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Clinical effects of coenzyme Q10 supplement in pediatric patients with chronic kidney disease

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Abstract
Background: Chronic kidney disease is a progressive condition characterized by functional and structural alterations of the kidney, Coenzyme Q10 is a lipophilic molecule that plays a vital role in cellular energy generation while having an important anti-inflammatory and antioxidant actions, an adequate supply of Coenzyme Q10 is crucial for maintaining physiological functions of the mitochondria.
Aims of the study: To observe the status of patients affected by chronic kidney disease clinically after starting them on Coenzyme Q10 enzyme supplement, and to compare their renal function, inflammatory markers, cardiac function before, during and after starting them on Coenzyme Q10 supplement.
Patients and methods: A prospective study was done which included forty patients between the ages of five years to eighteen years, with chronic kidney disease, they were started on Coenzyme Q10 supplement for the duration of six months, the duration of the study was a year and a half, during that period their clinical status was monitored, measurement of multiple parameters, including blood pressure, heart rate and weight was done, blood and urine sampling for multiple investigations of certain markers was also performed, an echocardiography was done for all participants before, during and the end of the study to monitor their clinical response and any hospital admission during that time was registered.
Results: According to the sex of the patients, 57.5% were females, regarding hemodialysis, 50% of them were on hemodialysis, after starting Coenzyme Q10, blood urea levels showed a decline, while serum creatinine values remained constant, no significant changes were observed in serum calcium and parathyroid hormone values while serum phosphorus values increased, body weight, blood pressure and ejection fraction was unchanged during the study while proteinuria declined, 25% of patients were admitted to the hospital (15% admitted once, 5% twice and 5% were admitted three times).
Conclusions: There was a decrease in blood urea, the values of serum cholesterol also declined and a decrease in protein in urine was noticed in patients after Coenzyme Q10 was administrated.

Keywords: Chronic kidney disease (CKD), Coenzyme Q10, Hemodialysis

Introduction

Chronic kidney disease (CKD) is a progressive condition causes structural and functional alterations to the functions of the kidney, it is characterized by damage to the kidney and its functions or a decrease in glomerular filtration rate, It is typically described as a decline in kidney function resulting in an estimated glomerular filtration rate [eGFR] of less than 60 ml/min/1.73m2 [1].

According to the eGFR, Chronic kidney disease is classified into five stages, having normal values generally in the range of 90-120. The prevalence of CKD in the UK population is around 10% [2].

Regarding the causes of CKD in the pediatric population, glomerular diseases and congenital abnormalities of the urinary tract or the kidney are amongst the most prominent [1].

In CKD, as GFR decreases, inflammatory processes surge, in order to interpret the causes of inflammation, multiple mechanisms are needed, such as increased oxidative stress, decreased cytokines elimination and levels of Vitamin D, metabolic acidosis, frequent infections, intestinal dysbiosis, periodontal disease, and factors related to dialysis [3].

Regarding coronary artery disease, the role of oxidative stress is well established, as high levels of certain inflammatory markers like high-sensitivity C-reactive protein has a predictive value for myocardial infarction, these markers are also detected in CKD patients and indicate inflammation like C-reactive protein [4].

Oxidative stress is likely to play a major role in the pathogenesis of many chronic diseases, and these diseases could in turn increase oxidative stress [5].

CoQ10 is a lipophilic molecule consisting of a benzoquinone nucleus and an isoprenoid side chain that has a vital role in cellular energy generation within the mitochondrial respiratory chain (MRC) while having important anti-inflammatory antioxidant properties [6]. Festenstein *et al*., 1955 and Crane *et al*., 1957 were the first to isolate and characterize this compound for the first time and established its electron carrier properties in the mitochondrial electron transport chain, this compound also plays a role in proton gradient formation in the endomembrane and the plasma membrane, and helps to maintain membrane structure and phospholipid status [7].

Plasma levels of CoQ10 have been found to be significantly lower in CKD patients (Whether or not on hemodialysis), compared to normal controls [8, 9].

The cause of this deficit in serum CoQ10 levels is still poorly understood, however, it could be related to the increased oxidative stress which occurs in CKD, it has been suggested that the enzymes involved in CoQ10 biosynthesis may exist in a super enzyme complex which is located in mitochondria in close proximity to MRC in the inner mitochondrial membrane [2, 10].

Patients and methods

This study followed the clinical status of patients with ESKD (On intermittent hemodialysis and patients with stage 4 and stage 5 of chronic kidney disease who are not on dialysis yet) before and after starting them on Coq10 enzyme supplement for the duration of 6 months, the patients were started on the supplement on different dates, as a result, data was collected over the period of one and a half years, from December 2022 to May 2024.

A prospective study was conducted on these patients over that duration, the number of the patients was 40 patients, half of them is on hemodialysis and the other half was on conservative treatment, all the patients participating in this study were from the pediatric nephrology and hemodialysis center in Al-Karama teaching hospital.

Inclusion criteria was any patient in the pediatric age group (From the ages of 5 to 18 years) with CKD (On intermittent hemodialysis and patients with chronic kidney disease, stage 4 and stage 5 who are not on dialysis yet).

Exclusion criteria was any patient who is not in that age group, or who dies during the duration of the study and patients with no compliance to treatment and poor follow up visits.

All of the clinical parameters, data and investigations were performed at Al-Karama teaching hospital, blood sampling was performed at the laboratories of the hospital and waste disposal was done according to their protocols, blood sampling and blood pressure monitoring for patients on HD was done before starting HD sessions.

Informed verbal consent was taken from patients' caregivers and when possible, the patients themselves.

Measurement of clinical parameters, including weight, height, heart rate, blood pressure, and blood sampling and urine sampling was done each visit for multiple investigations of certain markers.

An echocardiography to measure the ejection fraction was done for all participants of this study before starting and during Coq10 enzyme supplement.

The blood pressure and body weight measurements were compared to the standardized numbers of the world health organization charts according to the age and sex of the participants.

The Coq10 enzyme supplement was given orally, at a dose of 100 mg once daily, kept in room temperature and instructions were given to the caregivers and if possible, to the patients on how to use the supplements and the dosage, the formula was either as a syrup (100mg/5 ml) or tablets (100 mg).

After starting the supplement, every three months' visits were scheduled and performed to all participants, in these visits, the same clinical parameters measured at baseline, including heart rate, blood pressure, multiple investigations for certain markers and parameters with an echocardiography to measure the ejection fraction were repeated each 3 months for a total duration of 6 monthly visits, and data was collected to compare the results.

Any hospital admission for the participants that occurred during the time of the study is reported.

Statistical analysis

The data were entered and analyzed by SPSS version 26. The categorical data presented by frequencies and percentages and the change in positive cases numbers across the course of supplement with CoQ10 tested using Cochran's Q test. The numerical variables were tested for their normality and since they were normally distributed, they were presented by mean±standard deviations, the comparison between each two periods of supplement with CoQ10 were tested using paired t-test and the overall change in levels was tested by repeated ANOVA. The significant levels of P-value are 0.05 or below.

Results

The number of participants in this study were 40 patients, demographic features of these patients is shown in table No.1.

According to the sex of the patients, 17 of them were males (42.5%) and the 23 females (57.5%), regarding hemodialysis, 50% of them were on hemodialysis, the other half was on conservative measures.

Table No.1 demonstrate the values of specific parameters measured in this study, before starting, at 3 months and at six months of supplementing the participants with CoQ10 enzyme, the difference between the results was measured between the start and the second follow up visit, the second and the last visit, and between the results of before starting Coq10 supplement and at the end of the study, these parameters include hemoglobin, blood urea, serum creatinine, serum calcium, serum potassium, serum phosphorus, serum cholesterol, serum triglyceride and parathyroid hormone, statistical significance was found in blood urea, serum cholesterol and serum phosphorus values after Coq10 supplement.

Table 1: Comparison of laboratory parameters according to the treatment stage

Parameters	Supplement of CoQ10			P-value	P-value	P-value	P-value
	Before 0	After 3 months	After 6 months	0 vs.3	3 vs.6	0 vs.6	overall
Hemoglobin (g/dl)	10±1.7	10±1.3	9.9±1.6	0.826	0.46	0.83	0.827
Urea (mg/dL)	111±42.7	102.8±41.5	98.3±40.3	0.025*	0.264	0.013*	0.015*
Creatinine (mg/dL)	4.6±3	4.7±2.9	4.7±2.8	0.927	0.949	0.878	0.979
Ca (mg/dL)	8.4±0.8	8.4±1	8.6±0.8	0.506	0.251	0.075	0.194
PO4 (mg/dL)	4.5±1.1	4.6±1.1	4.8±1.1	0.136	0.067	0.038*	0.041*
Cholesterol (mg/dL)	180.1±65.1	175.4±54.6	171.2±47.3	0.082	0.062	0.022*	0.024*
Triglyceride (mg/dL)	141.5±89.2	137.8±80.9	138.3±81.5	0.286	0.801	0.288	0.287
Parathyroid hormone (ng/L)	614.3±515.5	620.8±534.3	617.7±509.4	0.672	0.799	0.858	0.884
Potassium (mEq/L)	4.6±1.1	4.5±1	4.5±0.9	0.047	0.754	0.162	0.118

*Significant at 0.05 level

Figure No.1 demonstrates the blood urea values across the stages of CoQ10 supplement, for which the value decreases during the period of the study, in comparing the values before starting and at the end of the study, the P-value was found to be 0.013.

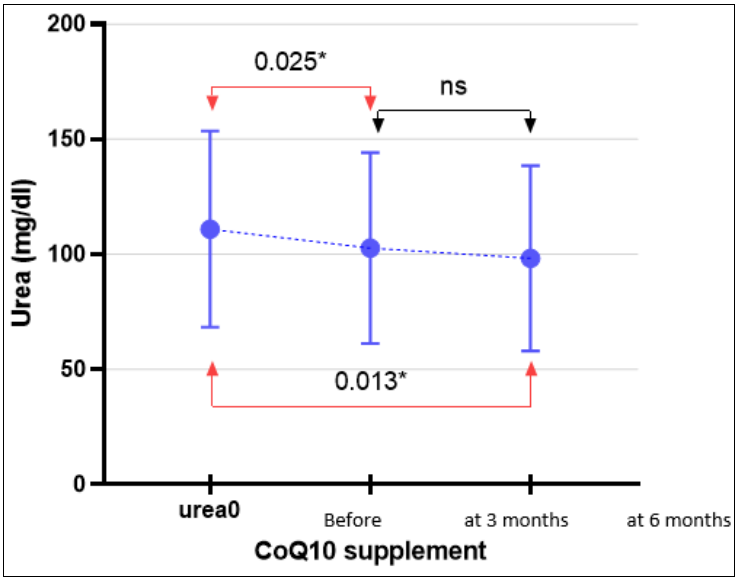

Fig 1: Comparison of urea according to stage of supplement with CoQ10

The number of patients in this study on hemodialysis with anuria is 14, table No.2 compares protein in urine in the other 26 patients before, during and after Coq10 supplement, there is a significance shown with a decreased protein in urine after starting CoQ10 supplement.

Table 2: Comparing protein in urine across the stages of CoQ10 supplement

Variables	Positive		Negative		
	Count	Percent	Count	Percent	P-value
Protein in urine 0	25	96.2	1	3.8	0.004*
Protein in urine 3	17	65.4	9	34.6	
Protein in urine 6	20	76.9	6	23.1	

*Significant at 0.05 level

Table No.3 compares the blood pressure and the body weight according to the standardized numbers of the world health organization charts according to the age and sex of the participants before, during and after Coq10 supplement, the values for both parameters were similar across the stages of CoQ10 supplement.

Discussion

In this study, there was a slight female predominance, with 57.5% of the participants, while the number of males were 17 out of the 40 patients,

In this study, certain parameters were measured before starting CoQ10 supplements, during and at the end of the study, regarding blood urea, there was a decrease in the values after starting CoQ10, while serum creatinine and eGFR changes were statistically non-significance, comparing these results to a study done in Australia, Mori T.A, *et al*. (2009) [11].

In this study, there was a decrease in serum cholesterol values while serum triglyceride remained fairly unchanged, comparing this to other studies, like Mori T.A, *et al*. (2009) [11], which showed no difference after starting CoQ10, Zuo X, *et al*, another meta-analysis done in patients with chronic kidney disease showed no effects of CoQ10 on serum cholesterol and triglyceride [12].

Table 3: Comparison of Blood pressure and body weight percentiles across the supplement with CoQ10 for patients

Stages	Blood pressure percentiles n (%)						P-value
	25th	50th	75th	90th	95th	99th+	
Before	8 (20)	16 (40)	8 (20)	2 (5)	2 (5)	4 (10)	0.998
After 3 months	8 (20)	18 (45)	6 (15)	2 (5)	3 (7.5)	3 (7.5)	
After 6 months	8 (20)	16 (40)	8 (20)	3 (7.5)	3 (7.5)	2 (5)	
	Body weight Percentiles n (%)						
	3rd	5th	10th	25th	50th	75th	P-value
Before	1 (2.5)	9 (22.5)	16 (40)	10 (25)	3 (7.5)	1 (2.5)	0.988
After 3 months	1 (2.5)	9 (22.5)	16 (40)	10 (25)	4 (10)	0 (0)	
After 6 months	1 (2.5)	7 (17.5)	18 (45)	10 (25)	4 (10)	0 (0)	

Serum calcium and phosphorous were also measured, serum calcium values remained constant while serum phosphorous increased after administrating CoQ10, while in Mori T.A, *et al*. (2009) [11], both remained fairly constant after starting CoQ10. Regarding protein in urine, in this study, a significant improvement was found after starting CoQ10, with a decrease in protein in urine during and at the end of the study, comparing this outcome to other studies, like the study in Perth, Australia in 2009, in which there were no significant differences at baseline between groups in 24-h albuminuria, which remained unchanged after intervention [11].

Conclusion

- There was a decrease in blood urea after starting the patients with CKD on CoQ10 supplements
- The value of serum cholesterol was less, but serum triglyceride remained fairly constant with CoQ10 administration, while serum phosphorous increased
- A decrease in protein in urine was noticed in patients after CoQ10 was administrated.
- Body weight, blood pressure, heart rate and C-reactive protein values didn't change during the study.

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