Effectiveness of Coenzyme Q10 on echocardiographic parameters of patients with Duchenne muscular dystrophy

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Abstract

Background: Myocardial damage is a common complication in patients with Duchenne muscular dystrophy (DMD) that occurs due to myocardial replacement by fat and fibrosis. In recent years, efforts have been made toward finding new pharmacological agents with fewer complications which can be used as prophylactic before the symptoms. Coenzyme Q10 plays a central role in production of bioenergy in heart muscle and antioxidant in reperfusion condition of myocardial damaged muscle and leads to membrane stability and prevents cell death.

Objective: This study aimed at comparing the Effectiveness of coenzyme Q10 on echocardiographic parameters of pediatric patients with Duchenne muscular dystrophy.

Methods: This randomized clinical trial study (RCT) was carried out on 25 pediatric patients with pre-diagnosed DMD who attended the Children’s Medical Center (CMC), Tehran, Iran from February 2013 to 2015. The patients were randomly divided into two groups. Group-1; (n=12) was treated with coenzyme Q10 for six months and group-2 ;(n=13) received placebo for the same time. The primary aim was to compare the myocardial performance index (MPI), between the two groups at the end of six months. Data were analyzed by SPSS software (ver-16) and using T-Test.

Results: Twenty-five patients under study were divided into two groups of (Q10=12) and (placebo=13). Mean ages were 8.9±1.7 and 8.6±1.4 in Q10 and placebo groups (P=0.66). No significant difference was detected in MPI at all three views of mitral and tricuspid and septum respectively in two groups after the end of treatment (0.41±0.13, and 0.43±0.6; P=0.59), (0.45±0.12, and 0.46±0.1; P=0.05), and (0.45±0.06, and 0.45±0.1; P=0.31).

Conclusion: According to the results obtained from this study, coenzyme Q10 had no significant effect on improving the performance of echocardiographic parameters in patients with DMD.

Trial registration: The trial is registered at the Iranian Clinical Trial Registry (IRCT.ir) with the IRCT identification number IRCT2015070223018N1.

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Keywords: Duchene muscular dystrophy, Coenzyme Q10, Echocardiography

1. Introduction

Duchenne muscular dystrophy (DMD) is an X-linked recessive myopathy which occurs in about 1 case in every 3,600 to 6,000 children (1-3). DMD occurs due to deletion or duplication by 70% and 30% due to point mutations in the dystrophin gene (1, 2). The disease is known as progressive weakness and wasting of skeletal muscle that leads to the loss of ambulation abilities at ages 7 to 13 years and death at the second and/or third decade of life due to

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cardio-respiratory insufficiency (1, 2, 4-6). Myocardial damage is a common complication in patients with DMD that occurs due to myocardial replacement by fat and fibrosis (1). Myocardial fibrosis leads to the left ventricular posterior wall thinning and dysfunction, and resulting in heart dilated cardiomyopathy and finally occasional mitral regurgitation and aortic valve regurgitation (1, 3). The myocardial fibrosis and infiltration can lead to cardiac conduction system involvement including atrioventricular (AV) node or sinoatrial (SA) node (1, 7, 8). However, most patients with DMD, despite the development of cardiac dysfunction, usually remain asymptomatic for several years because of limitation of daily physical activity; so, the diagnosis of cardiac involvement and also appropriate therapeutic intervention occur belatedly (2-4, 7, 9, 10). Glucocorticoids are currently taken, to slow down the loss of muscle strength and function and delay the onset and progression of cardiovascular complications (11). However, in all patients with DMD, response to glucocorticoid has not been the appropriate treatment also, these steroid medications have not been very well used in patients because of the known side effects, and indeed in about half of patients its consumption is cut due to the intolerance of side effects (2, 11-13). Therefore, in recent years, efforts have been aimed toward finding new pharmacological agents with fewer complications, which can be used prophylactically before the symptoms. Coenzyme Q10 is a natural substance made in the body that plays a central role in the production of bioenergy in the heart muscle and antioxidant in reperfusion condition of myocardial damaged muscle, and leads to membrane stability and prevents cell death. Idebenone acts also an antioxidant as a synthetic analogue of coenzyme Q10 drug that improves performance in mitochondrial respiratory chain, cellular energy production, and reducing oxidative stress (6, 13-15). So far, very few studies have shown that the use of idebenone can have beneficial effects on myocardial performance (6, 13-16). In the study of Buyse et al (12), which was conducted on mdx mouse model, it was shown that the use of idebenone has cardioprotective effects and can improve exercise performance in the dystrophin-deficient mdx mouse. Also, another randomized double-blind study (DELPHI) (17) has been done on 21 patients with DMD; idebenone favorable effects have been identified on cardiovascular function markers. And on the last attempt, in another study which was published in 2015 in the Lancet journal (9), idebenone could improve respiratory function in patients with DMD. The aim of this trial, was to study the effectiveness of coenzyme Q10 on improvement of heart function of patients with DMD using echocardiographic parameters.

2. Material and Methods

2.1. Study populations and design

This study was a randomized, prospective, and two-blinded clinical trial, which was carried out during 2 years from February 2013 to 2015 at the Children's Medical Center, Tehran, Iran. Children aged 6 to 10 years old were enrolled in a study in which Duchenne muscular dystrophy (DMD) was diagnosed and approved in them by DNA analysis and muscle biopsy (quadriceps or biceps). Exclusion criteria were: 1) A history of confirmed or suspected heart disease; 2) The presence of other concomitant illness; 3) Patients treated by herbal medicine, vitamins and enzymes; 4) Arrhythmia in ECG; 5) Inappropriate view in echocardiography.

2.2. Randomization and blinding

Patients were randomly assigned with the ratio of one to one using pre-encoded packets into two groups: Group 1) was treated with coenzyme Q10 for six months and Group 2) received placebo for the same time. In this study, none of the patients had been treated by the drug or placebo before, and after doing echocardiography the researchers prescribed a treatment regimen for the patients (Figure 1). The drug and placebo were isoshape and isoform moreover, the parents of the patients were not aware of the drug or placebo, and those who analyzed the gathered data of the patients were not aware of grouping. Consent was obtained from their parents.

2.3. Interventions

After registration of age and sex (based on phenotype), the patients were referred for basic laboratory tests such as: LDH (lactate dehydrogenase), CPK (Keratin phosphokinase), SGOT (Aspartate aminotransferase), SGPT (Alanine aminotransferase), TSH (thyroid-stimulating hormone), TU (Thyroid Uptake) and Aldolase. Thereafter, patients with confirmed DMD were examined by a pediatric cardiologist for exclusion criteria. In the case group, patients were treated by coenzyme Q10 capsules (30 mg capsules from WN Pharmaceuticals, Canada, Company Importer: Asia Karavran Teb, Packed in Atrak company, Tehran, Iran) for 6 months with a dose of 3-5 mg/kg/ daily and the control group were treated by the capsules of isoshape, isocolor and isodose (containing starch) for 6 months. Throughout the performance of study, and by calling once a week, investigators were in contact with patients' parents to ensure the accuracy of prescription drug consumption. All children were subsequently assigned to one of two groups, and twice (first visit before treatment and six months after treatment) went under echocardiography by Tissue Doppler Imaging (TDI).
2.4. Echocardiography

TDI was done by a My Lab esaote 60 echocardiography device (made in Italy) with the multifrequency 3.5 MHz transducer. The size of pulse Doppler sample volume was 3 mm and placed at a distance of 1 cm from tricuspid and mitral valve annuluses on the lateral wall of the right and left ventricles, and at 1 cm distance from the base of interventricular septum. TDI was carried out in three cardiac cycles with 100 mm/s sweep speed. The echocardiographic parameters include: 1) myocardial systolic wave (Sm) (in cm/s); 2) early diastolic wave (Em) (in cm/s); 3) atrial contraction (Am) (in cm/s) 4) isovolumic contraction time (IVCT); 5) isovolumic relaxation time (IVRT) and 6) ejection time (ET). Measurements and averages were calculated in three views of apical 4-chamber at the tip of the mitral and tricuspid valves and interventricular septum. Then, MPI was calculated for each view based on the formula MPI = (IVCT + IVRT) / ET.

2.5. Outcomes

The aim of this study was to evaluate the effectiveness of coenzyme Q10 in the myocardial performance of patients by comparing the myocardial performance index (MPI), between the two groups at the end of six months. The second objective of this study was to evaluate myocardial performance using determination and comparison of other echocardiographic parameters including Sm, Em, Am, IVCT, IVRT, and ET between the two groups.

2.6. Sample size

According to the study of Buyse et al. (2011), and using the formula "Comparison of two averages" with regard to probability of type I error (α) =0.05 and power (1-β) = 0.9, the sample size in each group was 12.

2.7. Ethics of research

This study was approved by the ethics committee of Tehran University of Medical Sciences, and all patients were in the process of content design before entering the study, and their data was used in the case of consent. Privacy and respect of patients were considered within the project. Information of patients was entered to the programs of statistical analysis with codes and published as an overall result.

2.8. Statistical analysis

The data of the project were extracted according to checklists and analyzed statistically by using independent-2-sample t-test and Chi-square and in comparing the means of the groups differences, less than 0.05 (P<0.05) was considered statistically significant.

Figure 1. Follow-up diagram of patients (According to consort statement)
3. Results

3.1. Basic information
During the 24 months of the study, 28 patients suspected of DMD were enrolled in the study and 3 patients (due to withdrawal of consent) were excluded due to exclusion criteria; finally, the results of 25 patients with DMS were statistically analyzed (Figure 1). Patients were randomly allocated into two groups of intervention (n=12) and placebo (n=13). The two groups were similar in terms of age, sex, weight, and previous use of corticosteroids (Table 1). Also, two groups had no significant differences at the beginning of the study in laboratory findings including: LDH, CPK, SGOT, SGPT, TSH, TU and Aldolase (Table 1).

3.2. Echocardiography
The results showed that the parameters of Sm, EM, AM, IVCT, IVRT, ET, MPI in two experimental and control groups had no significant differences at the beginning of the study in three views of the mitral valve, tricuspid and ventricular septum (Table 2). Patients after the intervention in either group were again under Tissue Doppler echocardiography six months later. In this section, echocardiographic findings were compared in two ways. In the first mode, primarily, the changes of echocardiographic findings in both groups were separately analyzed at the entrance time of study and then six months later. In the group treated by placebo, the significant changes had not occurred in any of the echocardiographic parameters before or after the intervention (Table 3). In the group treated with enzyme Q10, among echocardiographic parameters studied, only two parameters including Em Velocity in the view of the mitral valve (p=0.019) and ET (msec) in the view of the interventricular septum (p=0.012) showed significant differences before the intervention and six months later (Table 4). In the second way, the results showed that, although the two experimental and control groups at baseline had no significant differences in terms of echocardiographic parameters (Table 2), at the end of six months’ treatment, the parameter EH (msec) in the view of the tricuspid valve (p=0.05) and IVRT (msec) in the view of the interventricular septum (p=0.015) showed significant differences (Table 5). Two groups in terms of MPI at the end of six months’ treatment in any of the three views had no statistically significant differences (Table 5).

Table 1. Baseline characteristics of patients in treatment with Q10 and placebo group

| Variables          | Placebo group (n = 13) | Q 10 group (n = 12) | p-value |
|--------------------|------------------------|---------------------|---------|
| Sex (M.F)          | 7/15                   | 14/8                | 0.29    |
| Age (year), mean ± SD | 8.6±1.4              | 8.7±1.5             | 0.47    |
| Body weight (kg), mean ± SD | 31.2±12.9          | 30.3±13.5           | 0.18    |
| Heart Rate (beat. min), mean ± SD | 93.8±12.3        | 94.9±11.1           | 0.52    |
| Corticosteroid user (n), % | 13 (100%)           | 11 (91.6)           | 0.98    |
| SGOT (mg/dL), mean ± SD | 131.6±15.3         | 126.7±12.3          | 0.34    |
| SGPT (mg/dL) mean ± SD | 210.3±74.1         | 208.7±77.2          | 0.42    |
| LDH (mg/dL), mean ± SD | 1221.3±653.2       | 1207.6±611.1        | 0.23    |
| CPK (mg/dL), mean ± SD | 3622.4±1254.5      | 3471.4±1312.3       | 0.69    |
| TSH (mg/dL), mean ± SD | 3.5±0.18           | 3.3±0.12            | 0.74    |
| Aldolase (mg/dL), mean ± SD | 45.8±22.0          | 47.0±21.2           | 0.16    |
Table 2. Echocardiographic data of Q10 group and placebo group before the intervention

| Variables, Mean±SD | Q 10 group (n=12) | Placebo group (n=13) | p-value |
|--------------------|-------------------|----------------------|---------|
| Mitral valve view  |                   |                      |         |
| Sm (cm. s)         | 11.4±2.6          | 11.2±2.5             | 0.17    |
| EM (cm. s)         | 19.1±2.2          | 18.4±4.3             | 0.30    |
| AM (cm. s)         | 7.8±2.1           | 7.8±3.1              | 0.34    |
| IVCT (msec)        | 47.6±9.2          | 49.3±8.5             | 0.23    |
| IVRT (msec)        | 43.3±6            | 43.1±10.1            | 0.86    |
| ET (msec)          | 231.4±79.5        | 232.2±81.7           | 0.31    |
| MPI (Tei)          | 0.45±0.68         | 0.43±0.05            | 0.34    |
| Tricuspid Valve view |                 |                      |         |
| Sm (cm. s)         | 14.4±2.9          | 14.2±2.9             | 0.87    |
| EM (cm. s)         | 24.3±2.6          | 23.7±2.8             | 0.33    |
| AM (cm. s)         | 10.5±2.6          | 10.3±2.6             | 0.39    |
| IVCT (msec)        | 44.5±7.3          | 44.1±8.3             | 0.96    |
| IVRT (msec)        | 50.6±25.3         | 50.2±25.1            | 0.77    |
| ET (msec)          | 217.8±18.9        | 216.7±19.5           | 0.27    |
| MPI (Tei)          | 0.45±0.1          | 0.45±0.1             | 0.83    |
| Interseptal view   |                   |                      |         |
| Sm (cm. s)         | 9.4±1.6           | 9.4±1.4              | 0.83    |
| EM (cm. s)         | 13.4±1.7          | 13.6±1.8             | 0.46    |
| AM (cm. s)         | 7.4±1.3           | 7.2±1.1              | 0.3     |
| IVCT (msec)        | 53.7±16.3         | 51.7±9.2             | 0.33    |
| IVRT (msec)        | 44.3±11.5         | 43.8±11.1            | 0.21    |
| ET (msec)          | 209.7±18.7        | 208.9±18.5           | 0.94    |
| MPI (Tei)          | 0.46±0.05         | 0.46±0.07            | 0.89    |

Table 3. Echocardiographic data placebo group before and after intervention

| Variables, mean ±SD | Placebo group (Before intervention) (n = 13) | Placebo group (after intervention) (n = 13) | p-value |
|---------------------|---------------------------------------------|--------------------------------------------|---------|
| Mitral valve view   |                                             |                                            |         |
| Sm (cm. s)          | 11.2±2.5                                    | 11.4±2.6                                   | 0.17    |
| EM (cm. s)          | 18.4±4.3                                    | 19.0±4.8                                   | 0.30    |
| AM (cm. s)          | 7.8±3.1                                     | 7.1±2.1                                    | 0.34    |
| IVCT (msec)         | 49.3±8.5                                    | 47.0±9.6                                   | 0.23    |
| IVRT (msec)         | 43.1±10.1                                   | 43.2±9.6                                   | 0.86    |
| ET (msec)           | 232.2±81.7                                  | 231.1±79                                  | 0.31    |
| MPI (Tei)           | 0.43±0.05                                   | 0.45±0.68                                  | 0.34    |
| Tricuspid Valve view |                                             |                                            |         |
| Sm (cm. s)          | 14.2±2.9                                    | 14±2.9                                     | 0.87    |
| EM (cm. s)          | 23.7±2.8                                    | 24±2.6                                     | 0.33    |
| AM (cm. s)          | 10.3±2.6                                    | 10±2.6                                     | 0.39    |
| IVCT (msec)         | 50.2±25.1                                   | 50.1±25.2                                  | 0.77    |
| IVRT (msec)         | 216.7±19.5                                  | 216.3±18.1                                 | 0.27    |
| ET (msec)           | 0.45±0.1                                    | 0.46±0.01                                  | 0.83    |
| Interseptal view    |                                             |                                            |         |
| Sm (cm. s)          | 9.4±1.4                                     | 9.4±1.4                                    | 0.83    |
| EM (cm. s)          | 13.6±1.8                                    | 13.2±1.7                                   | 0.46    |
| AM (cm. s)          | 7.2±1.1                                     | 7.4±1.1                                    | 0.3     |
| IVCT (msec)         | 51.7±9.2                                    | 53.5±16.2                                  | 0.33    |
| IVRT (msec)         | 43.8±11.1                                   | 43.2±11.1                                  | 0.21    |
| ET (msec)           | 208.9±18.5                                  | 211.9±18.1                                 | 0.94    |
| MPI (Tei)           | 0.46±0.07                                   | 0.46±0.07                                  | 0.89    |
| Variables, mean ±SD | Q10 group (Before intervention) (n = 12) | Q10 group (after intervention) (n = 12) | p-value |
|--------------------|----------------------------------------|----------------------------------------|---------|
| Mitral valve view  | Sm (cm. s) 11.4±2.6                    | 12.4±3.5                               | 0.25    |
|                    | EM (cm. s) 19.1±4.2                    | 20.2±2.8                               | 0.01    |
|                    | AM (cm. s) 7.8±2.1                     | 9.1±2.8                                | 0.19    |
|                    | IVCT (msec) 47.6±9.2                   | 56.7±41                                | 0.50    |
|                    | IVRT (msec) 43.3±9.6                   | 48.5±5.7                               | 0.15    |
|                    | ET (msec) 231.4±79.5                   | 240.1±14.2                             | 0.80    |
|                    | MPI (Tei) 0.45±0.68                    | 0.41±0.1                               | 0.97    |
| Tricuspid Valve view | Sm (cm. s) 14.4±2.9                  | 14.3±2.8                               | 0.29    |
|                    | EM (cm. s) 24.3±2.6                    | 13.9±3.1                               | 0.94    |
|                    | AM (cm. s) 10.5±2.6                    | 12.7±3.8                               | 0.08    |
|                    | IVCT (msec) 44.5±7.3                   | 57.3±16.5                              | 0.10    |
|                    | IVRT (msec) 50.6±25.3                  | 45.7±14.2                              | 0.19    |
|                    | ET (msec) 217.8±18.9                   | 222.1±15.7                             | 0.52    |
|                    | MPI (Tei) 0.45±0.1                     | 0.46±0.1                               | 0.81    |
| Interaseptal view  | Sm (cm. s) 9.4±1.6                     | 11.3±5.9                               | 0.11    |
|                    | EM (cm. s) 13.4±1.7                    | 12.5±2.2                               | 0.97    |
|                    | AM (cm. s) 7.4±1.3                     | 9.6±5.3                                | 0.13    |
|                    | IVCT (msec) 53.7±16.3                  | 54.5±16.1                              | 0.85    |
|                    | IVRT (msec) 44.3±11.5                  | 57.4±16.5                              | 0.69    |
|                    | ET (msec) 209.7±18.7                   | 244.8±24.5                             | 0.012   |
|                    | MPI (Tei) 0.46±0.1                     | 0.46±0.1                               | 0.76    |

Table 5. Echocardiographic data of Q10 and placebo group after the intervention

| Variables, mean ±SD | Q 10 group (n = 12) | Placebo group (n = 13) | p-value |
|--------------------|---------------------|------------------------|---------|
| Mitral valve view  | Sm (cm. s) 12.4±3.5 | 11.4±2.6               | 0.34    |
|                    | EM (cm. s) 20.2±2.8 | 19.0±4.8               | 0.25    |
|                    | AM (cm. s) 9.1±2.8  | 7.1±2.1                | 0.08    |
|                    | IVCT (msec) 56.7±41 | 47.0±9.6               | 0.28    |
|                    | IVRT (msec) 48.5±5.7 | 43.2±9.6               | 0.09    |
|                    | ET (msec) 240.1±14.2 | 231.1±7.9              | 0.74    |
|                    | MPI (Tei) 0.41±0.1  | 0.45±0.68              | 0.59    |
| Tricuspid Valve view | Sm (cm. s) 14.3±2.8  | 14±2.9                 | 0.94    |
|                    | EM (cm. s) 13.9±3.1 | 24±2.6                 | 0.82    |
|                    | AM (cm. s) 12.7±3.8 | 10±2.6                 | 0.16    |
|                    | IVCT (msec) 57.3±16.5 | 44±7.3                | 0.05    |
|                    | IVRT (msec) 45.7±14.2 | 50.1±25.2             | 0.49    |
|                    | ET (msec) 222.1±15.7 | 216.3±18.1            | 0.05    |
|                    | MPI (Tei) 0.46±0.1  | 0.46±0.1               | 0.05    |
| Interaseptal view  | Sm (cm. s) 11.3±5.9 | 9.4±1.4                | 0.26    |
|                    | EM (cm. s) 12.5±2.2 | 13.2±1.7               | 0.44    |
|                    | AM (cm. s) 9.6±5.3  | 7.4±1.1                | 0.09    |
|                    | IVCT (msec) 54.5±16.1 | 53.5±16.2             | 0.33    |
|                    | IVRT (msec) 57.4±16.5 | 43.2±11.1           | 0.01    |
|                    | ET (msec) 244.8±24.5 | 211.9±18.1            | 0.16    |
|                    | MPI (Tei) 0.46±0.1  | 0.46±0.07              | 0.31    |

4. Discussion
This study was conducted to compare changes in echocardiographic parameters after six months’ treatment by Q10 in patients with DMD and placebo-control groups. The results showed that treatment by Q10 can cause significant changes in some echocardiographic parameters related to left ventricular systolic and diastolic functions. In this study, the control group, before and after treatment in any of the parameters and in any of the three views, did not
show the significant differences, while, in the Q10 group, except the two parameters of IVCT and MPI, an increase in the other parameters after six months’ treatment was observed which is due to intensity of the systolic dysfunction. But these changes were not statistically significant. However, the ratios of ET and Em increased significantly in the views of the mitral valve and interventricular septum. Increasing Em means that early diastolic flow velocity in mitral and tricuspid valves has improved. The comparison of TDI between the two groups at the end of interventions in the views of tricuspid and mitral valves and septum, showed deterioration of functions globally (systolic and diastolic). Furthermore, comparison of MPI and IVCT in the Q10 and control groups before and after intervention, showed a mild and non-significant increase that means that the drug is ineffective. As stated previously, DMD is a progressive disease associated with cardiac dysfunction that usually remains asymptomatic for several years. In these patients, the usage of energy and oxygen demand reduced by weak muscles and ultimately their necessity, decreased to cardiac out-put. Therefore, in these patients, cardiac signs are accompanied by severe cardiac dysfunction. So, early diagnosis and timely treatment of cardiac involvement are important to avoid irreversible left ventricular remodeling because this condition leads to death (1, 7, 18). We investigated and calculated the echocardiographic findings associated with systolic and diastolic function of right and left ventricles including; MPI, systolic and diastolic intervals and ejection time (IVRT, IVCT and ET) in the treated groups by Q10 and placebo, before and after treatment, and concluded that in spite of improvement of these parameters, changes did not occur in the cardiac global function parameters or MPI (which is also called Tei index) in treated groups by Q10 and placebo. According to the findings summarized in tables, it can be judged that myocardial damage in these patients are subclinical which is shown in MPI, and because of its progressive nature later engaged to involvement of EF and FS parameters. This process is justified through compensatory mechanisms that occur in the heart muscle (10, 19). In our study, tissue doppler showed a decreasing of IVRT in right and left ventricles in both groups, which is indicating improvement of left and right ventricular diastolic function after treatment. This finding is in line with the findings of Buyse et al. (12). These investigators studied the effects of coenzyme Q10 on dystrophin-deficient mice (mdx) and found that this drug has protective myocardial effects and leads to improvement of exercise tolerance tests. The results of their investigation showed that prescribing Q10 for 4-10 weeks at a dose of 200 mg/kg/day remarkably improved the diastolic function as well as end-diastolic volume, and also reduced the ratio of mortality associated with stress test with dobutamine. Moreover, it decreased inflammation and fibrosis in the heart muscle (12). In another study, the effectiveness of coenzyme Q10 in patients with heart failure were evaluated in 13 patients with Duchene muscular dystrophy and 8 people in the control group receiving placebo (20). The results of this study also showed that coenzyme Q10 increased peak systolic radial strain to 17.5% in the inferolateral wall of the left ventricle, while, this ratio was 7.5% in the placebo group, although this effect was not statistically significant. It seems that low sample size is one of the possible reasons for the lack of statistical significance, despite the numerical difference between the two groups (20). According to several studies, cardiac disorders in patients with DMD start from the posterobasal left ventricle because pressure on the longitudinal axis of the left ventricle is mostly applied to the posterior wall (3, 12). In our study, increasing and improving of Sm velocity (11± 2.6, 10.8± 3; PV=0.343) of the mitral valve was not shown in TDI on the samples before and after treatment in case and control groups and in comparing the two groups. Since different parts of the heart can be separately studied by TDI, evaluation of DMD patients seems to be more precise through this method. For example in Shabanian et al., despite the common parameters of echocardiography such as EF and FS, were in the normal range, but evaluation of MPI in their studied patients by using TDI, showed early global cardiac dysfunction (8). In present study, right ventricular MPI did not show difference between the two groups while, ET was significantly higher in the control group than case patients. In the evaluation of the right ventricle by TDI, Sm and Am velocities parameters had no significant differences in comparing the two groups. So, it can be concluded that the drug consumption had no effect in the MPI of right and left ventricles. However, based on the achieved results in this study, it seems that DMD patients had early subclinical cardiac dysfunction without clinical symptoms, and timely diagnosis of cardiac dysfunction in these patients leads to early treatment and ultimately a decrease in the progression of heart failure and delay of death caused by this problem. As for the limitations of this study, the major limitation was about small study sample size, due to the expenses involved, so larger sample sizes are suggested for future studies.

5. Conclusions
According to the obtained results from this study, coenzyme Q10 had no significant effects on improving of the MPI parameters in DMD patients. Therefore, based on our study, this drug cannot give hope to increase and improve the quality of life in these patients. However, the effects of the drug should be evaluated more precisely by greater sample size, more accurate methods particularly strain, strain rate by echocardiography and MRI, or by increasing the duration of the study.
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Trial registration:
The trial is registered at the Iranian Clinical Trial Registry (IRCT.ir) with the IRCT identification number IRCT2015070223018N1.

Conflict of Interest:
There is no conflict of interest to be declared.

Authors' contributions:
All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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