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Differences in Treatment of Schizoaffective Disorder and Schizophrenia in Real Clinical Practice in Slovakia

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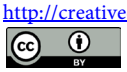

Abstract

Background: Schizoaffective Disorder (SAD), similarly to schizophrenia, is a potentially chronic mental disorder that negatively affects the functioning of a patient. Various issues in everyday clinical practice often arise from its diagnostic and therapeutic uncertainty. To date, there is a lack of a well-defined therapeutic algorithm used to treat the simultaneously manifesting schizophrenic and affective components. The aim of this study was to compare the therapeutic approaches in schizophrenia and schizoaffective disorders to identify the need of different treatment strategy for these diseases. Methods: In a retrospective study, we evaluated the therapeutic algorithms used in all patients with SAD (n = 99) hospitalized at the Department of Psychiatry, Comenius University in Bratislava, Faculty of Medicine and University Hospital Bratislava throughout the year 2010 and compared them with the therapeutic procedures used in all schizophrenia patients hospitalized in the same year (n = 120). Results: We found similarities between the groups of patients with schizophrenia and SAD in the number, type and length of hospitalizations and general patient management. Differences were identified in terms of the spectrum of used pharmacotherapy. For the treatment of both mental disorders, atypical antipsychotics were used the most. In the treatment of schizophrenia, we found the most frequent use of combined antipsychotic therapy, meaning oral and long-acting injectable forms. Patients with SAD mostly received antipsychotic monotherapy, but its complex effects were supplemented with other psychotropic drugs, mostly mood-stabilizers and anxiolytics. Conclusion: The results of our study show similarities between schizophrenia and SAD in terms of health care utilization, despite the fact that

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SAD is generally considered to be a "milder" disorder. On the other hand, this study indicates differences in the spectrum of pharmacotherapy used.

Keywords

Schizophrenia, Schizoaffective Disorder, Antipsychotics, Antidepressants, Mood-Stabilizers

1. Introduction

The diagnostic ambiguity of Schizoaffective Disorder (SAD) is a frequent issue in the daily clinical practice. Despite its long history of being recognized as a distinct disorder, the diagnostic criteria have not been clearly defined [1] [2]. Attaining a correct diagnosis of SAD requires not only the evaluation of the actual clinical state, but also a detailed history of the course of disease [3]. Similarly, to other psychiatric diagnostic entities, it includes a heterogeneous group of states within the disorder itself. Although the disorder psychopathologically consists of two groups of syndromes, schizophrenic and affective, it is a complex mental disorder. To achieve optimal therapeutic outcomes, patients with SAD therefore fundamentally require psychopharmacological treatment that affects all the aspects of the disease. Thus, SAD represents not only a therapeutic problem, but also a diagnostic one. When evaluating the incidence of SAD, we have to consider that coexistence of psychotic and affective symptomatology is more common in clinical practice than the incidence of SAD per se. Data concerning SAD incidence have been influenced by present-day understanding of the disease and by the diagnostic criteria used, however they are not based on biological evidence [3] [4]. As reported in the scientific literature, the annual incidence of SAD is about one quarter of the incidence of schizophrenia [5]. Kozak *et al.* [6] indicate that when comparing incidence at the time of hospital discharge, the diagnosis of SAD in the USA is even more frequent than the diagnosis of schizophrenia. The disorder is more common in women and its course follows the middle ground between schizophrenia and bipolar disorder [7].

In general, less attention has been given to the treatment of SAD than that of schizophrenia. Although many efforts have been devoted to create therapeutic algorithms for the treatment of various mental disorders, guidelines specifically focused on the treatment of SAD are rarely reported in the literature [7] [8]. Moreover, there are significant limitations presented. One important limitation is aforementioned diagnostic ambiguity of SAD [3] [4] [9]. Studies focused on evaluating the efficacy and safety of psychopharmacological treatments often include SAD patients together with schizophrenia patients or exclude SAD patients completely. In real clinical practice, it is not rare to use combinations of various psychotropic medications [7] [10] [11]. An individualized complex therapy including pharmacotherapy and psychosocial treatment is the basis for recovery for a severe mental disorder such as SAD [12].

There is an unmet need to find a satisfactory and practical therapeutic method for the treatment of SAD. The aim of our study was to evaluate the therapeutic algorithms used in patients with SAD hospitalized at the Department of Psychiatry, Comenius University in Bratislava, Faculty of Medicine and University Hospital Bratislava (DP Bratislava) throughout the year 2010, compare them with the therapeutic algorithms used in patients with schizophrenia in the same year, and identify the need for a different treatment strategy for both diagnoses.

2. Methods

This study was conducted as an open-label assessment of therapeutic strategies. The inclusion criteria for the study were 1) hospitalization at DP Bratislava during the year 2010 and 2) diagnosis of SAD or schizophrenia. Case records of all 219 in-patients discharged with the diagnosis of SAD (F25.y, n = 99) and schizophrenia (F20.y, n = 120) were used in the analysis. We recorded the demographic characteristics and selected clinical indicators such as age, gender, type of SAD, duration of disease, length of hospitalization, number of admissions, and medications at the time of hospital discharge. The spectrum of treatment strategies and psychopharmacologicals has been unchanged since 2010.

Categorical data were analyzed using chi-square tests. Other data were expressed as means with standard deviations (SD) and analyzed using analysis of variance (ANOVA). The overall level of statistical significance was defined as $p < 0.05$, eventually 0.1% ($p = 0.001$).

3. Results

In 2010, there were 1058 hospitalizations at the DP Bratislava altogether, 219 (20.7%) of which carried the diagnosis of SAD or schizophrenia. Out of those, the diagnosis of SAD at discharge appeared in 99 cases (SAD group, 45.2%), whereas 120 hospitalizations with the diagnosis of schizophrenia (SCH group, 54.8%). There were statistical differences between the groups due to age and gender distribution (Table 1). In the SAD group, the mean age at the time of hospitalization was higher and there was a higher proportion of women. In terms of diagnosis, the depressive type of SAD was more common than manic/bipolar SAD (Table 2). When comparing the mean age of patients with the manic and depressive type of SAD to the schizophrenia group, we found a statistically significant difference only in the depressive type of SAD (45.8 vs. 41.1 years; $p < 0.05$). In terms of gender distribution there was a greater representation of women in both types of SAD as compared to the SCH group. Duration of disease and length of hospitalization were similar in both groups (Table 1). First-time hospital admissions were rare and made up about 3% of cases. In both groups, hospital admission occurred mostly at the acute psychiatric unit (SAD 86.9%, SCH 80.8%).

The most frequently used psychotropic medications in SAD and SCH were antipsychotics. In the SCH group, they were prescribed in 100% of patients, and

in the SAD group, they were prescribed in 99% of cases. The use of atypical antipsychotics prevailed. At the time of hospital discharge, they were prescribed for 92.9% and 93.3% of patients in the SAD group and the SCH group respectively (Table 3). Conventional antipsychotics were used less often (SAD 29.3% SCH 41.7%), and rarely as monotherapy (SAD 6.1%, SCH 6.7%). Overall, a smaller proportion of patients in the SCH group underwent antipsychotic monotherapy than in the SAD group (SAD 67.7%, SCH 45.8%; $p < 0.001$). As expected, a combination of antipsychotics with various psychotropic medications was more frequent in the SAD group, mainly as a combination with mood stabilizers and

Table 1. Characteristics of SAD and SCH group.

		SAD (n = 99)	SCH (n = 120)	p
Age (years)	average ± SD median (interval)	44.3 ± 11.9 44 (21 - 78)	41.1 ± 13.8 40 (19 - 78)	<0.05
Gender (%)	male female	37.4 62.6	60.0 40.0	<0.001
Duration of disease (years)	average ± SD median (interval)	14.5 ± 9.8 5 (0 - 43)	14.1 ± 12.4 9 (0 - 60)	ns
Length of current hospitalization (days)	average ± SD median (interval)	15.6 ± 8.26 17 (0 - 31)	28.2 ± 21.6 23 (2 - 152)	ns
Number of hospital admissions (%)	first repeated	3.0 97.0	3.3 96.7	ns

ns: no statistically significant differences. Data are presented as the mean ± SD or the median (interval min./max.), or the percentage.

Table 2. Diagnostic spectrum of SAD and SCH group (according to ICD-10).

SAD (n = 99)		SCH (n = 120)	
F25.0	34%	F20.0	63%
F25.1	43%	F20.3	15%
F25.2	17%	F20.5	11%
other F25.y	6%	other F20.y	11%

Table 3. Psychopharmacotherapy in SAD and SCH group.

	SAD (n = 99)	SCH (n = 120)	p
Atypical antipsychotics (%)	92.9	93.3	ns
Conventional antipsychotics (%)	29.3	41.7	ns
Antipsychotic monotherapy (%) Combined antipsychotic therapy (%)	67.7 32.3	45.8 54.2	<0.001
Mood stabilizers (lithium, antiepileptics) (%)	48.5	9.2	<0.001
Anxiolytics (%)	43.4	28.3	<0.05
Hypnotics (%)	45.5	43.3	ns

ns: no statistically significant differences.

anxiolytics. In the depressive SAD subgroup, a combination with antidepressants was often used. Combinations of atypical antipsychotics were observed only in the SCH group. Similarly, combinations of atypical and conventional antipsychotics occurred more often in the SCH group than in the SAD group (SAD 6.1%, SCH 30.8%). In all cases, it was a combination of oral and long-acting injectable forms (LAI). LAI forms were administered at the time of discharge in 49.2% of hospitalizations with SCH and only in 24.2% of hospitalizations with SAD, even though atypical LAI forms being off-label treatments in Slovakia. LAI forms were prescribed for the manic type of SAD more often than the depressive type, with a ratio of 4:1. There were no statistically significant differences when comparing age, gender, length of the disorder and hospitalization between the subgroup of patients who used only oral medication and the subgroup of patients who used a combination of oral and LAI forms. The most frequent atypical antipsychotics used for the treatment of the manic type of SAD were (in descending order): quetiapine, olanzapine, zotepine. The depressive type of SAD was mostly treated with ziprasidone, olanzapine, clozapine and quetiapine. For the treatment of schizophrenia, the most frequently prescribed antipsychotic drugs were risperidone, olanzapine, haloperidol, and quetiapine.

At hospital discharge, patients were mostly referred to outpatient psychiatric care (SAD 87.9%, SCH 85.6%). Rehabilitation and resocialization at the day-treatment program, or hospitalization at a different ward, were less frequent.

4. Discussion

Schizoaffective disorder, like schizophrenia, is a potentially chronic mental disorder, with negative impact on a patient's functioning and quality of life. Data about its incidence are influenced by the current understanding of the disorder and the diagnostic criteria used in clinical practice. From an epidemiological point of view, SAD has a lower incidence than schizophrenia. However, its medical importance, for example in the context of health care utilization, is similar to that of schizophrenia, which has been further confirmed by the results of this study.

In accordance with published data, we found that the mean age in the SAD group was higher and that women predominated when compared to SCH [13] [14]. From a diagnostic perspective, the depressive type predominated in the SAD spectrum, as also previously reported by Doci *et al.* [15], although, Perlman *et al.* [16] found higher prevalence of the bipolar type. The course of SAD is generally described as more favorable than the course of schizophrenia [17]. It is characterized by an acute type of onset, a well-defined duration of episodes and generally good remissions with minimal residual symptomatology. Based on these reports, we had expected a faster achievement of remission and thus a shorter duration of hospitalizations in patients with SAD. However, this hypothesis was not confirmed by the results of our study. This could be explained by the predominance of the depressive type of SAD, which often has a chronic

course with negative consequences on all aspects of social functioning and on health care utilization [18] [19]. In contrast, association between psychosis and affective symptoms, including manic and depressive symptoms, has been identified as a positive prognostic factor [20]. Moreover, in our study, there were repeated hospitalizations and a longer course of the mental disorder in both groups, in which case even the course of SAD could turn into progressive with residual symptoms. The groups did not differ in the need for extended care in the day-treatment program in order to provide rehabilitation and resocialization.

Psychotropic medication is the main tool used for the treatment of SAD, with antipsychotics being the most common type, but antidepressants and mood stabilizers are also prescribed [21]. Combined pharmacotherapy is often indicated in connection with the presence of schizophrenic and affective symptoms. Studies of the efficacy and safety of antipsychotic monotherapy are available in the literature. Nowadays, the efficacy of a therapy is measured not only by achieving remission during the acute phase, but emphasis is placed also on its long-term effect. The aim of maintenance treatment is to retain good remission without relapses that worsen psychosocial functioning and lower the quality of life. For each treatment option, prescription of medication at hospital discharge should be carefully evaluated against the risk of suicidal behavior [22] [23]. Improvement of schizophrenic and affective symptomatology with conventional antipsychotics used as monotherapy has been described by several authors [24] [25] [26]. The problem seems to be the lack of efficacy on affective, especially depressive symptomatology and the depressogenic potential of conventional antipsychotics and their negative side effect profile. Better acute and long-lasting efficacy, higher quality of life, greater safety and better patient compliance are achieved with atypical antipsychotics, mainly thanks to their more complex pharmacological effects. The results of our study show that atypical antipsychotics dominated in the spectrum of prescribed drugs. Conventional antipsychotics were hardly ever used as monotherapy. They were used mainly in the LAI form, which was influenced by the unavailability of atypical LAI antipsychotics on the pharmaceutical market in Slovakia at the time of data collection for our study. In clinical practice, there were only risperidone and olanzapine in LAI forms, but they were prescribed twice as all conventional LAI antipsychotics,. Preference for atypical antipsychotics in the treatment of the whole spectrum of psychotic disorders was also confirmed by Correll *et al.* [27], who stated that they are used in 88.6% of the cases. The same result, however, this time in patients on the schizophrenic spectrum, was noticed by Pickar *et al.* [28]. In the analysis of hospitalizations and prescribed psychotropic medication in the year 2010 in patients suffering from the schizophrenia spectrum disorder in the Slovak Republic, Aziri and Pečeňák [29] state that atypical antipsychotics were prescribed in 67.3% of cases.

Huhn *et al.* [30] have confirmed that antipsychotics differ more in their side-effects than in their efficacy. However, in both groups we found a preference in terms of mechanism of action of different groups of antipsychotics. The

fact that Serotonin and Dopamine Antagonists (SDA), risperidone and ziprasidone, ranked at the top for the treatment of schizophrenia and the depressive type of SAD could be explained by the expectation for obtaining considerable therapeutic benefit on negative, depressive and cognitive symptomatology as compared with the effect on positive symptomatology. The greater need to influence the affective (manic) and positive schizophrenic symptomatology in the treatment of the manic type of SAD could explain the more frequent use of Multi-Acting Receptor Targeted Agents (MARTA), with quetiapine in the first place. We have not identified a study that had separately analyzed how often the specific antipsychotics are used for the treatment of patients with SAD. Correll *et al.* [27], as well as Procyshyn *et al.* [31] have reported the use of olanzapine-quetiapine-risperidone, in declining order, in the treatment of a whole spectrum of psychiatric diagnoses. Our findings in the SCH group are supported by Faries *et al.* [32], who also described the order in which antipsychotics were administered as risperidone-olanzapine-quetiapine, but in patients treated for different psychoses from the schizophrenic spectrum. Broekema *et al.* [33] found that the most frequent antipsychotics used in the treatment of patients with mental disorders were risperidone-clozapine-olanzapine. The frequent use of haloperidol for the treatment of schizophrenia in our study may seem surprising. A likely explanation is that it could be used as the LAI form in 45% of cases. We think that haloperidol as a conventional antipsychotic drug has the advantages implied from the long-lasting clinical experience. Although many studies proved its reliable efficacy, they simultaneously pointed at the risks of side effects, mainly in case of high dosing. However, the view on the treatment with smaller doses of haloperidol differs. Marder *et al.* [34] present haloperidol in low doses (5 mg/day) as an efficient enough and at the same time a much safer antipsychotic drug. The results of the study of Green *et al.* [35] documented comparable neurocognitive effect and impact on psychosocial functioning in the therapy with risperidone (5.7 mg/day) and haloperidol (4.5 mg/day) in a two-year trial.

In clinical practice, combinations of psychotropic medications are often used to influence all symptoms of SAD. Among the advantages of properly chosen combinations of antipsychotics may be the more complex and optimized influence they exert on key neurotransmitters, and thus affect a wider range of symptoms. The potential disadvantages are possible adverse effects associated with pharmacokinetic or pharmacodynamic interactions, subsequent need for corrective co-medication, a higher cost of treatment, and possible worsening of the patients' adherence to treatment [27] [36]. The results of our study showed a relatively high representation of combinations of antipsychotics in both groups. Combinations of antipsychotics were more frequent in the SCH group. It was mostly a combination of oral and LAI form of antipsychotics. A certain influence had also the high percentage of recurrent hospitalization in patients with SCH.

A higher proportion of antipsychotic monotherapy in the SAD group can be explained, on the one hand, by the more frequent use of different psychotropic

drugs from other groups, especially antidepressants and mood stabilizers, on the other hand, by the rarer use of LAIs in the treatments. In none of the groups, we found preference for a particular combination of psychotropic drugs.

A number of studies have dealt with the use of antipsychotic monotherapy and combined psychopharmacotherapy in psychiatric patients. Most of them have documented less common use of antipsychotic monotherapy. Faries *et al.* [32] reported antipsychotic monotherapy for a one-year period in only 35.7% of patients. Broekema *et al.* [33] reported the use of monotherapy in the treatment of a whole range of psychiatric diagnoses in 47.1% of patients. In contrast, only 25.7% of combined antipsychotic treatment was reported by Procyshyn *et al.* [31]. Combination of antipsychotics with other commonly used psychotropic medications was observed in our study, particularly in patients with depressive type of SAD. In 2002, we published the results of a study that monitored the use of various psychotropic drugs in patients with SAD, where we reported that combined therapy of antipsychotics with antidepressants occurred in 23.7% of patients, while mood stabilizers were used in 37.1% of cases [37]. Later on, we revealed the higher antipsychotic efficacy and tolerability of risperidone in comparison to haloperidol-sertraline combination for the acute treatment of SAD, depressed type [8]. Both treatments were comparable in terms of antidepressant efficacy. For the treatment of SAD, Doci *et al.* [15] found that antidepressants represented 65%, while mood stabilizers only 5% of the cases. In the treatment of schizophrenia spectrum disorders Pickar *et al.* [28] found the use of antipsychotic and antidepressant combination treatment in 38.0% of patients, where use of the combination occurred significantly more often in the case of re-hospitalizations and in achieving higher score on Montgomery Asberg Depression Rating Scale (MADRS). The combination of an antipsychotic drug with a mood stabilizer occurred in 44.5% of the patients. They indicate the diagnosis of SAD, as well as aggressive behavior and a high score on Positive and Negative Syndrome Scale (PANSS) as the important predictive factors for the combined use. The use of mood stabilizers has its place especially in persistent residual positive symptoms while antidepressants are used when depressive and/or negative symptoms occur [38]. Olfson *et al.* [39], in accordance with our results, postulated the status of SAD as a separate therapeutic entity.

Our study is limited by the open-label design, and the fact that the study was performed at one psychiatric center, where clinical practice can be influenced by particular workplace practices. We realize that some effects on the obtained results are likely due to psychiatric comorbidity, which we did not research in our study. Since 2010, other atypical antipsychotics came to the pharmaceuticals market in Slovakia, including in LAI, but no new medication brought a new unique mechanism of action.

5. Conclusions

Diagnosing and treating SAD pose a problem in everyday clinical practice, and it

is not sufficiently researched in evidence-based studies, even in the new revisions of DSM-5 and ICD-11 [3] [4]. So far, there has not been a well-defined therapeutic algorithm to treat patients with simultaneously present schizophrenic and affective symptoms.

We can confirm the findings of other authors that despite differences in the prevalence of schizophrenia and SAD in the general population, there are similarities between these disorders, for example, in terms of health care utilization.

In the SAD group, we found a higher proportion of the depressive type of the disorder, which also represents a significant therapeutic challenge. As expected, in the treatment of SCH and SAD groups, atypical antipsychotics were the most commonly used. Conventional antipsychotics were administered primarily in the LAI form. A more frequent occurrence of combinations of antipsychotics in the SCH group was associated with the combination of oral and LAI antipsychotic medication, as well as the prevalence of repeatedly hospitalized (potentially treatment-resistant) patients. In the SCH group, the most prescribed antipsychotic agent was risperidone, which is, according to the recommendations, considered to be the drug of the first choice. For the treatment of patients with SAD, antipsychotic monotherapy was often used. Its efficacy was often supplemented by antidepressants and mood stabilizers, particularly in patients with a depressive type of SAD. The manic type of the disorder was most often treated with quetiapine, an atypical antipsychotic agent from the MARTA group.

The results of our study show similarities between schizophrenia and SAD in terms of health care utilization, despite the fact that SAD is generally considered to be a "milder" disorder. Nevertheless, our data point to differences between these two disorders as reflected in the spectrum of pharmacotherapy used to treat them.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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