The effect of coenzyme Q10 in comparison with placebo on CD4 in HIV-infected patients

Farid Yousefi[a], Fatemeh Roozbeh[b,*]

[a] Health Research Institute, Infectious and Tropical Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[b] Mazandaran University of Medical Sciences, Sari, Iran

ABSTRACT

Background: We planned this study to evaluate the effects of coenzyme Q10 (CoQ10), a substance with known effects on the immune system, on the occurrence of opportunistic infections and CD4$^+$ T-cell count of HIV-infected patients as markers of their immunologic status.
Methods: This was a parallel, double-blind, placebo-controlled, randomized clinical trial in adult (> 18 years old) patients with HIV infection on antiretroviral therapy (ART) referring to Ahvaz Behavioral Diseases Consultation Center. The intervention group was given CoQ10, one 200 mg capsule per day, and the controls received placebo, each for 3 months.
Results: There was no statistically significant difference in the mean CD4$^+$ T-cell count at the beginning of the study (p = 0.232) and also in it's increase after 3 months (p = 0.114) between the two groups; however, the mean CD4$^+$ T-cell count increased significantly by the end of the study in each group (p = 0.045 for intervention, p = 0.001 for controls).
Conclusion: This study suggested that CoQ10 had no remarkable effect on the CD4$^+$ T-cell count and the incidence of opportunistic infections in adult HIV-infected patients on ART.

1. Introduction

Few decades after of HIV/AIDS diagnosis, it has been still a health problem and impact will continue in the next decades.[1] In 2015, HIV/AIDS was the 12th cause of death in the world and it's estimated that 1.2 million people was died of HIV/AIDS this year.[2] In the global epidemiological study of AIDS in 2014, the overall prevalence of this disease was reported to be 0.05% in individuals aged 15–49 years and the highest frequency of HIV/AIDS has been reported in Sub-Saharan Africa and then in Asia.[3] Considering the progression of HIV/AIDS and the disability and mortality that followed the disease, it was tried to produced different drug against it and there has been a remarkable development in this field. Among with main antiviral drugs, there has been some efforts in auxiliary drugs effects, but these findings are not adequate and studies are not enough.[4] One of these drugs is Coenzyme Q10 (CoQ10). Naturally, this enzyme there is in the body. The function of this coenzyme as a cofactor is in the electron transmission chain in mitochondria that acts in the synthesis of adenosine triphosphate (ATP).[5] In addition, it increases the activity of macrophages, as well as the proliferation of granulocytes.[6] CoQ10 also works an intracellular antioxidant at the mitochondrial surface.[7] So, theoretically, it seems that this drug is useful in patients with HIV due to increased proliferation of granulocytes and it prevents cardiomyopathy and oxidative stress induced lipidostrophy by antioxidant activity.[8,9]

HIV infection includes a wide range of nutrition deficiencies and immunological impairments and it seems that to eliminate nutrition deficiency and increased ATP production, although it may not improve HIV, can help prevent weight loss and improve the overall immune system's function. So, regarding to potential effects of CoQ10 on the immune system, the aim of this study was to determin the effect on the effects of CoQ10 on CD4 count in HIV-infected patients.

2. Material and methods

This randomized, double blind, placebo controlled, parallel group clinical trial was performed on 73 patients with human immunodeficiency virus infected. This study registered in the clinical trial registry with code IRCT201108027197N1. The studied population was HIV-infected adults that HIV confirmed with 2 positive results of ELISA and western blot test and they are in treatment with ART. The sample size according to the pilot study in 10 people at 95% confidence level and 80% power were obtained 37 patients in each group by two sample

comparison of means formula. Exclusion criteria included: immunodeficiency diseases for other causes, including lymphoma or other malignancies, Use of drugs that affect the immune system, such as corticosteroids, autoimmune diseases, advanced pulmonary tuberculosis and pregnant women. In these patients, the baseline level of CD4 was measured with flowcytometry. The levels of liver enzymes, BUN, Cr, and CBC were also measured and recorded. Patients selected with convenience method and then randomly assigned to two groups with using random table and the drug or placebo was received by a third person (nurse) without the information. One group received CoQ10, 200 mg daily and the other group received placebo, were completely consistent with CoQ10 in terms of shape, color, and size. After 3 months, the above parameters are measured again and were compared in two groups. The initial outcome was change in the rate of CD4 and the secondary outcome was change in the values of ALKP, ALT, AST, BUN, creatinine, white blood cells, hemoglobin and platelets. Data were analyzed by SPSS19 and statical test such as t-test, paired t-test and chi-square test and the per-protocol method was used in the therapeutic effect analysis and p < 0.05 was considered as a significant level. Normality was checked by histogram.

3. Results

Finally, 37 patients in the intervention group and 36 patients in the placebo group were studied. There was only one loss to follow up case in the placebo group. The distribution of the demographic parameters of the subjects in intervention and placebo groups are shown in Table 1. The mean age of the patients in the intervention and placebo groups was 39 ± 10 and 41 ± 10, respectively (p = 0.423). In the intervention group, 83.8% and in the placebo group, 69.4% were male (p = 0.175). There was no significant difference between addiction and hepatitis B and C in both groups (P > 0.05).

Level of CD4 and other blood parameters in patients before and after intervention are presented in Table 2. The mean of the CD4$^+$ level before treatment in the intervention and placebo groups was 161.5 ± 291.1 and 159.9 ± 337.4, respectively (P = 0.232), which increased after treatment in both groups to be 336.5 ± 155 (P = 0.045) and 246.5 ± 440.9 (P = 0.001). There was no significant difference between ALKP, ALT, AST, BUN, creatinine, white blood cells, hemoglobin and platelets in both intervention and placebo groups before and after treatment (P > 0.05).

4. Discussion

This study was conducted to determine the therapeutic effect of CoQ10 in HIV infected patients and the result of this study shows that auxiliary treatment with CoQ10 likewise placebo along with routine treatment improved the immune system's activity and increased CD4 + levels without affecting the hepatic function test and hematologic indexes. It should be noted that the demographic parameters,

Table 1
Baseline characteristics of HIV-infected patients in two groups.

Variable		Placebo N (%)	CoQ10 N (%)	P-value
Sex	Female	11 (30.6)	6 (12.6)	0.175*
	Male	25 (69.4)	31 (83.8)	
Addiction	No	16 (44.4)	12 (32.4)	0.341*
	Yes	20 (55.6)	25 (67.6)	
HCV	No	23 (63.9)	19 (51.4)	0.346*
	Yes	13 (36.1)	18 (48.6)	
HBV	No	33 (91.7)	35 (94.6)	0.674*
	Yes	3 (8)	2 (5.4)	
Age (mean ± SD)		39 ± 10	40.9 ± 10	0.423**
Weight (mean ± SD)		65.6 ± 10.6	70.7 ± 11.9	0.057**
Height (mean ± SD)		170.1 ± 8.1	166.7 ± 13.7	0.200**

*Chi-square, ** t-test.

Table 2
CD4 and other blood parameters changes in HIV-infected patients before and after intervention.

		Placebo	CoQ10	p-value*
CD4	Before	337.44 ± 159.96	291.18 ± 167.59	0.232
	After	440.97 ± 246.55	336.54 ± 155.04	0.035
	p-value**	0.001	0.044	
Bill	Before	1.03 ± 0.29	1.14 ± 0.34	0.270
	After	0.99 ± 0.19	1.16 ± 0.34	0.031
	p-value**	0.43	0.356	
ALKP	Before	165.33 ± 42.02	180.71 ± 65.8	0.329
	After	170.12 ± 68.05	190.6 ± 81.35	0.334
	p-value**	0.713	0.106	
ALT	Before	39.69 ± 29.3	41.32 ± 27.05	0.806
	After	40.05 ± 36.87	44.08 ± 25.21	0.587
	p-value**	0.953	0.54	
AST	Before	38.6 ± 27.5	42.81 ± 28.31	0.525
	After	38 ± 29.86	39.78 ± 25.21	0.785
	p-value**	0.895	0.365	
Cr	Before	0.9 ± 0.29	0.82 ± 0.3	0.239
	After	0.96 ± 0.3	0.87 ± 0.3	0.189
	p-value**	0.151	0.165	
BNU	Before	12.19 ± 4.25	12.21 ± 3.3	0.981
	After	12.66 ± 4.78	12.27 ± 4.65	0.724
	p-value**	0.619	0.943	
WBC	Before	5597.1 ± 1916.2	5362.16 ± 1525.77	0.520
	After	6651.4 ± 10605.5	6061.62 ± 3522.071	0.750
	p-value**	0.552	0.211	
HB	Before	12.72 ± 1.83	12.66 ± 1.73	0.726
	After	12.77 ± 1.78	12.6 ± 1.63	0.682
	p-value**	0.85	0.799	
PLT	Before	220971.4 ± 89053.3	238864.9 ± 148140.7	0.496
	After	224971.4 ± 64002.5	208594.6 ± 77082.01	0.332
	p-value**	0.748	0.198	

*Paired t-test, ** t-test.

including the weight, were not significantly different between the two groups. In 2001, Batterhman et al. in Australia examined the effects of using antioxidants, including CoQ10, on viral load in 48 HIV infected patients who referred to outpatient clinics for treatment. A twelve week regimen full of high dose antioxidant was administered in half of these patients and the other patients received low dose antioxidant regimen and they concluded that such component increases oxidative defense parameters, but in viral load didn't change significantly[10] which is somewhat similar to the present study.

In 1978, in a study by Bliznak et al. in one of the colleges of California on mice show that the immune impairment was significantly associated with a decrease in CoQ10 levels[11] and this effect was corrected by CoQ10 treatment.[12] In 1982, Folker et al. studied 8 patients with chronic disease in Russia and administered CoQ10 for 27–98 days in these patients and an increase in serum immunoglobulin G level was observed in all patients and this result suggest that CoQ10 may have a role in the prevention and reversal of immune system deficiencies related to chronic disease.[7] Folker et al. in another study reported that blood level of CoQ10 in HIV patients is lower than the general population, also, blood level of this concentration in patients with AIDS is less than asymptomatic HIV positive patients. They treated 6 AIDS patients with 200 mg CoQ10 daily, one patients excluded the study because, he didn't participate in follow up, but the other patients didn't show any evidence of opportunistic infectious after 4–7 months. Also, in 3 of these 6 patients T cell helper/suppressor increased and it was normalized in one patient. Folker et al. study show that reduction in CoQ10 level is common in HIV patients and CoQ10 supplement rise the immune level in HIV patients and decrease the opportunistic infections.[13] Kitayama et al., in 2008 in Japan show that Macrophage infected HIV virus secrete a substance called VPR (viral protein R) that cause neural cells damage and suppress neural cells precursors, but, CoQ10 anchor this effect and can protect neural cell against VPR.[14]

The strong point of this study comparing other studies is that unlike

other studies on experimental animal or observational studies, the present study was double blind clinical trial study to minimize the bias effect and so, we can use its result with more power, although we need more studies with more sample size and more follow up time to study more accurately, because 3 month fallow up was our limitation.

Finally, we conclude that CoQ10 auxiliary treatment along with routine antiviral therapy improve immune system function and increase CD4 level without any side effect on hepatic function and hematologic parameters.

Funding

Availability of data and materials

The datasets analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

FY designed the study, FR collected the data, FR analyzed the data, FY and FR drafted the manuscript.

Conflicting interests

The authors declare that they have no conflicting interests.

Acknowledgements

References

1. GBD 2015 HIV Collaborators. Estimates of global, regional, and national incidence, prevalence, and mortality of HIV, 1980-2015: the Global Burden of Disease Study 2015. *Lancet HIV*. 2016;3(8):e361–e387.
2. GBD 2015 Eastern Mediterranean Region HIV/AIDS Collaborators. Trends in HIV/AIDS morbidity and mortality in eastern mediterranean countries, 1990-2015: findings from the global burden of disease 2015 study. *Int J Publ Health*. 2018;63(Suppl 1):123–136.
3. Fettig J, Swaminathan M, Murrill CS, Kaplan JE. Global epidemiology of HIV. *Infect Dis Clin*. 2014;28(3):323–337.
4. Manary M, Ndekhat M, van Oosterhout JJ. Supplementary feeding in the care of the wasted HIV infected patient. *Malawi Med J*. 2010;22(2):46–48.
5. Soni S, Agarwal P, Sharma N, Chander S. "Coenzyme Q10 and periodontal health"-A review. *Int J Oral Maxillofac Pathol*. 2012;3(2):21–26.
6. Barbieri B, Lund B, Lundström B, Scaglione F. Coenzyme Q10 administration increases antibody titer in hepatitis B vaccinated volunteers–a single blind placebo-controlled and randomized clinical study. *Biofactors*. 1999;9(2-4):351–357.
7. Folkers K, Shizukuishi S, Takemara K, et al. Increase in the level of IgG in serum ofd patients treated with coenzyme Q10. *Res Commun Chem Pathol Pharmacol*. 1982;38:335–338.
8. Cohen IS, Anderson DW, Virmoni R, et al. Congestive cardiomyopathy in assoation with the aqueired immune difficiency syndrome. *N Engl J Med*. 1986;315:628–630.
9. Rabing Christensen E, Stegger M, Jensen-Fangel S, et al. Mitochondrial DNA levels in fat and blood cells from patients with lipodystrophy or peripheral neuropathy and the effect of 90 days of high – does coenzyme Q treatment:A randomized,double blind, placebo-controlled pilot study. *Clin Infect Dis*. 2004;39:1371–1379.
10. Batterham M, Gold g, NaidooD, et al. A prreliminary open lable dose comparhson using an antioxidant regimen to determine the effect on viral load and oxidative stress in men with HIV/AIDS. *Eur J Clin Nutr*. 2001;55(2):107–114.
11. Bliznak ov EG, Watanabe T, Saji S, Folkers K. Coenzyme Q difficieney in aged mice. *J Med*. 1978;9:337–346.
12. Bliznak EG. Immunological senescence in mice and its reversal by Coenzyme Q10. *Mech Ageing Dev*. 1978;70:189–197.
13. Folkers k, Cangsjoen p, Nara Y, et al. Biochemical deficiencies of coenzyme Q10 in HIV infection and exploratory treatment. *Biochem Biophys Res Commun*. 1988;153:888–896.
14. Katayama H, Yoshihara M, Yoshinori A, et al. Human Immunodifficiency virus type 1 VPR inhibhts axonal outgrowth induction of mitochondrial dysfunction. *J Virol*. 2008;82:2528–2542.