCM and severe myocardial lipid accumulation[11]. A rapid, dramatic clinical response characterised by improvement in cardiac function has been noted in patients with systemic carnitine deficiency treated with supplemental carnitine[11,12]. However, a recent case report of a child with DCM secondary to type II 3-methylglutaconic aciduria has been described where supplementation with L-carnitine led to rapid deterioration in the cardiac status and was reversible with large doses of pantothenic acid. Carnitine may perhaps be contraindicated in this condition[13].

The possible therapeutic value of carnitine for congestive heart failure secondary to ischaemic or hypertensive heart disease was evaluated in 38 elderly patients, where patients on carnitine demonstrated an improvement in both echocardiographic and electrocardiographic parameters and a more marked decrease in the requirement of digoxin[14].

There are no reports on the effects of L-carnitine in children with idiopathic DCM. In our study we were unable to estimate the plasma carnitine levels in patients before initiating treatment, and thus were unable to exclude from the study children with DCM secondary to carnitine deficiency. However, these were consecutive cases of DCM and unlikely to have DCM due to primary carnitine deficiency.

Although the number of patients in this study is small, the results suggest that L-carnitine therapy is beneficial for children with idiopathic DCM and leads to a modest improvement in myocardial function.

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