

Sudden Death in Antipsychotic Therapy of Patients with Schizophrenia

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Abstract

The analysis of cases of sudden death among 882 patients with schizophrenia died in the period from 1952 to 2010 inclusive was carried. The vast majority of them are caused by cardiac pathology, that is, there is a sudden cardiac death. In the suppressing majority it is sudden cardiac death owing to a chronic ischemic heart disease and a neuroleptic cardiomyopathy. The part of cases is caused by exchange infringements at schizophrenia (attrition or adiposity). The data obtained confirm the serious role of antipsychotic drugs, both classical, and atypical, in the genesis of sudden cardiac death of patients with schizophrenia.

Keywords: *Schizophrenia; Sudden Cardiac Death; Antipsychotics; Side Effects*

Introduction

Sudden death (SD) is a rapidly occurring, unexpected nonviolent death against the background of apparent health from a latent or atypical chronic or sudden acute disease [1]. Most often there is a sudden cardiac death (SCD), that is death from cardiac arrest, which is caused by severe arrhythmias due to electrical instability of the myocardium [1,2]. Electrocardiographic predictor of these disorders is a significant extension of the QT interval [1,3].

Among hospitalized mentally ill SCD observed in about 5% of all deaths in psychiatric hospitals [1,4]. It is believed that this is largely due to the side cardiotoxic effect of antipsychotics (AP) [1,5,6], in particular the prolongation of the QT interval [1,5,7].

At the same time, proven or latent cardiovascular pathology is another serious modifying factor in SCD associated with antipsychotic therapy (APT) [1,3].

The SCD in mental patients was first described in 1849, and the assumption of its connection with the reception of AP was expressed more than 50 years ago [1,6]. However, there are still very few the qualitative pathoanatomical studies of SCD among psychiatric inpatients [1,4,8]. The aim of this work is to fill the existing gap if possible.

Material and Methods

At my disposal were clinical and pathological data on 882 patients with schizophrenia who died in the Tver regional M. P. Litvinov's psychiatric hospital № 1 from 1952 to 2010 inclusive.

The collected sectional material is divided into three groups depending on the observation period. Group 1 includes the information on 66 schizophrenics who died before 1956, when chlorpromazine was first used in the hospital. Group 2 consisted of the material on 195 deaths over two periods, from 1963 to 1967 and from 1975 to 1980. At this time, the use of AP was very limited. Into the group 3 got

data Group 3 includes the material (621 cases) for 1988-2010, when APT became the main method of treatment of schizophrenia, which includes a wide range of AP of the first and second generations.

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 and Discussion

Of the 882 deaths of patients with schizophrenia in 109 (12.4%) recorded SD. Generalized gender and age data of deceased patients are shown in table 1.

Age	21 - 30	31 - 40	41 - 50	51 - 60	61 - 70	71 years and older	In all
Sex	years	years	years	years	years	years	
Man	2	8	18	23	15	-	66
Woman	-	2	11	11	15	4	43
Both sexes	2	10	29	34	30	4	109

Table 1: Gender-age composition of patients with schizophrenia who died suddenly in APT.

The presented figures show that 62.4% of the cases are over the age of 51 years. In general, the SD was more often registered among men (60.6%), the ratio with women is 1.5 : 1.

At the same time, 34.9% of the total studied contingent are men from 51 to 70 years, and 25.7% of men die suddenly younger (up to 50 years). The difference in this figures is statistically insignificant. In contrast, the incidence of SD among women under 50 years (11.9%) is statistically significantly lower than in older ones.

Thus, according to my data, the frequency of SD in schizophrenia is almost not too dependent on the sex and age of patients. To a much greater extent it is determined by other factors, among which the side effects of APT play an important role [1,6].

The analysis of the nosological profile of the material (Table 2) shows that the vast majority of cases of SD in schizophrenia (97%) are associated with cardiac pathology, that is, can be attributed to SCD. This corresponds to the literature concerning SCD of mentally healthy persons [9].

Groups Period	I	II	III	In all
Cause of death	1952-1955	1963-1967 1975-1980	1988-2010	
Cardiac pathology	-	6	76	82
1. Atheroscler. cardiosclerosis	-	2	31	33
2. Postinfarc. cardiosclerosis	-	-	16	16
3. NCMP	-	4	23	27
4. Other heart diseases	-	-	6	6
Cachexia (wasting of the heart)	-	-	17	17
Obesity (one of the heart)	-	-	7	7
Other pathology	-	1	2	3
In Total	-	7	102	109

Table 2: Nosological profile of patients with schizophrenia who died suddenly in APT.

At the same time, SCD was not registered in the 1st group of observations and was noted in a small number of cases in the 2nd group. On the contrary, group 3 is characterized by a sharp jump in the frequency of SCD. Indeed, the average annual frequency (the ratio of the absolute number of SCD cases to the number of years of observations) in group 2 is 0.5, and in group 3 this parameter increases 6.6 times, reaching 3.3. These data confirm the causal relationship between the increase in the frequency of SCD and the ongoing APT, which first appeared in the hospital by the early 60s and reached a peak of intensity by the end of the century.

According to my data, the main cardiac pathology, in which there is SCD during APT (45,0% of the whole sun), is a chronic coronary heart disease, manifested in two variants: more often (30.2%) in the form of atherosclerotic cardiosclerosis, less often (14.8%) - postinfarction one.

In second place in the frequency of SCD is neuroleptic cardiomyopathy (HCMP) - one of the most dangerous complications of APT, developing due to the side cardiotoxic action of AP [10-13].

So, 24.8% of 109 cases are associated with NCMP, and of 52 people who died, according to my observations, from NCMP for 23 years (1988 - 2010), SCD was found in 23 (44.2%), which is 32.9% in relation to all 70 patients with schizophrenia identified by me in combination with NCMP.

A peculiar group of patients with schizophrenia, who died suddenly, are patients suffering from severe obesity (6.4% of the case of the SD), this is the most externally noticeable component of the metabolic syndrome. This pathology was detected in the last group of observations, which is undoubtedly associated with the widespread use of atypical AP since the late 80-ies, one of the undesirable side effects of which is an increase in body weight [1,14].

Diametrically different from the above, another group of patients who died as a result of SCD. These are patients with a continuously progredient form of the disease, often with an outcome in a pronounced mental defect. Rapidly progressive schizophrenic process with the defeat of the higher vegetative centers of the hypothalamus leads to the development of cerebral cachexia in such patients. At the same time, metabolic processes in the body also capture the myocardium, leading to its dystrophy and atrophy [15]. These pathological changes of the heart serve as the basis for the occurrence of electrical instability of the heart muscle [16], which significantly increases the risk of SCD even at a relatively young age.

Indeed, in my material, this pathology was detected in patients with schizophrenia mainly under the age of 50 years - 13 of 17 patients (9 of them men). The fact that VSS in schizophrenia, complicated by cachexia, was established only in the last two decades (group 3 of observations), does not exclude that there is a layering of adverse effects of AP on the myocardium, which is already in a serious pathological condition due to cachexia.

Conclusion

Summarizing the above, it should be emphasized that 93.6 % of all cases of SCD in schizophrenia were registered in the last decades studied (group 3), when psychopharmacotherapy reached its peak. This is especially evident in the group of patients who died from diseases of the circulatory system. These data confirm the concept that SCD among those suffering from schizophrenia is largely due to the side effects of cardiotoxic AP, both classical and atypical.

It should be assumed that the appropriate awareness of practitioners in this matter will help to keep the number of cases of SCD patients with schizophrenia caused by APT at a minimum level.

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