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Analysis of cardiac exams: electrocardiogram and echocardiogram use In Duchenne muscular dystrophies

Análise dos exames cardiológicos: eletrocardiograma e do ecocardiograma em Distrofia Muscular de Duchenne

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Abstract

Introduction: Duchenne Muscular Dystrophies (DMD) is a genetic muscle disorder that causes degeneration and atrophy of skeletal muscle and heart. **Objective**: The aim of this survey is accomplish an evaluation electrocardiographic and echocardiography in the patients bearers of Duchene Muscular Dystrophies (DMD), to observe which alterations, which the degree of cardiac compromising these patient present and the effectiveness of these exams in the evaluation cardiologic. **Methods**: Nine patients of the sex male bearers of DMD, with medium age of 14.12 $\pm$ 4.19 years, varying of 7 to 23 years were appraised. All were submitted to the evaluation physiotherapy and the cardiologic: electrocardiogram and echocardiogram. **Results**: The experimental conditions of the present survey we propitiate the observation of the alterations echocardiography, as well as: significant increase in the diastolic diameter of the left ventricular (LV), increase in the systolic diameter of the left atrium (LA), and significant decrease of the ejection fraction of the LV, characterizing global systolic function reduced, and of the alterations electrocardiographic suggested possible overload of RV, septum hypertrophy, blockade of left previous fascicle and overload of atrium left. Compatible alterations of hypertrophy left ventricular were not observed. **Conclusion**: The evidences corroborate with the data described in the literature in the characterization of an important heart compromising that these patient present, like this the evaluation

cardiologic, through the complemented exams of the echocardiography and electrocardiography provide important information for the prognostic, the accompaniment, and the treatment of patient bearers of DMD.

Keywords: Muscular dystrophies. Cardiomyopathy. Physical Therapy.

Resumo

Introdução*: A Distrofia Muscular de Duchenne (DMD) é uma desordem muscular de origem genética que causa degeneração e atrofia da musculatura estriada esquelética e cardíaca.* ***Objetivo****: Realizar uma avaliação eletrocardiográfica e ecocardiográfica dos pacientes portadores de Distrofia Muscular de Duchenne, observando quais as alterações presentes, o grau de comprometimento cardíaco e a eficácia destes exames na avaliação cardiológica.* ***Métodos****: Foram avaliados 9 pacientes do sexo masculino portadores de DMD, com idade média de 14,12 ± 4,19 anos, variando de 7 a 23 anos. Todos foram submetidos à avaliação fisioterápica e aos exames cardiológicos: eletrocardiograma e ecocardiograma.* ***Resultados****: As condições experimentais do presente trabalho nos propiciam a observação de alterações ecocardiográficas, bem como: aumento significativo no diâmetro diastólico do ventrículo esquerdo, aumento do diâmetro sistólico do átrio esquerdo, e diminuição significativa da fração de ejeção do ventrículo esquerdo, caracterizando função sistólica global diminuída, e das alterações eletrocardiográficas que mostraram possível sobrecarga de ventrículo direito, hipertrofia septal, bloqueio de fascículo anterior esquerdo e sobrecarga de átrio esquerdo. Não foram observadas alterações compatíveis de hipertrofia ventricular esquerda no eletrocardiograma.* ***Conclusão****: As evidências corroboram com os dados descritos na literatura na caracterização de um comprometimento cardíaco importante apresentado por estes pacientes, assim a avaliação cardiológica, através dos exames complementares de ecocardiográfica e eletrocardiografia, nos proporcionam informações importantes para o prognóstico, o acompanhamento, e o tratamento dos pacientes portadores de DMD.*

Palavras-chave*: Distrofia muscular. Miocardiopatia. Fisioterapia.*

Introduction

Duchenne muscular dystrophy (DMD) is a muscle disorder of genetic origin. It is caused by dystrophin gene mutations on chromosome Xp21 and causes degeneration and atrophy of cardiac and skeletal striated muscles (1, 2, 3, 4). Its incidence is about 1 in 3,500 live-born males. (5, 6).

The disruption of dystrophin function as a cytoskeletal protein leads to an abnormal intracellular Ca2+ homeostasis (7, 8), whose actual source and functional consequences remain obscure (9). It is known, however, that these anomalies have a nuclear pathogenesis (10). Over 90% of all DMD patients develop cardiomyopathy and many die of cardiac failure (11). Despite the progress in skeletal muscle gene therapy, few attempts have been made to treat cardiomyopathy (12). The most common cardiac abnormality found in these patients is dilated cardiomyopathy (13, 14) and the heart may be affected to varying degrees, depending on the stage of the disease (15). Pathoanatomic evidence of cardiac involvement in DMD is the replacement of the myocardium by fibrous tissue or fat (16). In DMD the left ventricular posteriobasal and lateral walls are most extensively affected, sparing the right ventricle and atrium. Cardiac involvement usually remains subclinical even in advanced stages of the disease. (15), (17, 18).

The electrocardiogram (ECG) is a complementary cardiac test of great value in the diagnosis of heart diseases due to its ease of performance. When present, electrocardiographic changes constitute the so-called dystrophic pattern, considered as a differential diagnosis element for DMD and other dystrophinopathies. In Duchenne's form of muscular dystrophy, the occurrence of this electrocardiographic pattern in the early phase of the disease provides evidence of early heart involvement (15), (19).

The main electrocardiographic abnormalities found in DMD are sinus tachycardia, shortening of the PR interval, occurrence of deep Q waves in D1,

aVL and left precordial leads, broad R wave in V1-V6 leads, suggesting diagnosis of ventricular overload (19 ,20, 21, 22).

Echo-Doppler cardiography is a technique to anatomically and functionally evaluate the cardiovascular system (23). It allows a qualitative assessment of left ventricular contraction (24), being a useful tool for the early diagnosis of left ventricular dysfunction and providing useful information for the treatment of DMD patients (25). The most common abnormalities seen in the echocardiogram are heart muscle contractility disorders (26, 27). Electrocardiographic and echocardiographic changes are due to a degenerative process involving fibrosis and replacement of primary tissue by fatty tissue (28, 29). Ventricular dysfunction and arrhythmias occur in conjunction with the increased fibrosis and, in the final stages of the disease, impaired systolic function can lead to heart failure and sudden death (15).

The aim of this study was to conduct a cardiac evaluation through specific complementary tests, such as electrocardiogram and echocardiogram. We observed the changes that were present, the degree of cardiac involvement and the efficacy of these tests, which may contribute to an early therapeutic intervention.

Methods

This study was approved by the Research Ethics Committee of the University of Franca, protocol number 083/04. Parents and/or guardians signed an informed consent form providing authorization for the participation of their children in this study.

We evaluated 9 male patients with DMD who were undergoing physical therapy. Mean age was 14.12 ± 4.19 years, ranging from 7 to 23 years of age. Mean weight was 45.62 ± 19.03 kg. A cardiologist was responsible for conducting the tests and making the diagnoses. In all patients, the clinical diagnosis of DMD was confirmed by muscle biopsy, specific genetic testing (PCR) and characteristic clinical signs: calf pseudo-hypertrophy, Gower´s sign and changes in the spinal column.

The study group underwent electrocardiographic examination on a conventional 12-lead electrocardiogram. Tests were performed while the patients were at rest and positioned supine. The device used for the graphic recording of electrocardiographic waves was a TEB ECG PC 150 AC model. The analysis of the tracings comprised the QRS complex morphology, analysis of the ST segment and T wave in order to assess the presence or absence of left ventricular hypertrophy and other possible changes.

Echocardiographic examination was performed in all patients by conventional transthoracic Doppler echocardiography with the aid of a Hewlett Packard Sonos 500, 100, 200 or 5500 (model SIM 7000 CFM – Challenge). The left ventricle (LV) M-mode measurements were taken in the parasternal long-axis view (30), with the patient in the left lateral decubitus position. The systolic and diastolic diameter of the LV was measured in sectional images between the end-diastolic dimension and the cross-dimension (31).

Fractional shortening of the LV was calculated as the end-diastolic dimension minus the end-systolic dimension, divided by the end-diastolic dimension The apical two-dimensional view of the fourth chamber was used to calculate the left-ventricular ejection fraction (LVEF), adopting a single method of length measurement (31). Systolic LV impairment was defined as a fractional shortening < 25% or decreased ejection fraction (< 58%) (31, 32). Dilated cardiomyopathy was diagnosed by the demonstration of an increased end-diastolic diameter (33).

Echocardiographic variables were corrected for body surface area and referred to as indexes consolidated in textbooks (34, 35). All echocardiographic measurements were performed according to the standards established by the American Society of Echocardiography (30). The following variables were studied: left ventricle diastolic diameter (LVDD), left atrium systolic diameter (LASD), aortic diastolic diameter (ADD), aortic valve opening and LV thickness.

For the statistical analysis of the data concerning the ejection fraction (EF), we compared the normal baseline value described in the literature (> 58%) with the values obtained by using the paired Student's t-test. Values are expressed as mean + SEM and a p value < 0.05 was considered statistically significant. For statistical data on the LVDD, LASD, ADD, aortic valve opening and LV thickness, we compared the average of the normal baseline values described in the literature with the values obtained by using the nonparametric Mann-Whitney test, considering $p < 0.05$. Values are expressed as mean + SEM.

Results

Results of the electrocardiographic and echocardiographic examinations showed cardiac involvement in 90% of patients, but only 33% were symptomatic patients. The other cases had only sub-clinical evidence. Among the existing echocardiographic changes are: significant increase in LVDD (Figure 1) and in LASD (Figure 2), and significant decrease in LVEF (Figure 3), indicating decreased global systolic function.

For the parameters ADD and aortic valve opening no significant difference was observed compared to baseline values (34) (Table 1).

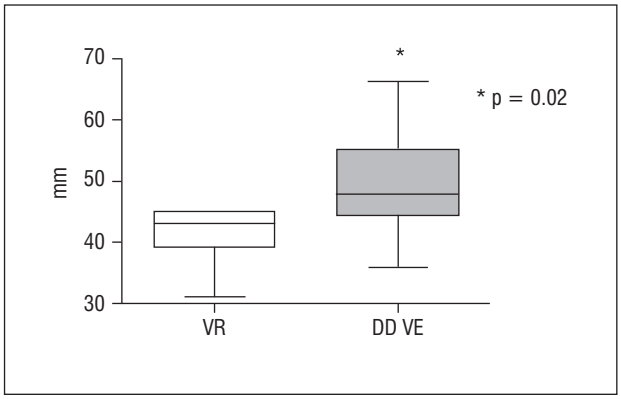

Figure 1 - Comparison of baseline values with the values obtained in the echocardiogram for the variable left ventricle diastolic diameter * (LVDD), where p = significance level

Source: Research data.

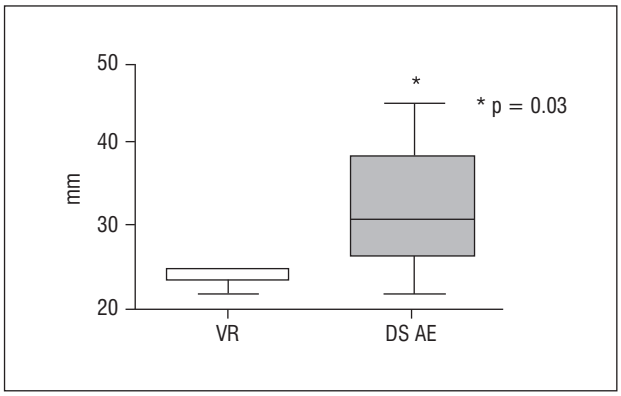

Figure 2 - Comparison of baseline values with the values obtained in the echocardiogram for the variable do left atrium systolic diameter * (LASD), where p = significance level

Source: Research data.

The conventional 12-lead electrocardiographic evaluation showed shortening of the PR interval, deep Q waves in D1, AVL and left precordial leads, wide R waves in V1-V6 leads (Figure 4), which can be translated into possible right ventricular overload, septal hypertrophy, left anterior fascicular block and left atrial overload, according to Table 2.

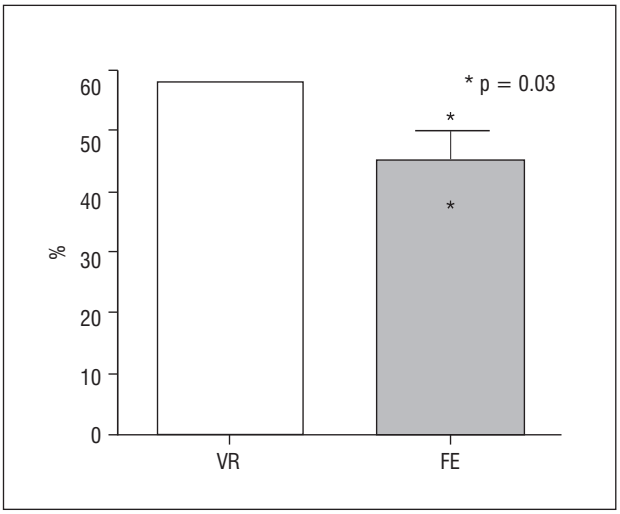

Figure 3 - Comparison of baseline values with the values obtained in the echocardiogram for the variable Left-ventricular ejection fraction * (LVEF), where p = significance level

Source: Research data.

Table 1 - Comparison of normal baseline values with the values obtained in the echocardiogram

Variable	Obtained	Reference	p
LVEF (%)	43.75 + 12.17	> 58	0.03
LVDD (mm)	49.52	37.5 + 3.84	0.02
LASD (mm)	33.5 + 11.5	28.4 + 3.2	0.03
ADD (mm)	18	21 + 3.4	NS
AVO	13.5 + 0.5	20 + 0.44	NS
LV thickness	6.65	6.0	NS

Note: LVEF = left-ventricular ejection fraction; LVDD = left ventricle diastolic diameter; LASD = left atrium systolic diameter; ADD = aortic diastolic diameter; AVO = Aortic valve opening; NS = not significant.

Source: Morcerf et al. (34).

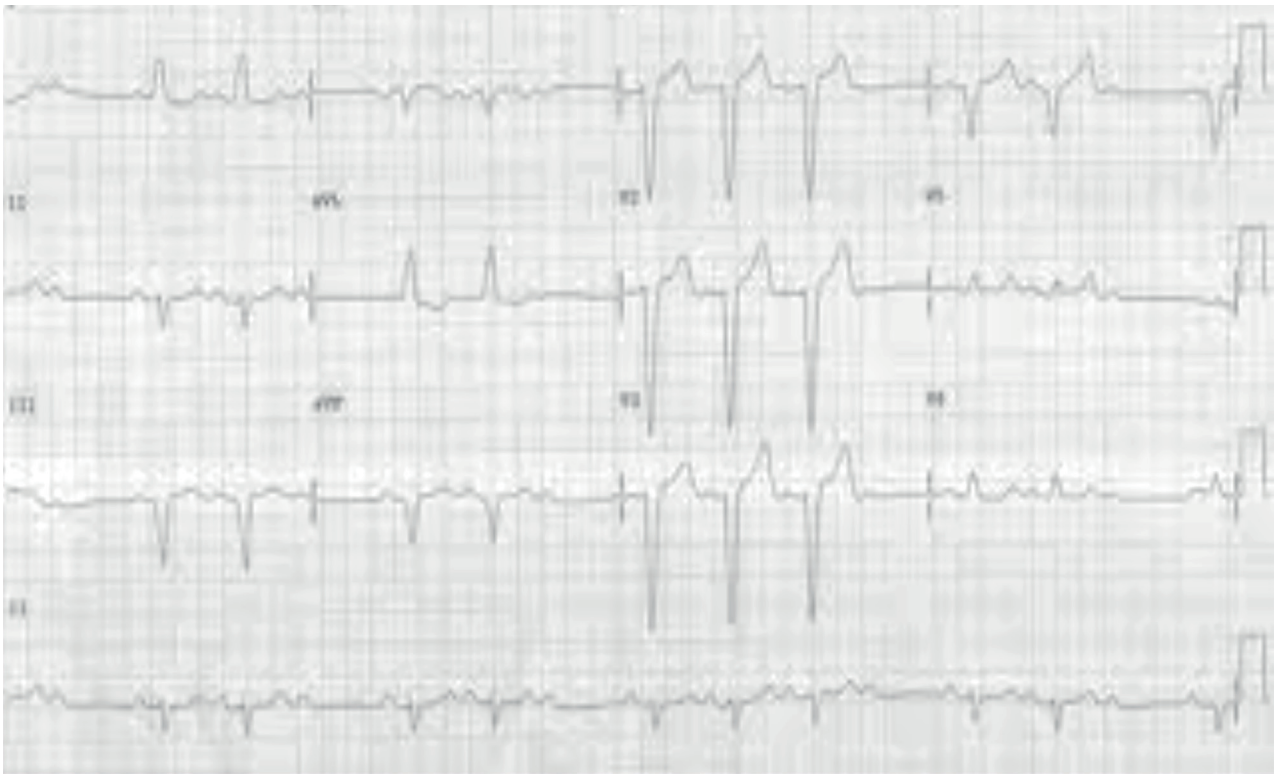

Figure 4 - ECG changes compatible with right ventricular overload
Source: Research data.

Table 2 - Types of electrocardiographic changes in the group studied (in percentages)

SH	RVO	LAFB	LAO
44.4 %	44.4 %	2.2%	22.2%

Note: SH = Septal Hypertrophy; RVO = Right Ventricular Overload; LAFB = Left Anterior Fascicular Block; LAO = Left Atrial Overload.
Source: Research data.

Discussion

The heart of DMD carriers is affected to various degrees, depending on the stage of the disease and the type of mutation (15). Pathoanatomic evidence of cardiac involvement in dystrophinopathies is the replacement of the myocardium by fibrous tissue or fat (16). In this study, we observed cardiac involvement in 90% of patients. Corresponding percentages have been elucidated by other authors (11), (15), (35). Despite the high level of cardiac involvement found, only about 30% of subjects are symptomatic carriers of DMD (36), as can be seen in our study.

The involvement of the heart muscle can be visualized by using electrocardiographic and echocardiographic tests (15), (19), (20). Echocardiography allows qualitative assessment of LV contractility (24). The most frequently found abnormality in DMD is the LV contractility dysfunction (26), (27). This functional change generates systolic deficiency (37), which can be observed in our study through a decrease in EF. A recent case report showed a 35-40% reduction in EF in a patient with dilated cardiomyopathy (38). We found very similar values in our study (43.75 on average).

The mean LVDD value in our study was 49.52 mm. Similar values were reported by Saito et al. (22). Many DMD patients suffer from dilated cardiomyopathy (11), (14), this type of cardiac involvement was seen in most patients analyzed in our study group. Studies show the effectiveness of echocardiography in detecting cardiac abnormalities in DMD carriers (39), and evidence the ventricular systolic function as the parameter that best indicates myocardial involvement in the myopathic process (39, 40, 41).

Electrocardiographic tests evidence alterations in patients with DMD. Studies such as those conducted

by Nigro et al. (20) and D'Orsogna (42) revealed alterations in the whole study population, which was also seen in this study. The most common changes were shortening of the PR interval, deep Q waves in D1, AVL and left precordial leads, wide R waves in leads V1-V6 (19), (22), (43). Other studies have shown and classified these changes as typical DMD alterations (ECG pattern) (20, 21). Some studies also report the presence of frequent sinus tachycardia (19, 20) which was not corroborated by our study, as it was only found in 11% of the patients studied.

The alterations mentioned above may be translated into possible left ventricular overload, septal hypertrophy, left anterior fascicular block and left atrial overload. This shows the importance of cardiac monitoring, through the use of these tests. Experimental studies in mice provide the first evidence that dystrophin plays a mechanical role in cardiomyocytes similar to its role in skeletal muscle (2). An experimental model in mdx mice applied the ECG method and observed significant tachycardia, with a 15% faster heart rate when compared with the control group. This finding shows an imbalance in the autonomic nervous system modulation of heart rate, with increased sympathetic and decreased parasympathetic activity (20).

A study analyzed the prognostic value of ECG and echocardiography of 56 DMD patients and found an 18%prevalence of cardiac abnormalities. 7% of patients had significant LV dilation and decrease in EF. Echocardiography was more often abnormal than ECG (44). This finding is corroborated by our results. Hoogerwaard et al. (21) suggest that DMD carriers should be assessed by a cardiologist at least once a year so that they can initiate a timely therapy. This author evaluated cardiac tests of DMD patients and found that 47% had ECG alterations, 36% had echocardiographic alterations and 18% had dilated cardiomyopathy. In our study, 44% showed electrocardiographic alterations and 80% had echocardiographic alterations.

One of the indexes commonly used for the prognostic evaluation of cardiomyopathy is the LVEF. LVEF greater than 28% correlates with the annual mortality rate of < 13%. LVEF lower than 28% associated with LV diameter to thickness ratio higher than 4 during diastole shows an annual mortality rate of 25% (45).

An early diagnosis of impaired cardiac function makes is possible to initiate drug therapy, following the established cardiological recommendations, due to its protective effect.

Based on the data and observations discussed above, we believe that the findings of this study allowed us to identify the important cardiac involvement found in DMD patients. This evidences the importance of cardiac monitoring, which is not yet part of the control routine for the analyzed group. This information, however, require further confirmation by prospective studies designed for this purpose.

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