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Electrocardiogram Changes with Neuroleptic Cardiomyopathy: The influence of age factor

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Abstract

By calculating the Cohen coefficient, the force of the influence of an age factor on the dynamics of electrocardiographic parameters at development of a neuroleptic cardiomyopathy is determined. It is established that in patients of different age crucial importance plays not the age factor, but side cardiotoxic effect of antipsychotics leading finally to development of the cardiac pathology.

Keywords: Antipsychotics; Cardiotoxicity; Neuroleptic cardiomyopathy; Electrocardiogram changes; Age effect

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As a result of active therapy of both the main mental and concomitant somatic pathology, the life expectancy of mental patients, in particular those suffering from schizophrenia, has increased significantly [1-5]. This process is accompanied by a significant increase in the duration of antipsychotic therapy (APT), thereby significantly lengthening the time of damaging cardiotoxic effects of antipsychotics (AP) on the heart, which is fraught with the development of severe life-threatening iatrogenic pathology-neuroleptic cardiomyopathy (NCMP) [6].

The various pathological changes on the electrocardiogram (ECG) serve as a reflection of the deep structural changes of the myocardium in the process of morphogenesis of

NCMP [3,4,7,8]. In parallel, natural ontogenetic involutional processes develop in the heart [9]. So, the features of the ECG of the practically healthy elderly people are the correct sinus rhythm; sinus bradycardia; extrasystole; blockade of the legs of the GIS beam; EOS deviation to the left; expansion, flattening and deformation of the P wave; lengthening of the PQ and QT intervals, broadening, splitting and reducing the voltage of the QRS complex; reducing the amplitude of the T wave in all leads [10-12]. In connection with the above, the question arises naturally, how do these two factors (APT and age) interact and what is the value of the direct action of the age factor in the formation of changes recorded on the ECG in the development of NCMP? In the special literature any information on this problem is not found.

Meanwhile, the clarity is of a great practical importance, since AP is usually prescribed by the psychiatrists, who are usually poorly informed about the nuances of cardiology [13]. In addition, the study of ECG equivalents of cardiotoxic side effect of AP is extremely important for clinical practice [9], since it is the appearance of abnormal signs on the ECG that is one of the relatively early signs of the developing cardiac pathology [14,15]. Based on the above, the purpose of this study was to try to find an answer to this question. Such a study is necessary to determine the possibility of differentiation of age-related changes of the ECG and ones due to cardiotoxic side effect of AP and the development of NCMP. This is important for the early diagnosis of a dangerous complication of APT and the beginning of its timely treatment.

Material and Methods

The case histories of 43 patients with schizophrenia (men - 27, women - 16) who died at the age under 40 years and over 60 years were analyzed in retrospect. During their lives the patients received various antipsychotic (neuroleptic) drugs (AD) in quantities corresponding to the therapeutic standard; these medicines are not rarely received in combination with each other. Patients of groups I and II received AP relatively short time-from six months to one and a half years. In groups III and IV APT lasted for many years, sometimes up to 30 years or more. All diagnostic procedures, including ECG studies, as well as psychotropic treatment of patients with schizophrenia were performed for medical reasons and did not require the consent of patients.

The observations were divided into four groups: I and II were respectively 8 young and 12 elderly patients receiving AP, but had no heart disease and died of non-cardiac causes; groups III and IV included 6 young and 17 elderly patients suffering from NCMP. The final diagnosis of each deceased was verified at the

autopsy. The criteria of an exception were the expressed signs of a metabolic syndrome (the increased body weight, arterial hypertension, a diabetes mellitus), a chronic pulmonary pathology with hypertension in a small circle of blood circulation, heart defects, a cachexia.

A total of 133 ECGs were studied, divided into groups as follows: 23, 34, 21 and 55, respectively. In each group, eight pathological electrophysiological parameters (ECG signs) were ranked by their frequency. One of them is the corrected Qt interval (QTc) calculated by the formula H.C. Bazett [16,17]. Mathematical analysis of the obtained quantitative data included the calculation of such an index as the effect's size by J. Cohen [18,19], which in quantitative terms determines the effect of the studied factor on a particular object of study [18,20]. It is believed that the inclusion of the Cohen coefficient (d'C) in the mathematical data processing tool strengthens the rigor of the study and gives more weight to the analysis, conclusions and recommendations [21]. The following gradation of d'C is accepted: insignificant - less than 0,20; small - 0,20-0,49; average - 0,50-0,79; big - 0,80 and above [18,20,22]. Negative d'C values indicate the opposite direction of the effect [22]. The obtained quantitative results were processed statistically (computer program "Statistica 6.0") with the level of significance of differences of 95% and more ($p \leq 0.05$). The d'C calculation is performed automatically using a computer calculator [22].

Results and Discussion

The comparison of the studied ECG indices in groups I and II (Table. 1) identifies the pronounced and statistically significant ontogenetic changes in six of the eight ECG parameters. So, with age the frequency of tachycardia which is a side effect of most AP [4] decreases. Apparently, this is due to a noticeable increase in the frequency of conduction disturbances, including prolongation of the QTc interval.

ECG signs Groups	Rhythm disturbances	Extension of the QTc interval	Conduction disturbances	Diffuse muscle changes	Overload of the right parts	Left ventricular hypertrophy	Reduction of myocardial electrical activity	EAH deviation to the left
I	83,9±15,1 2, 4	8,6±4,2 2, 3, 4	7,4±4,9 2, 3, 4	15,3±4,4 2, 3, 4	8,7±4,7 3, 4	2,4±1,4 3, 4	1,4±1,0 2, 3, 4	3,8±2,5 2, 3, 4
II	56,4±10,8 1	21,2±7,1 1, 4	22,4±8,3 1, 4	25,4±8,8 1, 4	12,0±5,7 3, 4	9,6±7,7 4	7,9±3,3 1	15,7±4,9 1, 4
III	67,7±15,7	21,9±11,2 1, 4	33,7±10,8 1	34,7±4,8 1	24,9±9,2 1, 2	13,5±6,1 1	11,6±6,1 1	19,2±5,9 1
IV	64,1±8,6 1	47,4±6,8 1, 2, 3	35,4±7,3 1, 2	38,8±5,7 1, 2	27,5±6,4 1, 2	21,2±5,8 1, 2	21,3±7,7 1, 2	28,2±7,3 1, 2

Table 1: The frequency of ECG signs [%] in the study groups.

Note: 1-4 - statistically significant differences between the groups. The certain frequency shifts demonstrating age-related changes of a myocardium of the mainly left ventricle are observed from such ECG signs as diffusion muscular changes, a decrease in electric activity of a myocardium and a deviation of the electrical axis of heart (EAH) to the left. The listed pathological shifts of the ECG parameters are most likely due to the influence of the age factor, since APT in these groups of observations was relatively short. However, the cardiotoxic effect of AP cannot be completely excluded. In particular, the change of such ECG sign as QTc interval, as we know, is caused by the direct effect of AP on the ion channels of cardiomyocytes, and the disturbances of a cardiac rhythm, manifested mainly by sinus tachycardia [3, 8], are constantly observed at reception of the majority of AP [1,3,4,13,14]. The listed pathological shifts of the ECG parameters are caused, most likely, by influence of an age factor as APT in these groups of observations was rather short. However, it is impossible to exclude completely and cardiotoxic effect of the Apostle. In particular, change of such ECG sign as QTc interval, as we know, is caused by direct impact of AP on ion channels of cardiomyocytes [1]. The calculation of d'C in the compared groups I and

II (Table. 2) shows that the influence of an age factor only on such an indicator as the deviation of the EAH to the left corresponds to an average degree, on almost all the others - a small one, and on the ECG-sign "overload of the right departments" - an even insignificant one. The data presented in both tables are fully consistent. In general, it is possible to note that age changes of an ECG against the background of short APT, though take place, but are expressed quite poorly.

In the process of the morphogenesis of NCMP (group III and IV) there is a leveling effect of the latter on the degree of severity of ontogenetic ECG shifts (table. 1). On the pathological background created by the presence of NCMP age-related changes in ECG signs are practically not expressed and are statistically significant only in such an indicator as the lengthening of the QTc interval. The values of d'C for the vast majority of ECG indices compared in groups III and IV (Table. 2) are within the boundaries of small and insignificant quantities. The exception is again the frequency of increasing the QTc interval, in which d'C corresponds to an average degree. Thus, the force of the influence of an age factor on the dynamics of ECG parameters in patients suffering from NCMP is extremely small, and all the identified changes are caused by the

development of the specified iatrogenic pathology. The results of a comparative analysis of ECG changes in paired groups I-III and II-IV, that is in persons of the same age respectively without NCMP and in the presence of one (Table. 1), once again confirm the put-forward position. So, in young patients with the development of this cardiac pathology almost all ECG parameters, excluding arrhythmias, substantially and statistically significantly deteriorate. In this case, the force of the influence of NCMP development on ECG changes is more noticeable in young people - d'C in the compared pair of groups I and III in three indicators corresponds to a small degree, in four - an average one and one (diffuse muscle changes) - a high one (Table 2). The frequency of the absolute majority of ECG signs, except for cardiac arrhythmias, also significantly

changes in elderly mental patients suffering from NCMP (Table 1). From eight d'C values in the compared groups II and IV (Table 2) of the average level reach two (and one of such indicators - all the same lengthening of an interval of QTc); the small size of d'C is inherent in five indicators and insignificant only to one (rhythm disturbances). In conclusion, two significant circumstances should be noted. First, with age the severity of arrhythmia, associated with the reception of AP, regardless of the presence or absence of NCMP significantly decreases. This indicates a certain adaptation of the organism to the cardiotoxic action of these drugs. Secondly, at assessment of the given ECGs of the patients receiving APT, paramount attention should be paid to lengthening of an interval of QTc as to the most labile indicator.

ECG signs Groups	Rhythm disturbances	Extension of the QTc interval	Conduction disturbances	Diffuse muscle changes	Overload of the right parts	Left ventricular hypertrophy	Reduction of myocardial electrical activity	EAH deviation to the left
I-II	- 0,41	0,389	0,396	0,258	0,117	0,224	0,464	0,545
I-III	- 0,23	0,350	0,696	0,922	0,491	0,560	0,521	0,755
II-IV	0,122	0,571	0,254	0,286	0,381	0,265	0,317	0,291
III-IV	- 0,054	0,510	0,033	0,123	0,059	0,215	0,218	0,213

Table 2: Cohen's coefficient (d'C) in the study groups.

Conclusion

Thus, the carried-out analysis of the dynamics of changes of the ECG parameters in the aspect of ontogenesis and at the development of NCMP shows lack of significant influence of an age factor on the frequency of registration of pathological ECG signs at mentally ill patients in the presence of NCMP. Generalizing everything told, it is possible to note that at the development of NCMP in patients of different age the crucial importance in the genesis of

various pathological changes of an ECG has not an age factor, but the side cardiotoxic effect of AP leading eventually to the development of NCMP. This conclusion has the great practical value for the clinic. The matter is that such vital dangerous iatrogenic cardiac pathology as NCMP associated with the reception of AP can develop at any age. At the same time, it is the side cardiotoxic effect of AP that is the determining factor. The dynamics of the ECG parameters in this group of patients is a reflection of the process of a morphogenesis of

NCMP. Therefore, when carrying out APT at all patients irrespective of their age regular performance of an ECG researches is necessary for early detection of the developing iatrogenic cardiac pathology.

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