ECRONICON OPEN ACCESS

EC CLINICAL AND EXPERIMENTAL ANATOMY
Research Article

To the Problem of the Beginning of Development of Neuroleptic Cardiomyopathy: Organometric Study of the Heart

Volkov VP*

Tver Center of Judicial Examinations, Russia

***Corresponding Author:** Volkov VP, Tver Center of Judicial Examinations, Russia.

Received: June 26, 2019; **Published:** July 12, 2019

Abstract

By a morphometric method of research the macroscopic changes of the heart in the process of antipsychotic therapy and in neuroleptic cardiomyopathy as a whole, and at various stages of the disease was determined. The analysis of the obtained results shows that the development of neuroleptic cardiomyopathy in its latent stage begins gradually after 10 years of psychotropic treatment.

Keywords: *Antipsychotics; Cardiotoxicity; Duration of Antipsychotic Therapy; Neuroleptic Cardiomyopathy; Clinical Stages of Disease; Pathomorphology of a Heart; Organ Level of Organization; Morphometry*

Introduction

Neuroleptic (antipsychotic) cardiomyopathy (NCMP) is one of serious complications of psychotropic therapy caused by side cardiotoxic effect of antipsychotic preparations [1-4].

As showed my researches, in its development NCMP passes three clinical stages: 1) a latent one, it is clinically fully compensated, 2) a full-scale (developed. manifesting) one, when cardiac disorders are clearly detected, but without the expressed signs of CHF, and 3) a terminal one, when the clinical picture of CHF comes to the foreground [5,6].

Demonstration NCMP occurs usually after prolonged treatment with antipsychotics [7-9]. For example, according to the systematic literature review conducted by M Alawami., *et al.* (2014) [8], after the start of receiving clozapine, perhaps the most cardiotoxic antipsychotic drug, symptoms of the disease appear after an average of 14.4 months. B Makhoul and colleagues (2008) [7] describe a patient even with seven years of experience using this antipsychotic. Overall, however, the timing of the disease is still not exactly specified. At the same time, more or less accurate knowledge of the timing of the beginning of the possible development of NCMP is of great importance for the clinic, opening the possibility of timely therapeutic and preventive measures.

Aim of the Study

The goal of this study is to verify these preliminary data by morphometric study of macroscopic parameters of the heart at different stages of NCM and at different time of APT, followed by a comparison of the results.

Materials and Methods

To characterize cardiac changes in NCMP at the macroscopic level, cardiac organometry was performed in 80 deceased patients with schizophrenia (60 men and 20 women; age from 16 to 77 years), who suffered during the life of NCMP, verified at autopsy.

In 30 of dead patients the disease was in the latent stage (group II), in 21 patients it was in the full-scale stage (group III), and in 29 patients it was in the terminal stage (group IV).

In addition, autopsy protocols of 70 patients with schizophrenia (41 men and 29 women) who died at the age from 22 to 77 years were analyzed. 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, a cachexia.

During their lives the patients received various antipsychotic in quantities corresponding to the therapeutic standard; these medicines are not rarely received in combination with each other. The duration of APT ranged from six months to 30 years or more.

Depending on the duration of the APT material is divided into four groups (V-VIII): V - up to 10 years (20 dead); VI - from 11 to 20 years (25); VII - from 21 to 30 years (19); VIII - over 30 years (6).

The original author's method developed by me for such studies [10] was used for the analysis of the obtained data.

The following parameters were measured on the macroscopic level: heart mass (m), linear dimensions, perimeter of venous valve openings, and thickness of a wall of ventricles.

For this analysis the outer volume of heart without atria (V) was determined and two relative parameters (both in percent) were calculated: 1) C_v - coefficient of volume, this coefficient shows a part of the total volume of heart (without atria), and this part falls on the volume of cavities of ventricles; and 2) C_l - coefficient of the left ventricle, this coefficient shows the volume size of the left ventricle with respect to the total volume of both ventricles. In addition, two other parameters were calculated which use a gravimetric characteristic of the heart (m): mass-volume ratio (MVR) and index of density of myocardium (IDM).

A growth of MVR is evidence of a hypertrophy of myocardium, and its diminution is an indication for dilatation of cavities of heart ventricles. IDM clearly shows a strongly expressed correlation with such objective parameters of microstructure of cardiac muscle as stromal-parenchymatous ratio and rate of interstitial edema [10], which quantitatively describe a condition of its intercellular matrix.

The obtained quantitative results were processed statistically (computer program "Statistica 6.0") with the level of significance of differences of 95% and more ($p \leq 0.05$).

Results

In table 1 presents the data obtained in the course of the study.

Situations / Groups	m	V	C_v	C_l	MVR	IDM
I	359 ± 10[5]	165,4 ± 6,8[5]	42,1 ± 1,1[5,8]	40,3 ± 0,6	2,17 ± 0,04[5]	6,20 ± 0,14[5]
II	355 ± 9	162,8 ± 5,2	41,4 ± 1,0	40,2 ± 0,7	2,18 ± 0,03	6,06 ± 0,06
III	358 ± 12	165,9 ± 6,7	42,6 ± 1,7	40,3 ± 0,8	2,16 ± 0,05	6,24 ± 0,08
IV	361 ± 10	167,5 ± 5,4	43,2 ± 1,5	40,6 ± 0,7	2,15 ± 0,03	6,36 ± 0,05
V	317 ± 7[1]	141,4 ± 5,4[1]	34,5 ± 0,6[1]	39,7 ± 0,6	2,24 ± 0,04[1]	4,57 ± 0,08[1]
VI	355 ± 8	163,5 ± 5,8	41,4 ± 0,4	40,2 ± 0,5	2,17 ± 0,04	6,06 ± 0,07
VII	359 ± 8	166,7 ± 6,3	42,6 ± 0,5	40,4 ± 0,4	2,15 ± 0,04	6,29 ± 0,04
VIII	364 ± 5	168,7 ± 6,3	43,8 ± 0,6[1]	40,8 ± 0,4	2,16 ± 0,03	6,38 ± 0,06

Table 1: *Macroscopic cardiac changes at NCMP and in APT.*

Note: 1, 5, 8 - statistically significant differences between the groups.

Discussion

Analysis of the results of organometric study of the heart (Table 1), conducted in the direction of the goal of work, showed that the differences between groups I and V are statistically significant in the vast majority of indicators. At the same time, there are no differences in the parameters in group I compared to those in subsequent groups of observations.

When comparing organometric indicators characterizing the state of the heart at different stages of development of NCMP and observed at different periods of AP administration, it was found that statistically significant differences in these indicators at all stages of the disease (group II-IV) were observed practically only with those with a relatively short duration of APT - up to ten years (group V). At the same time, pathological changes in the structure of the heart, characteristic of the latent clinical stage of NCMP (group II), correspond to those in group VI. The expanded stage of the disease (group III) with its inherent organometric cardiac signs as accurately as possible correlates with group VII, and the terminal (group IV) fits into the picture of changes detected in groups VIII. The relationship of studied parameters in their absolute value in all the considered pairs of groups on a scale of Chedoke direct and functional ($\rho = 1{,}000$).

Thus, organometric changes of the heart observed during its remodeling in the process of morphogenesis of NCMP and after ten years of APT are almost identical. This indicates that the ten-year period of AP intake can be considered as a certain threshold, at which the complex of quantitative macroscopic changes of the heart passes into a new quality - the development of NCMP.

Conclusion

Organometric approach to the comparative study of the heart in NCMP as a whole, and at various stages of the disease, on the one hand, and in different periods of APT, on the other one, showed that the risk of development of severe iatrogenic complications - NCMP, which is due to the side cardiotoxic effects of antipsychotic drugs, increases abruptly after ten years of psychotropic treatment.

In other words, the disease begins about 10 years after the start of APT. the disease In this period the disease is in a latent stage. Clinical manifestations of NCMP occur much later (after 20 years of taking antipsychotics) thanks to the compensatory-adaptive processes occurring during this period in the heart.

The detected long enough period preceding the beginning of clinical manifestation of NCMP allows to diagnose this pathology in a timely manner and to start the necessary medical measures in time.

Bibliography

1. Volkov VP. "Cardiotoxicity of phenothiazine neuroleptics (review of literature)". *Psichiat Psychopharmacotherapy* 12.2 (2010): 41-45.
2. Volkov VP. "Phenothiazine dilated cardiomyopathy: some aspects of clinic and morphology". *Klinicheskaia Meditsina* 87.8 (2009): 13-16.
3. Buckley NA and Sanders P. "Cardiovascular adverse effects of antipsychotic drugs". *Drug Safety* 23.3 (2000): 215-228.
4. Coulter DM., *et al*. "Antipsychotic drugs and heart muscle disorder in international pharmacovigilance: data mining study". *British Medical Journal* 322.7296 (2001): 1207-1209.
5. Volkov VP. "Clinical characteristic of an antipsychotic cardiomyopathy". In: VP Volkov (ed.) Actual problems of therapeutic clinic: collective scientific monograph. Novosibirsk: SibAC Publ (2013): 94-116.
6. Volkov VP. "Morphometric aspects of a morphogenesis of an antipsychotic cardiomyopathy". *Russian Journal of Cardiology* 95.3 (2012): 68-73.

7. Makhoul M., *et al*. "Dilated cardiomyopathy: an unusual complication of clozapine therapy". *Nature Clinical Practice Cardiovascular Medicine* 5.9 (2008): 566-570.

8. Tanner MA and Culling W. "Clozapine associated dilated cardiomyopathy". *Postgraduate Medical Journal* 79.933 (2003): 412-413.

9. De Berardis D., *et al*. "Update on the adverse effects of clozapine: focus on myocarditis". *Current Drug Safety* 7.1 (2012): 55-62.

10. Volkov VP. "New method of an organometry of heart". In: Paraklinicheskie discipliny: novye metody i diagnosticheskie vozmozhnosti: kollektivnaya monografiya/pod red. V.P. Volkova. Novosibirsk: SiBAK Publ (2014): 78-100.

Volume 2 Issue 6 August 2019