ISSN: 2635 - 2826

Journal of Clinical & Biomedical Research

SCIENTIFIC Research and Community

Research Article

Open Access

Sudden Cardiac Death in Schizophrenia

Volkov V.P

Tver center of judicial examinations, Russia, 170008, Tver, A. Zavidov St., 24, of. 6

ABSTRACT

Under the special scheme materials of archive of the Tver regional psychiatric clinical hospital with 1952 for 2010 are studied and statistically analysed. Sudden death is ascertained at 12.4 % died in-patient of schizophrenia without dependence from their sex and age. In the suppressing majority it is sudden cardiac death owing to a chronic ischemic heart disease and an neuroleptic cardiomyopathy. The part of cases is caused by exchange infringements at schizophrenia (attrition or adiposity). The sudden cardiac death among suffering by schizophrenia is connected to some extent with side cardiotoxic effect of various antipsychotic drugs, both classical, and atypical.

***Corresponding author**

Volkov V.P, Tver center of judicial examinations, Russia, 170008, Tver, A. Zavidov St., 24, of. 6. Tel: +7-915-701-58-68; Email: patowolf@yandex.ru

Received: July 06, 2019; **Accepted:** Aug 05, 2019; **Published:** Aug 09, 2019

Keywords: Schizophrenia, Sudden Cardiac Death, Antipsychotics; Side Cardiotoxic Effect

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]. In this case, most often there is death from cardiac arrest, that is, the so-called sudden cardiac death (SCD), caused by severe arrhythmias due to electrical instability of the myocardium [1, 2]. The predictor of these disorders is a significant elongation of the electrical systole of the ventricles of the heart – the QT interval on the electrocardiogram [1].

Almost all antipsychotic drugs (AP) to some extent cause prolongation of QT interval [1, 3, 4]. It is no accident, therefore, that SCD in patients of psychiatric hospitals often observed during antipsychotic therapy (APT). The armed forces account for about 5% of all deaths in psychiatric hospitals [1, 5].

However, the most serious modifying factor in SCD associated with the use of antipsychotics is proven (or latent) cardiovascular disease [1, 6].

Although the sun in persons with mental disorders was first described in 1849, and the assumption of its connection with the reception of AP was expressed more than half a century ago [1, 7], to date, there are no qualitative publications on a series of pathological studies of psychiatric cases of SCD [1, 5, 8]. In order, if possible, to fill this gap, a study was conducted in the dynamics of some aspects of SCD in schizophrenia, and an attempt was made to link some of its manifestations with the side effect of APT.

Material and methods

The materials protectory and partially the medical history of the Tver regional M.P. Litvinov's psychiatric hospital № 1 from 1952 to 2010 inclusive were analyzed. A kind of "probe" method of material selection was applied. Given that treatment with chlorpromazine in the hospital began in 1956, assembled sectional material for a 1952–1955 years followed by another four studied periods: 1963–1967, 1975–1980, 1988–1997 and 1998–2010 years. While I studied period is fundamentally different from the others, in that at this time neuroleptic treatment of schizophrenia has not yet been performed. As a result, data on 882 deceased patients with schizophrenia were collected.

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

A general description of the material collected, relating to the number of observations, sex and age of the deceased for each time period, is presented in table 1.

Table 1: General characteristics of the studied material

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

In recent years, life expectancy in schizophrenia has increased significantly. Thus, in the IV and V periods of deceased patients with schizophrenia older than 51 years significantly more (66.5%) than in the I period (16.7%). In general, the number of deaths of patients with schizophrenia over 50 years of age is 1.5 times higher than in the younger. The ratio of men to women is 1.7 : 1.

SD was found in 109 cases, representing 12.4% of all deaths in patients with schizophrenia. Their sex and age are summarized in table 2.

Table 2: Age composition of patients with schizophrenia in SD

Time period	Number of autopsies in schizo-phrenia	Man	%	Woman	%	Up to 50 years	%	Over 51 years old	%
I	66	23	34,8	43	65,2	55	83,3	11	16,7
II	38	17	44,7	21	55,3	16	42,1	22	57,9
III	157	101	64,3	56	35,7	72	45,9	85	54,1
IV	353	235	66,6	118	33,4	109	30,9	244	69,1
V	268	182	67,9	86	32,1	99	36,4	169	63,1
IN TOTAL	882	558	63,3	324	36,7	351	39,8	531	60,2

The figures presented show that 62.4% of the cases are over the age of 51 years. At the same time, slightly more ⅓ (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 the figures is insignificant. In contrast, the incidence of SD among women under 50 years is statistically significantly lower than in older women, accounting for only 11.9%. In general, the SD was more often registered among men (60.6%), the ratio with women is 1. 5 : 1.

When comparing the data characterizing the age-sexual composition of patients with schizophrenia who died suddenly (table 2), with similar general indicators in this disease (table 1), a slightly different picture is revealed. Thus, the SD among men is 11.8% of all male deaths, while this figure among women reaches 13.3%. At the same time, the SD in patients with schizophrenia younger than 50 years was noted in 11.7%, and older than 51 years – in 12.8% of all deaths with schizophrenia in the appropriate age range. The differences in the above indicators by gender and age are statistically random.

Thus, according to our data, the frequency of SD in schizophrenia is practically independent of the sex and age of patients. It is mainly determined by other factors, among which the side effects of APT play an important role [1, 7].

The analysis of the nosological profile of the material (table 3) 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 the armed forces of mentally healthy persons [9].

Table 3: Nosological profile of SCD in schizophrenia

Period / Cause of death	I	II	III	IV	V	I all
CARDIAC PATHOLOGY	-	-	6	35	41	82
1. Atheroscler. cardiosclerosis	-	-	2	12	19	33
2. Postinfarc. cardiosclerosis	-	-	-	8	8	16
3. NCMP	-	-	4	11	12	27
4. Other heart diseases	-	-	-	4	2	6
Cachexia (wasting of the heart)	-	-	-	10	7	17
Obesity (one of the heart)	-	-	-	6	1	7
Other pathology	-	1	-	1	1	3
IN TOTAL	-	1	6	52	50	109

On our material, the incidence of cardiovascular diseases leading to the death of schizophrenia, sharply and statistically significantly increased in the 60s compared to the previous period (31.6% and 4.5%, respectively). Subsequently, until the end of the 90s, it remained stable at a high level, amounting to about ⅓ (29.4%–35.4%) of all causes of death in schizophrenia. However, in the last V period revealed a substantial (11.6%) and statistically significant increase in this indicator, approaching almost half of all deaths of patients with schizophrenia (47.0%). This "two-humped" nature of the increase in the frequency of cardiac pathology among the studied contingent of schizophrenia confirms its causal relationship with APT, which first appeared by the early 60s and reached its peak by the end of the century.

However, the observed increase in the life expectancy of the mentally ill cannot be completely discounted. Thus, we revealed a direct and very strong correlation (ρ=0.92) between the increase in the age of patients throughout the study time and the frequency of cardiac pathology leading to their death.

According to my data, in increasing the frequency of death in schizophrenia from diseases of the circulatory system observed during the previous almost half-century period and especially the last 13 studied years, the main role is played by various variants of chronic coronary heart disease. It is mostly atherosclerotic cardiosclerosis, and rarely postinfarction one. The difference in the V and IV periods (27.6% and 16.8% respectively), not to mention earlier (7.9%–4.5%), is statistically significant. In this case, a pronounced positive correlation (ρ=0,64) between the increase in the age of patients and the frequency of chronic coronary heart disease was revealed. However, only 41.2% of the changes are due to shifts in the age composition of schizophrenia sufferers, and the predominant part of other factors. It is fair to assume that such pathogenic agents may be AP, having to some extent the effect of cardiotoxicity [3].

In particular, AP-induced myocardial ischemia leads to partial depolarization of cardiomyocytes and changes in the transmembrane potential of different severity in different parts of the myocardium [10], which contributes to the formation of its electrical instability. Increasing over time, age-related coronary atherosclerosis further exacerbates the picture [10]. Hence the increased risk of SCD in this kind of patients.

As shown by the study (table 3), 49 patients (45.0% of all aircraft) died suddenly in the presence of established coronary heart disease. Thus, the share of diffuse atherosclerotic cardiosclerosis accounts for 30.2%, and the share of focal postinfarction one – 14.8% of cases. SCD in all these observations is most likely due to myocardial electrical instability and is associated with various arrhythmias and conduction disturbance [2, 9].

A special place in the genesis of SCD in schizophrenia is neuroleptic cardiomyopathy (NCMP) [11], which is a form of dilated

cardiomyopathy (DCMP) [12]. Although this pathology was singled out as an independent nosological unit only in 1965 [3, 13], retrospective analysis of autopsy reports and case histories revealed this disease in previous years, although it did not sound in the pathological diagnosis. At the same time, it is noteworthy that in the first period of observations (1952–1955), DCMP was not detected even once. Starting from the 60s (II period) and in the future, this disease was constantly encountered with almost the same frequency (5.3%–6.5% of autopsies of deceased patients with schizophrenia). If we consider only cases where DCMP was also present as a comorbidity, the prevalence of schizophrenia will increase significantly. So, for 23 years (1988–2010) DCMP discovered at autopsy died from various causes in patients with schizophrenia in 70 cases, accounting for 1.9% of all autopsies (3635), produced in a psychiatric prosecture for a specified period. When comparing the last indicator (1.9%) with the literature data concerning the frequency of DCMP in mentally healthy individuals, a substantial and statistically significant prevalence of it is revealed. In addition, according to my sectional data, in schizophrenia, the number suffering from DCMP, significantly higher than the gross sectional material on the psychiatric prosecture as a whole (11.3% and 2.5% respectively).

This form of DKMP, which are the result of side cardiotoxic effects of AP [3], should be considered as NCMP. In this regard, it becomes clear the absence of this disease in the I ("pre-neuroleptic") observation period.
Patients with idiopathic DKMP are considered to be at high risk of SCD [13]. This situation is true for NCMP [11]. Thus, 24.8% of 109 cases are associated with NCMP, and of 52 people who died from NCMP in 23 years (IV and V periods), SCD was found in 23 (44.2%), which is 32.9% in relation to all 70 patients with schizophrenia in combination with NCMP.

A peculiar group of patients with schizophrenia who died as a result of SCD, are patients suffering from severe obesity (6.4% of cases of SCD), this is the most externally noticeable component of the metabolic syndrome. This pathology was detected in the IV and V periods, which is undoubtedly associated with the widespread use of atypical AP since the late 80s, one of the undesirable side effects of which is an increase in body weight [1, 14].

The accumulation of practical experience in the use of new psychotropic drugs, the introduction of methods of correction of their undesirable dysmetabolic side effects allowed in the future to practically exclude this pathology from the list of causes of SCD in schizophrenia.

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. A 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 [13]. These pathological changes of the heart serve as the basis for the occurrence of myocardial electrical instability [10], which significantly increases the risk of SCD even at a relatively young age.

Indeed, on our material, this pathology was revealed in patients with schizophrenia mainly under the age of 50 years – 13 of 17 patients (9 of them men). The fact that the SCD in schizophrenia, complicated by cachexia, stated only in the last two decades (IV and V periods), does not yet find a convincing justification. It is possible that there is a layering of the 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 BCC in schizophrenia were registered in the last decades (IV and V periods), 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 cardiotoxic effects of 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 of patients with schizophrenia caused by APT at a minimum level.

References

1. Abdelmawla N, Mitchell AJ (2006) Sudden cardiac death and antipsychotics. Part 1: Risk factors and mechanisms. Adv Psychiatr Treat. 12: 1: 35-44.
2. Engdahl J, Holmberg M, Karlson BW et al. (2002) The epidemiology of out-of-hospital "sudden" cardiac arrest. Resuscitation 52: 3: 235-245.
3. Volkov VP (2018) Cardiotoxicity of antipsychotic drugs. Tver: Triada Publ 622.
4. Reilly JG, Ayis SA, Ferrier IN et al. (2000) QTc-interval abnormalities and psychotropic drug therapy in psychiatric patients. Lancet 355: 1048-1052.
5. Reilly JG, Ayis SA, Ferrier IN et al. (2002) Thioridazine and sudden unexplained death in psychiatric in-patients. Br J Psychiatre 180: 515-522.
6. Montanez A, Ruskin JN, Hebert PR et al. (2004) Prolonged QTc interval and risks of total and cardiovascular mortality and sudden death in the general population: a review and qualitative overview of the prospective cohort studies. Arch Int Med ; 164: 9: 943-948.
7. Titier K, Girodet PO, Verdoux H et al. (2005) Atypical antipsychotics: from potassium channels to totsade de pointes and sudden death. Drug Safety 28: 1: 35-51.
8. Maron B J (2003) Sudden death in young athletes. N. Engl. J. Med. 349: 11 1064-1075.
9. Volkov VP (2008) On the role of phenothiazine neuroleptics in the development of dilated cardiomyopathy syndrome. Verkhnevolzhsky Med J 4: 13-17.
10. Constant J (2004) Clinical diagnosis of diseases of the heart/ translated from English. Moscow: Binom-Press Publ: 448.
11. Volkov VP (2015) Morphological basis of sudden cardiac death in patients with schizophrenia. In: Volkov VP (ed.). Morphological basis of pathology: monograph. Novosibirsk: SibAK Publ 30-57.
12. Tereshchenko SN, Jayani Nah (2001) Dilated cardiomyopathy today. Consilium medicum 3: 2: 58-60.
13. Kushakovsky MS (1997) Chronic congestive heart failure. Idiopathic cardiomyopathy. SPb. Folio Publ: 320.
14. Malin DI (2000) Side effect of psychotropic drugs. Moscow: University book Publ 270.