Review

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Schizophrenia and cerebrovascular disease. A description of a series and bibliographic reivew

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Introduction. The state of health of patients with schizophrenia is a field of growing interest that has probably not received sufficient attention in the past. It is currently held that physical health should form a part of the overall therapeutic strategy in these patients since reference is made to certain treatable conditions that may affect the final prognosis. One example is cardiovascular disease and its associated reduction in life expectancy.

Development. We carried out a retrospective study in which we described the consultations held between the psychiatric acute care service and the neurology service during a one-year period. We have analyzed the frequency of cerebrovascular complications in our sample and have included a summary of the most relevant published data regarding cerebrovascular disease (CVD) in patients with schizophrenia.

Conclusions. We have described the high frequency of CVD in both our series of patients with severe mental illness receiving attention as well as in those from the neurology service (25.7%), and in the subgroup presenting psychotic disorders (25%). There are several studies focusing on the possible causes of increased cardiovascular morbidity and mortality, especially in schizophrenia. However, in regards to CVD specifically, little has been found in the literature and that found shows contradictory results. Given the direct relation between cardiovascular disease and CVD, a consistent relation between CVD and schizophrenia is to be expected.

Key words: Cardiovascular disease, Cerebrovascular disease, Schizophrenia, Antipsychotic drugs, Stroke, Psychotic disorders

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Esquizofrenia y enfermedad cerebrovascular. Descripción de una serie y revisión bibliográfica

Introducción. El estado de salud de los pacientes con esquizofrenia es un campo de creciente interés que probablemente no ha recibido la atención necesaria en el pasado. Actualmente se considera que la salud física debería formar parte de la estrategia terapéutica global en estos pacientes ya que hace referencia a algunas patologías tratables y que pueden modificar el pronóstico final. Un ejemplo es la enfermedad cardiovascular y la reducción en la esperanza de vida asociada a ella.

Desarrollo. Realizamos un estudio retrospectivo en el que describimos las interconsultas realizadas desde la unidad de agudos de psiquiatría al servicio de neurología durante un año y analizamos la frecuencia de complicaciones cerebrovasculares en nuestra muestra. Exponemos asimismo, un resumen de los datos más relevantes publicados acerca de la enfermedad cerebrovascular (ECV) en pacientes con esquizofrenia.

Conclusiones. Describimos una alta frecuencia de ECV tanto en el global de nuestra serie de pacientes con enfermedad mental severa a los que se realizó una interconsulta a Neurología (25,7%) como en el subgrupo que presenta Trastornos psicóticos (25%). Hay diferentes estudios centrados en las posibles causas de la elevada morbimortalidad cardiovascular, especialmente en esquizofrenia, pero respecto a la ECV en concreto hay poca literatura y con resultados contradictorios. Dada la relación directa entre enfermedad cardiovascular y ECV, se puede esperar una relación consistente entre ésta y la esquizofrenia.

Palabras clave: Enfermedad cardiovascular, Enfermedad cerebrovascular, Esquizofrenia, Fármacos antipsicóticos, Ictus, Trastornos psicóticos

INTRODUCTION

It has been estimated that more than one third of the European population develop some type of mental disorder. Together with neurological diseases, these are responsible for more than one fourth of the cases of incapacity in present day Europe.[1] In recent years, psychiatry has been acquiring greater awareness of the physical problems of their patients as these have a repercussion on the final well-being of the patient, on treatment adherence, on self-esteem and finally on life expectancy.[2,3] In schizophrenia, the somatic pathology that has been described is extensive: metabolic syndrome, hyperprolactinemia, sexual dysfunction, cardiovascular disease, smoking, consumption of abuse drugs, sexual transmission diseases and physical inactivity. The consequences of a sometimes inadequate style of life with decreased self-care, possible institutionalization and the potential side effects of the drugs are added to all of this.[4,5]

Schizophrenia is related with a two to three times risk of premature death[6] and an up to 3 times greater risk of unexpected sudden death.[7] It is associated to 20% reduction in the levels of life expectancy regarding the general population.[7,8] This means a loss of 20 years of life for men and 15 for women.[9] As life expectancy has been increasing in the population, the difference between it and life expectancy in patients with mental diseases has been increasing.[10] The intervention strategies applied up to date do not seem to be sufficiently effective. At present, these strategies have only been able to slightly improve life expectancy in patients with mental diseases, even when applied in Nordic countries with very good health care models.[11]

Even though patients with schizophrenia have 10 to 20 times more likelihood of committing suicide (10% *vs* 1%),[8,12] this excess of premature death is only partially caused by suicide (28%) and accidents (12%).[3] If the causes of natural death account for 97% of total deaths in the general population, in schizophrenia patients this percentage is reduced to only 75-80%.[9,14] Within these, cardiovascular disease is the most frequent cause of premature death,[12] followed by neoplasms, respiratory and infectious diseases.[9,10,15]

It is currently known that the morbidity-mortality due to cardiovascular disease in patients with schizophrenia is increased in both sexes, this increase being greater in men than in women.[6,16,17] It is also known that while the proportion of deaths due to coronary disease is 75% in patients with schizophrenia, this proportion is 50% in the general population (RR 1.5).[8,12] One study[18] calculates the *standardized mortality rate* (or number of deaths observed divided by number of deaths expected) for each one of the causes of death in patients with schizophrenia. This study observed that while deaths due to neoplasms, circulatory or respiratory problems were maintained in the same proportions as in the general population, the mortality rates from cardiovascular disease (CVD), diabetes mellitus (DM) and epilepsy were very elevated.

As a result of that previously stated, cardiovascular disease, CVD and factors that make schizophrenic patients especially vulnerable to develop them are of focus of growing interest in medicine.[19-22]

PATIENTS AND METHODS

Case Series

We have performed a retrospective analysis of the specialty consultations made by the acute psychiatric unit to the neurological department of the Parc Sanitari Sant Joan de Déu during a one-year period including June 2006 to June 2007.

Sources

The registry and computerized clinical history were used and variables were collected on the social-demographic characteristics, medical and pharmacological history and admission in which the neurological evaluation was performed.

The CVD variables were recorded after both the clinical and radiological data were obtained. During a first analysis, coding was performed in the groups as 0-Absence of CVD; 1-Transient ischemic attack; 2- Clinically established stroke; 3- Leukoaraiosis in the imaging tests and clinically silent; 4- Lacunar lesions in the imaging tests that are clinically silent and 5-Other ischemic lesions observed in the imaging tests that are clinically silent. After, they were codified again as: Absence of CVD (group 0), symptomatic CVD (groups 1 and 2) that are clinically silent CVD (groups 3, 4 and 5). Those cases in which the CVD was not considered to be responsible for any of the symptoms present in the patients, whether they were or were not the reason for specialty consultation, were defined as "silent CVD." Cognitive deterioration, also that of vascular type, were included within the symptoms.

The resulting data were analyzed with IBM SPSS Statistics 20.0 using the Chi Square test for categorical variables and the T-test for continuous variables after verifying that they fulfilled the application conditions.

Bibliographic review. Sources

We performed a bibliographic search from January 1995 to December 2011 with different combinations of the

terms "Psychotic Disorders," "Schizophrenia," "Antipsychotic Agents," "Cerebrovascular Disorders," "Stroke" and "Cardiovascular Diseases" in the PubMed platform. Preference was given to the most recent text, clinical trials and texts that used the Formula Framingham Score (FRS)[23] to measure cardiovascular risk since this measurement is the one used most in somatic conditions and includes the different cardiovascular risk factors (CVRF) in a final single value. Herein, we present the most relevant and recent data found in the publications resulting from the search.

RESULTS

Case series. Description of the series

In the period studied, 1149 admissions in the psychiatric acute unit were recorded. Specialty consultation with neurology for 70 patients was carried out. Criteria used to request this evaluation were: presence of known neurological disease with implications in the psychiatric condition, suspicion of undiagnosed neurological disease, no control or debut of neurological symptoms secondary to the treatment and alterations in the neuroimaging tests. The most frequent reason for specialty consultation was suspicion of cognitive deterioration (28, 40%), followed by gait disorders (8, 11.4%), evaluation of alterations in complementary tests (5, 7.1%), the sum of extrapyramidal syndrome with cognitive deterioration (4, 5.7%), headache (4, 5.7%) and tremors (3, 4.3%). Other reasons accounted for less than 4 cases each one. On the part of the neurology service, the following were requested: a total of 14 tomographies, 11 resonances, 1 brain SPECT, 2 electroencephalograms, 4 electromyogram, 3 carotid Dopplers and 2 lumbar punctures were performed (Table 1).

The main psychiatric condition most frequently found in patients requiring neurological evaluation was major depressive or recurrent depressive disorder (15, 21.4%) followed by bipolar disorder (7, 10%) and schizophrenia (6, 8.6%). Other frequent diagnoses were schizoaffective disorder, psychotic disorder secondary to toxic agents and/or cranioencephalic trauma (CET) and chronic delusional disorder (4, 5.7% each one).

We found 18 cases of CVD, which account for a 25.7% prevalence of all the specialty consultations made. Only two out of the CVD cases diagnosed showed symptoms. The remaining diagnoses resulted from a casual finding when imaging tests were requested for other reasons. White matter diffuse lesions (leukoaraiosis) were diagnosed in 8, lacunar lesions in 6 and other types of asymptomatic ischemic lesions in 2 patients.

Regarding CVD in patients with psychotic disorders, some of the following diagnoses were found in our sample of 20 patients: Schizophrenia, Schizoaffective disorder, Chronic delusional disorder, Acute/brief psychotic disorder or not otherwise specified psychotic disorder. Mean age was 58.4 years (range 36-79). Some type of silent CVD was diagnosed in 5 (25%) off these 20 patients, with a mean age of 65 years (range 41-75). None had symptomatic CVD. We excluded patients in whom the psychotic symptoms were considered secondary to toxic agents, cognitive deterioration or previous CETs from this group (Table 2).

Case series. Comparison of the groups with and without CVD

Except for age, which was greater in the CVD group of patients (p=0.003), we did not find a statistically significant association between the variables described in table 1 and the presence or not of CVD.

It stands out that the frequency of HBP was practically the same in both groups and that the frequency of DM, dislipidemia (DLP), active smoking and active or past consumption of second generation antipsychotics (SGA) was lower in the CVD group.

Cardiovascular risk factors

The frequency of CVRF in the general population is considered to be 25-40% for HBP, 4-8% for DM, 20-40% for smoking and 6-40% for DLP.[24] In patients with schizophrenia, significantly higher rates have been described for all the CVRFs: HBP (27%), DM (13%), smoking (68%), physical inactivity and DLP.[25-27] Some series have been found in which up to 70% were smokers and 70% more were obese or overweight. Style of life, diet, toxic agents and diseases associated to these also play an important role and contribute to the fact that patients with schizophrenia have up to three times more risk of developing the so-called metabolic syndrome.[19,28,29]

While several texts and reviews have been published on the predisposition of patients with schizophrenia to have cardiometabolic diseases in recent years,[30] there are few studies that show the possibility of performing effective interventions on them. Furthermore, none of them are long-term, perspective studies that show the impact of these on mortality.[25]

Global cardiovascular risk is commonly measured with the Framingham formula that takes into consideration age, systolic arterial pressure levels, HDL cholesterol and total cholesterol, gender, taking of antihypertensive drugs in the presence or not of DM and smoking, obtaining a percentage (Framingham Risk Score, FRS). The FRS interprets what the risk is of presenting a cardiovascular event at 10 years. A previous study[31]

Table 1 Results of the case series. Distribution of the variables studied

Variable	Total specialty consultations	Group without CVD	Group with CVD
Number of patients	70	52	18
Age (years)	Mean 62.0 SD=15.0	Mean 59.1 SD=14.8	Mean 70.4 SD=12.6
Most frequent principal diagnosis[a]	MDD/R 15/70 (21.4%) SD=41.5 CI:12.5%-32.8%	MDD/R 8/52 (15.4%) SD=36.7 CI:8.0%-27.5%	MDD/R 7/18 (38.9%) SD=50.1 CI:20.3%-61.4%
Duration of hospitalization (days)	Mean 49.8 SD=34.4	Mean 51.3 SD=37.7	Mean 45.5 SD=21.5
Most frequent reasons for specialty consultation[a]	Suspicion of cognitive deterioration 28/70 (40.0%) SD=49.6 CI:28.5%-52.4%	Suspicion of cognitive deterioration 20/52 (38.5%) SD=49.12 CI:26.4%-52.1%	Suspicion of cognitive deterioration 8/18 (44.4%) SD=51.4 CI:24.5%-66.2%
No. of neurological visits	Mean 2.9 SD=2.7	Mean 2.7 SD=2.5	Mean 3.7 SD=3.2
Males[a]	27/70 (38.6%) SD=49.0 CI:27.2%-50.1%	18/52 (34.6%) SD=48.0 CI:23.2%-48.2%	9/18 (50%) SD=51.4 CI:29.0%-70.9%
SGA consumption[a]	52/70 (74.3%) SD=44.0 CI:62.9%-83.08%	40/52 (76.9%) SD=42.5 CI:63.9%-86.2%	12/18 (66.7%) SD=48.5 CI:43.7%-83.7%
Arterial hypertension[a]	24/70 (34.3%) SD=47.9 CI:23.3%-46.5%	17/52 (32.7%) SD=37.36 CI:21.5%-47.1%	7/18 (38.9%) SD=50.7 CI:20.3%-61.3%
Diabetes mellitus[a]	14/70 (20%) SD=40.3 CI:11.4%-31.2%	11/52 (21.2%) SD=41.23 CI:12.2%-34.0%	3/18 (16.7%) SD=38.3 CI:5.8%-39.2%
Dislipidemia[a]	27/70 (38.6%) SD=49.1 CI:27.2%-50.1%	23/52 (44.2%) SD=50.15 CI:31.5%-57.6%	4/18 (22.2%) SD=43.7 CI:9.0%-45.2%
Active smoker[a]	14/70 (20%) SD=41.2 CI:11.4%-31.2%	12/52 (23.1%) SD=43.7 CI:13.7%-36.2%	2/18 (11.1%) SD=32.3 CI:3.1%-32.8%
BMI (kg/m^2)[b]	Mean 25.7 SD=7.1 [25][b]	Mean 24.9 SD=7.6 [19][b]	Mean 28.4 SD= 4.7 [6][b]
FRS[b]	10.7% SD=8.8 [16][b]	10.9% SD=9.4 [14][b]	9.0% SD=1.6 [2][b]

[a] Fraction: absolute number of cases divided by absolute number of the group; percentages between parenthesis: mean of the total of the group (column)
[b] Between brackets - number of patients for whom sufficient data could be obtained when there were losses.
SD: Standard deviation. CI: 95% Confidence Interval 95%. MDD/R: Major Depression disorder/or recurrent. BMI: Body mass index. FRS: Framingham risk score.

showed that patients with schizophrenia had significantly elevated levels of this index, this occurring both in men (9.4% *vs* 7.0%) and in women (6.3% *vs* 4.2%), when they were compared with the controls paired by age, race, and gender and after controlling the body mass index.

Some difficulties are present in the management and diagnosis of somatic pathology in schizophrenic patients. It may be difficult to differentiate between the appearance of somatic symptoms or side effects of the antipsychotics.[21] The patients have physical complaints in more advanced stages of their somatic diseases and may have problems to recognize and cope with their symptoms.[32] Furthermore, primary care physicians in general do not have clinical guidelines adapted to the management of somatic comorbidity in psychiatric patients. When a study is made on how the general action guidelines are applied in these patients, it is observed that patients with psychotic backgrounds do not receive the same treatments aimed at the control of CVRF and at the treatment of the risk situations recommended in the medical guidelines even though they have a greater mortality than in the general population. Data exist on the lower use of statins (OR 0.51), beta blockers (OR 0.82) and on the lower indication of cardiac bypass (OR 0.35).[33] It also seems that fewer brain arteriographies are performed and that anticoagulation treatment is initiated less than in the general population.[16,33] One example is a review from 2006 on visits to the emergency service in diabetic patients that was carried out for 4.5 years. This review observed that patients with psychiatric comorbidities had less possibilities of being hospitalized (OR 0.65) than those who did not have it.[11] The fact that these patients do not receive the optimum treatment may be related with the excess of premature

death. Therefore, it should be studied and controlled,[34] evaluating what the reasons are and up to what point they are avoidable.

In order to minimize these risks and differences, a series of guidelines and recommendations aimed at controlling cardiovascular risk in patients with schizophrenia were developed between the years 2000 and 2012. By order of frequency, the measurements recommended are fasting glucose, body mass index, triglycerides, waist diameter, total cholesterol, HDL, LDL, blood pressure and monitoring the appearance of symptoms of diabetes. Furthermore, physical activity, diet, psychoeducation of the patient and of the family, treatment of the alterations of lipids, glucose, smoking abstention and sending the patient to the medical specialist of reference in the case of needing treatment are recommended.[19]

Cerebrovascular disease

Little data has been published on the prevalence of CVD in patients with schizophrenia.

In the 2010 meeting of the Spanish Society of Neurology, two posters were presented with a series of 58 and 42 cases of specialty consultations made from psychiatry to neurology in which only one case diagnosed of CVD was described. However, these series only reported the principal diagnosis and did not mention the already present or nonrelevant comorbidity in the evaluation of this moment.[35,36] In an extensive bibliographic review of 2006, the authors specifically stated that patients with schizophrenia did not have higher rates of stroke than the general population.[37] In another bibliographic review up to the year 2006 on the physical health of schizophrenic patients, it was described that the prevalence of stroke in them was the same as in the general population, except in the subgroup of schizophrenics who were hospitalized where it appears to be lower.[37,38] However, some texts have described an increased risk of CVD in patients with schizophrenia and certain characteristics in the evolution of CVD in these patients.[38,39] In a study performed in 2008, the authors observed how in the 5 years after having required admission for acute exacerbation of their baseline psychiatric disease, schizophrenic patients younger than 45 years had 2 times more likelihood of stroke compared with controls without schizophrenia who had been hospitalized for an appendicetomy.[40] This risk was much greater in women than in men.[40] Another study observed that after having a stroke, patients with schizophrenia had less mortality in the first 90 days than patients without schizophrenia adjusted for demographic characteristics and comorbidity. [39]

In the patients with schizophrenia or paranoid psychosis of late onset with clinical characteristics different from those of early-onset,[41] up to 3 times more white matter hyperintensities have been described. These could have an ischemic origin in the magnetic resonance,[41] above all in the periventricular areas[42] and in the thalamus.[42,43]

Table 2 Cases of Silent Cerebrovascular Disease (CVD) in the subgroup of patients with Psychotic Disorders

Psychotic Disorder	Number of patients	Cases of silent CVD
Schizophrenia	6	2
Schizoaffective D.	4	0
Chronic delusional D.	4	1
Acute/brief psychotic D.	3	1
Unspecified psychotic D.	3	1
TOTAL	**20**	**5**

Cases in which the psychotic symptoms were considered secondary to toxic agents, cognitive deterioration or previous CETs were excluded.

It is difficult to know up to what degree the frequency of silent CVD in patients with psychotic disorders observed in our sample (5/20, 25%) was increased above that expected in their age group and comorbidity since the data on the frequency of silent CVD in the general population are unequal. It seems that their global prevalence in the general population is between 5.8% and 17.7%,[44,45] which is considered to be up to 5 times more frequent than the symptomatic CVD. We have found literature that reports prevalences going from 0.7% in a healthy population of 20-60 years[46] forming a part of the control group and some studies, from 8% in a healthy population of 60-64 years,[47] 8.1% in patients with migraines with aura,[46] up to 35% in an age group of 85-90.[47] It does seem to be clear that age and high blood pressure (HBP) are the most important risk factors to develop it[48] and that it should be considered as an independent risk factor from the remaining CVRF both for ischemic stroke and hemorrhagic stroke. [24,45]

Antipsychotic drugs

Second generation antipsychotics (SGA) are the treatment of first choice in schizophrenia. Compared with those of the first generation, they are better tolerated, cause fewer extrapyramidal effects and produce more metabolic and cardiovascular adverse effects.[49-51] There is much evidence, both related with cardiovascular side effects and metabolic syndrome,[3,17,52] that these effects are not the same in all the SGA. Therefore, individualized use is necessary for each one of them.[50,52-54]

In order to identify both efficacy and side effects of the antipsychotics, the Clinical Trial CATIE (Clinical Antipsychotic Trials of Intervention Effectiveness) was performed between

2001 and 2004 in the United States. This was an extensive randomized and controlled multicenter study on patients with schizophrenia receiving antipsychotic treatment.[55,56]

A review was published in 2007 comparing the rates of obesity and DM among patients with schizophrenia versus non-schizophrenic controls within the population of hospitalized patients. Between 1988 and 2002, a period during which the use of SGAs was initiated and spread, an increase of both CVRFs was described.[57]

The choice of neuroleptics to be used in each patient should be based on their antipsychotic efficacy. However, if two medications are similar in efficacy, their possible adverse effects and their reversibility should be taken into account.[58-60] The reason for this, for example, is that when the medication is switched from risperidone (RSP) to olanzapine (OLZ), cardiovascular risk may increase up to 33%.[60,61] In a 2007 Spanish clinical trial, it was observed that if the initial atypical antipsychotic was switched to ZPR, it was possible to reduce weight, glycemia, total cholesterol and triglycerides after 6 months without loss of clinical efficacy. [62]

It is known that race and gender play a moderate role in metabolic side effects of antipsychotics.[63] Although males are more vulnerable globally to CVRF, cardiovascular death is disproportionally increased in the women who take them.[54,64] Furthermore, it is known that there is significant individual susceptibility and some young patients with schizophrenia who have never received antipsychotic treatment have been identified as forming a population that is especially vulnerable to weight gain and to suffering changes in glucose metabolism with the SGAs in their first psychotic episode.[20]

Globally, it seems clear that the SGAs that have the most metabolic effect are clozapine (CLZ) and OLZ (risk of metabolic syndrome 43.9%-34.8%)[65,66] followed by RSP and quetiapine (QTP). Those having the least metabolic side effects are ziprasidone (ZPR) (risk of metabolic syndrome 37.7%-29.9%) and aripiprazole (ARIP). There are contradictory results on the effect of RSP, QTP, ZPR and ARIP on glycemias and lipids.[67-70]

More specifically, the following have been described:

- Weight gain. Above all with CLZ and OLZ and less with ZPR, ARIP, RSP and QTP.[65,71] The differences between SGA are reduced over time.[68] The increase seems to be more important at the onset of the treatment and is maintained up to 8 years after it. Weight loss has been described when switching from CLZ or OLZ to ZPR or ARIP that may be due to having stopped taking the former[72] more than due to the real effect of weight loss with the latter.
- Changes of the FRS. In the CATIE study, an increase with OLZ (+0.5%) and QTP (+0.3%) and reduction with perphenazine (-0.5%), RSP (-0.6%) and ZPR (-0.6%) were observed. Another study[15] described a statistically significant increase of 7.69% of the FRS with OLZ and decrease of 11.6% with ZPR in men. The sign of these differences in women was maintained, but not significantly.
- Hyperglycemia. An incidence of up to 10.1% of DM was described 6 weeks after taking antipsychotics that was not always weight-increase dependent.[62,66,69,73] With those of the first generation, there is an increased risk of type 2 DM in spite of its low effect on abdominal obesity and dislipidemia.[67] In the CATIE study, an increase of glucose metabolism was described with CLZ, QTP and OLZ.[63] It is estimated that the risk of developing DM when taking a first generation antipsychotic versus a SGA varies from 46 to 53 new cases/1000 patients.[74]
- Hypertriglyceridemia. An increase of triglycerides has been described with OLZ and QTP and a reduction with RSP and perphenazine. Both lack of effect and reduction of its levels have been described with ZPR.[75,76]
- CVD. In a review of more than 10,000 elderly patients during 7 years who were under treatment with SGA, greater risk of CVD was not found when comparing them with those who took first generation antipsychotics. However, it was described that chronic use (more than 30 days) of both first and second generation antipsychotics was associated to a greater risk of cerebrovascular adverse effects.[76]

DISCUSSION

In recent years and in response to the growing interest regarding the physical health of patients with mental diseases, different studies have sought to identify the causes of the elevated cardiovascular morbidity-mortality in schizophrenia. These causes have been identified as poor control of CVRF, the effects of certain antipsychotic drugs, style of life, possible presence of unhealthy habits and a certain genetic predisposition. Added to all of these are the difficulties that the physicians have found in the clinical practice to apply the same clinical guidelines for somatic pathology in psychiatric patients as in the general population, worsened by the lack of knowledge by the physicians of this increased risk in said population.[9] The final consequence is that patients with schizophrenia sometimes do not receive the optimum treatment in spite of being a population at risk.[16,33,34]

Taking typical antipsychotics should be studied as an independent risk factor for the development of cardiovascular disease, above all in certain patients who are especially vulnerable and with some drugs.[62] Among the different SGA, they differ in their effects. Furthermore, the long-term

consequences that these differences have on morbidity -mortality have not been well-studied.[34]

In our case series, we observed a 25.7% (18/70) global prevalence of CVD in all the sample of patients with severe mental disease. This prevalence was 25% (5/20) in this subgroup of patients with psychotic disorder. These values greatly exceed those described in the general population, which is 10.7% for silent CVD[45] and much less for the symptomatic one.

All the data herein presented should be interpreted taking into account the following limitations.

Our sample comes from patients hospitalized in the Psychiatric Acute Unit. It is likely that this is not representative of the general population of patients with schizophrenia but only of the subgroup of more serious patients. In fact, as has been commented in this text, a greater risk of suffering a cerebrovascular event in relation with exacerbations of psychotic disorders has been sporadically described.[40]

The real prevalence of silent CVD in the general population (with and without psychiatric condition) is unknown and has probably been underestimated. The reason is that silent CVD can only be diagnosed by imaging tests that are usually justified due to the appearance of neurological and/or psychiatric symptoms. Our sample, therefore, is made up of patients in whom neurological evaluation was requested. It does not include all the patients who were hospitalized. This is a limitation for extrapolating the results to all of the population of patients with schizophrenia. It is also a common problem when reviewing the literature and the evidence that we have on silent CVD.

Even so, given that CVD is directly related with cardiovascular disease and metabolic syndrome, in our opinion, finding a greater frequency of CVD in patients with schizophrenia is to be expected. This relationship may only be due to an increase of global cardiovascular risk or may have an added risk because both conditions present common, potential physiopathological grounds such as early cerebral aging. These are interesting aspects to keep in mind in future studies. We consider that knowing if the patients with schizophrenia have a greater risk of CVD than the general population of their same social demographic characteristics is the first step needed to develop effective preventive and therapeutic strategies.

CONFLICT OF INTERESTS

It is declared that there are no conflicts of interests.

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