

To a Question of Structural Stereotype of Myocardial Response to Various Damaging Influences

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Abstract

By morphometric method myocardium of 50 dead persons was studied who had schizophrenia and had received various anti-psychotic drugs. A part of them died of acute non-cardiac pathology (control), of sudden cardiac death, another one died of sudden cardiac death, and the third part died of neuroleptic malignant syndrome.

The conducted studies of changes in myocardium developing in cases of SCD and NMS has discovered significant differences compared to control. However, there were no significant differences in myocardial structural changes in SCD and NMS.

These results objectively confirm the fact that the CMC's responds to any negative destructive influences with a very limited set of the stereotypical nonspecific structural changes.

Keywords: *Changes of Myocardium; Sudden Cardiac Death; Neuroleptic Malignant Syndrome; Morphometric Research*

Abbreviations

SCD: Sudden Cardiac Death; NMS: Neuroleptic Malignant Syndrome; AD: Antipsychotic (Neuroleptic) Drugs; APT: Antipsychotic Therapy; ZPD: Zone of Pericapillary Diffusion; KI: Kernogan Index; SPR: Stromal-Parenchymatous Ratio; RIE: Rate of Interstitial Edema; CMC's: Cardiomyocytes; SVHC: Specific Volumes of Hypertrophied CMC's; SVAC: Specific Volumes of Atrophied CMC's; SVDC: Specific Volume of Dystrophic CMC's.

Introduction

As is well-known, myocardium, as a kind of biological system, reacts to the impact of various damaging factors relatively limited set of standard cellular and tissue reactions [1-3].

This set of changes is standard and very limited - microcirculation disorders, extracellular matrix pathology, parenchymal lesions [4-7].

However, these data were obtained in the study of the state of the myocardium in various pathological conditions using the classical descriptive method.

At the same time, at the present stage of development of science purely descriptive approach to studying of pathological processes is insufficient for exact and, the main thing, objective characteristic of observed pathological changes.

Therefore, there is insistently necessary an application of morphometric methods of a research that answers the principles of the modern evidence-based medicine [8] and gives to the received results and the drawn conclusions objectivity and actual scientific value [9,10].

Based on the above, it is of some interest to study the response of the myocardium to various stress situations (for example, the onset SCD and/or the development of NMS) with the help of morphometric research method in order to clarify the level of stereotyping of structural changes.

Materials and Methods

As a model changes in the myocardium in such acute pathological conditions associated with the side cardiotoxic effects antipsychotic drugs as the onset of sudden cardiac death and the development of neuroleptic malignant syndrome were considered.

The myocardium of 50 dead patients with schizophrenia (men - 31, women - 19; age from 26 to 6 years) was studied by a morphometric method of research.

During their lives the patients had received various AD in quantities corresponding to the therapeutic standard; these medicines had often received in combination with each other. The duration of APT had ranged from six months to 20 years or more.

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

The material of study had divided into the three groups: I (control) - 20 patients without any heart pathology who died of acute non-cardiac causes; II - 13 patients in whom SCD was found; III - 17 lethal cases of NMS without concomitant heart diseases.

Myocardium slices from various departments of the left ventricle were filled in paraffin, cuts were painted by hematoxylin and eoziny. Respective objects were studied in 10 different fields of microscope, with necessary magnifications with the help of an ocular micrometer, the point count method was also used [9, 10]. Such parameters as ZPD, KI, SPR, and RIE were calculated. Karyometry and cytometry of CMC's were performed, SVHC, SVAC, and - by the method of polarization microscopy - SVDC were determined. The above-named parameters describe a condition of three structural components of myocardium: of microvasculature (ZPD and KI), intercellular matrix (SPR and RIE), and parenchyma (SVHC, SVAC, and SVDC).

The received results were statistically processed by the nonparametric Mann-Whitney U-test with significance level of 5%.

Analysis of data has been conducted in two directions. First, the changes of myocardium microstructure were traced in the cases of SCD and NMS in comparison with the group I (comparison of groups I-II and I-III). Second, the same study were conducted on patients with SCD and NMS (comparison of groups II-III).

Results

Groups	Microvasculature		Intercellular Matrix		Cardiomyocytes		
	ZPD	KI	SPR	RIE	SVHC	SVAC	SVDC
I APT	128.5	1.42	10.3	9.8	16.9	8.4	5.7
II SCD	176.1*	1.27*	9.1	34.8*	15.1	8.6	28.1*
III NMS	177.5*	1.48	7.8	33.4*	8.9	7.6	17.8*

*Table 1: Morphometric indicators of a myocardium.
Note: *: Statistically significant differences with group I.*

The changes which develop in the case of SCD (comparison of I-II groups) had an acute character. They serve as a reflection of the statistically significant ($p < 0.05$) shifts was compared to control of the corresponding quantitative parameters: decrease in KI, the seeming increase in ZPD, RIE and SVDC.

Development of NMS was accompanied by statistically significant deviations of such parameters as ZPD, RIE, SVDC (comparison of I-III groups). A reliable negative dynamics like in the cases of SCD was observed.

Discussion

Myocardium morphology of the patients who received AD are strongly affected both by SCD and NMS [4,7,10-12].

After sudden cardiac death the considerable acute disturbances of microcirculation in the form of paresis of myocardium microvessels are observed, the decrease of value of KI is an evidence of it. It causes the onset of tissue hypoxia with a subsequent increase of permeability of walls of capillary network and with a growth of interstitial edema (apparent increase of RIE). The edema promotes the disconnection of nutritional capillaries and CMC's (growth of ZPD) [13] what seriously impairs the trophism of the latter and is a cause of a quick development of intracellular dystrophic processes (increase of SVDC) [10,13].

The described changes are the material basis of electrical instability of myocardium and it is fraught with development of severe rhythm disturbances and SCD [11,12,14].

Myocardial injuries in course of NMS are a relatively acute process too and are characterized by serious disturbances of microcirculation, interstitial edema and apparent dystrophic degenerative changes of CMC's.

Thus, when SCD occurs and/or NMS manifests itself in mentally ill patients pathomorphological changes in myocardium are a standard and rather limited set of disturbances of all its structural components and these disturbances arise acutely. At the same time the reactivity of myocardium is on a quite high level.

Conclusion

The conducted morphometric studies of changes in myocardium developing in cases of SCD and NMS has discovered significant differences compared to control.

In these two sharply developing pathological conditions (SCD and NMS), structural myocardial damage is also characterized by acute microcirculation disorders, interstitial edema, and dystrophic-degenerative changes in CMC.

On the other hand, there were no significant differences in myocardial structural changes in SCD and NMS.

These results objectively confirm the fact that the CMC's responds to any negative destructive influences with a very limited set of the stereotypical nonspecific structural changes.

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