Switching Antipsychotics in Inpatient Schizophrenia Care: Predictors and Outcomes

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Background: Within a pharmacoepidemiologic study, characteristics of patients with schizophrenia switched from first- to second-generation antipsychotics (FGAs and SGAs, respectively) or to antipsychotic polypharmacy were compared with those of patients maintained on treatment with FGAs. The primary aim was to assess factors associated with antipsychotic switching and to compare disease course with regard to mental state and social functioning.

Method: Adult inpatients with an ICD-10 diagnosis of schizophrenia or schizoaffective disorder were assessed in 7 psychiatric hospitals. Data were collected between 2001 and 2002. For those patients (N = 847) with an antipsychotic prescription at discharge, t tests and covariance and logistic regression analyses were used to evaluate the relationship between demographic and clinical characteristics and antipsychotic switching.

Results: Patients switched from FGAs to SGAs had fewer previous psychiatric admissions, a shorter illness duration, fewer substance disorders, and a higher probability of working in a competitive setting but more pronounced symptoms than those maintained on treatment with FGAs. Mental state and social functioning after case-mix adjustment were more favorable in the group switched to SGA monotherapy but not in those patients administered FGAs and SGAs concurrently at discharge. Logistic regression controlling for demographic and clinical variables revealed that a short disease duration ($p < .05$), fewer previous psychiatric hospitalizations ($p < .01$), voluntary admission ($p < .05$), and pronounced thought disorder ($p < .05$) were significantly associated with switching from FGAs to SGAs. Hospital differences were also observed.

Conclusion: Remaining on FGAs or switching to SGAs in schizophrenia care depends strongly on institutional practices in addition to the previous disease course and health care utilization.

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With the increasing availability of new single interventions in mental health care, the need to transfer results from efficacy studies to the real world and to replicate evaluations from experimental settings becomes even more pertinent.[1] The lack of effectiveness data might be one reason for the poor use of guidelines in day-to-day clinical work. The Patient Outcomes Research Team's finding that treatment recommendation conformance rates in schizophrenia are at best moderate[2,3] stimulated a great amount of research into quality indicators and guideline implementation.[4,5] Important issues in the treatment of schizophrenia, not yet based on solid evidence, are recommendations on switching patients from first- to second-generation antipsychotics (FGAs and SGAs, respectively).[6] In randomized controlled trials, some SGAs have been more efficacious than FGAs in short-[7] and long-term relapse studies,[8] whereas other SGAs have not. Short-term, prospective, controlled studies have shown that switching stable patients from conventional antipsychotic drugs to olanzapine or aripiprazole was not associated with an increased relapse rate or with withdrawal symptoms.[9,10] Different switching strategies can be applied without running the risk of increased adverse events. In naturalistic switching studies, the majority of, but not all, patients benefited from switching to SGAs.[11] In most outpatients, switching to an SGA resulted in significant improvement in positive symptoms, general psychopathology, and quality of life.[12] However, general recommendations about antipsychotic switching in acutely ill patients are difficult to formulate.

Although the interpretation of the available clinical trial evidence for superior effectiveness of SGAs is an area of debate,[13] it is obvious that medication preferences must take into account side effect profiles, compliance, and long-term effects. Newer guidelines and meta-analyses generally recommend the first-line use of SGAs for most patients[7,14] and advise switching those patients never treated with SGAs.[15] Some guidelines consider FGAs appropriate for those patients who have responded well to conventional agents without unacceptable side effects.[16,17] Others, including the American Psychiatric Association and the German Schizophrenia Guidelines, give little information facilitating the decision between SGAs and FGAs in first-line treatment.[18,19] In addition to trial evidence, it is essential to evaluate clinical decisions concerning medication switching in real world settings and to understand when and under which conditions psychiatrists may deviate from guideline recommendations. Thus, pharmacoepidemiology can support guideline implementation. It is well known that the likelihood of being switched, especially to the more expensive SGAs, is influenced by ethnic factors, family status, duration of disease, and other demographic and clinical factors.[20,21] However, it remains unclear if patient characteristics and institutional practices have a greater influence on antipsychotic choice than clinical factors, as was shown for antipsychotic dosage.[21]

The aim of the present study was to evaluate which factors contribute to antipsychotic switching in inpatient schizophrenia treatment to find out which patients are more likely to have their antipsychotic medications switched. We compared characteristics and disease course, with regard to mental state and social functioning, of patients maintained on an FGA regimen with those of patients who were switched to SGAs or to antipsychotic polypharmacy.

METHOD

Data for this study were collected as part of a quality management project among 7 psychiatric hospitals in Germany: 5 were state mental hospitals and 2 were university hospitals. Inclusion criteria for the 1-year systematic data collection conducted between 2001 and 2002 were an ICD-10 diagnosis of schizophrenia or schizoaffective disorder, age between 18 and 65 years, and provision of informed consent. Patients with a substance abuse comorbidity or a serious physical illness were not excluded.

Measures

Besides demographic and clinical variables at time of admission, detailed diagnostic and therapeutic process measures in addition to outcome parameters in the mental state (Positive and Negative Syndrome Scale [PANSS][22]) and social functioning (Global Assessment of Functioning [GAF][23]) were recorded. Trained physicians assessed patients weekly and at the end of their hospital stay. In accordance with Kay,[22] we calculated the PANSS positive and negative subscores, the paranoia subscore, the thought disorder subscore, the depression/anxiety subscore, and the schizophrenia subscore, including the thought disorder cluster, the activation cluster, and the paranoid/belligerence cluster. Interrater reliability according to Kay was > 0.7.[22]

Benperidol, bromperidol, clopenthixol, flupenthixol, fluphenazine, haloperidol, perazine, perphenazine, pimozide, sulpiride, trifluoperazine, trifluperidol, and zuclopenthixol were classified as FGAs irrespective of their mode of administration. Amisulpride, clozapine, olanzapine, quetiapine, risperidone, and zotepine were classified as SGAs. Prescriptions of the low-potency antipsychotics chlorpromazine, levomepromazine, melperone, pipamperone, prothipendyl, and thioridazine were not considered FGA prescriptions for our purpose because after individual case reviews, it was clear that these medications were used as sedatives in addition to other antipsychotics in all cases.

Statistical Methods

We used t tests for continuous variables and χ^2 tests for proportions. Data were analyzed using 2-tailed tests of significance with 95% confidence intervals. Patients initially treated with SGAs, FGAs, or antipsychotic polypharmacy were compared with analysis of variance. A p value of $< .05$ delineates a significant difference between demographic and/or clinical characteristics among the 3 groups. This analysis was also used to compare switched and maintained patients. By means of covariance analysis, case-mix adjusted outcomes were compared between the switching groups. Outcomes were controlled for the case-mix variables sex, age, age at illness onset, duration of illness, number of previous hospital stays, PANSS thought disorder subscore, concurrent substance disorders, and PANSS total score at admission. With the exception of sex and age, case-mix variables were chosen because in simple correlation analysis they were associated with better or worse outcome as assessed by PANSS at discharge ($p < .05$).

With logistic regression analysis, patient and clinical predictors for switching from FGAs to SGAs or to polypharmacy were evaluated. Adjusted odds ratios (ORs) were calculated controlling for case-mix variables in multivariate analysis. Additionally, a sensitivity analysis was performed to check if results remained robust when those patients who stayed fewer than 7 days in the hospital were excluded.

Analyses presented are based on 847 patients with medication data who were prescribed an antipsychotic at discharge. Results are shown separately for those main-

Table 1. Demographic and Clinical Characteristics of Patients Initially Treated With SGAs, FGAs, or FGAs and SGAs Concurrently[a]

Variable	N	SGA, %	FGA, %	FGA + SGA, %	p Value
Total	847	35.2	50.1	14.8	
Female	841	47.3	43.1	46.3	NS
Independent living (alone, original or new family)	831	77.7	81.0	67.0	.001
Involuntary admission	838	28.9	39.1	19.7	.001
> 6 previous admissions	713	36.0	36.4	46.4	NS
First episode	822	5.5	7.0	6.6	NS
Self-harming behavior history	762	28.6	28.7	36.0	NS
Substance abuse comorbidity	847	13.7	12.5	18.2	NS
		Mean (SD)	Mean (SD)	Mean (SD)	
Age, y	806	38.4 (12.5)	39.3 (11.0)	39.6 (12.4)	NS
Age at illness onset, y	738	27.4 (14.8)	27.7 (14.2)	30.7 (19.9)	NS
Illness duration, y	717	11.4 (10.3)	13.2 (11.2)	13.3 (10.6)	< .01
GAF score	829	39.7 (17.2)	34.8 (16.0)	34.9 (18.4)	.001
PANSS					
Total	834	86.2 (24.2)	88.0 (26.3)	95.5 (25.1)	.007
Positive	834	19.8 (7.7)	21.9 (8.7)	23.3 (8.8)	< .001
Negative	834	22.7 (9.7)	21.9 (9.4)	23.9 (8.8)	NS
Schizophrenia	834	27.3 (10.0)	30.0 (11.3)	31.9 (11.4)	< .001
Thought disorder	834	11.4 (4.5)	12.4 (5.1)	13.4 (5.2)	< .001
Anxiety/depression	834	11.9 (4.8)	10.5 (5.0)	12.0 (4.8)	< .001

[a]Complete data were not available for all patients for some variables.
Abbreviations: FGA = first-generation antipsychotic, GAF = Global Assessment of Functioning, NS = not significant, PANSS = Positive and Negative Syndrome Scale, SGA = second-generation antipsychotic.

tained on FGAs, those switched to SGAs, and those switched to antipsychotic polypharmacy.

RESULTS

Patient Characteristics and Medication

The majority of patients admitted during an acute psychotic episode were treated with an FGA. Five percent of patients did not receive any antipsychotic during the first 3 hospital days. As shown in Table 1, only one third of the patients were initially treated with SGA monotherapy. Remarkably, 14.8% of patients were prescribed an FGA and SGA concurrently early within the first 3 hospital days. At admission, the respective medication rates for all patients were: benperidol, 8.2%; flupenthixol, 12.3%; fluphenazine, 6.9%; haloperidol, 35.2%; perazine, 7.2%; perphenazine, 0.8%; pimozide, 0.4%; zuclopenthixol, 2.9%; amisulpride, 9.2%; clozapine, 9.7%; olanzapine, 17.5%; quetiapine, 4.1%; risperidone, 9.7%; and zotepine, 0.7%. At admission, 20.5% of patients were taking a depot antipsychotic. In the majority of cases of antipsychotic polypharmacy, the medication regimen was a continuation of outpatient treatment before admission.

There were no sex differences among the different initial medication groups. However, patients initially prescribed SGAs had significantly shorter illness duration, higher GAF scores, lower PANSS total scores, and lower PANSS positive, schizophrenia, and thought disorder subscores but higher anxiety/depression subscores than those patients initially prescribed FGAs. Patients initially treated with FGAs had a higher chance of living independently compared with those treated with FGAs and SGAs concurrently and were more likely to be involuntarily admitted. Patients with antipsychotic polypharmacy at admission had more previous psychiatric hospitalizations, the highest rate of substance comorbidities, and higher PANSS total scores including all subscores compared with those initially treated with FGA or SGA monotherapy. Thus, while those patients with initial polypharmacy were not much older than were monotherapy patients, they were the most mentally disturbed and the most chronically ill patients. Length of stay did not differ among patients initially prescribed SGAs, FGAs, or both (43.5, 45.2, and 47.9 days, respectively).

Eighty-eight patients (21.3%) initially treated with FGA monotherapy were switched to SGAs, and 64 (15.5%) were switched to polypharmacy at discharge. In contrast, only 17 patients (5.7%) initially treated with SGA monotherapy were switched to FGA monotherapy, and 28 (9.4%) were switched to polypharmacy. Reasons for this type of switching were not evaluated.

Switch From First- to Second-Generation Antipsychotics Versus Maintained Treatment

At admission, patients switched from FGAs to SGAs (N = 88) had a lower level of social functioning and a higher PANSS total score as well as positive, schizophrenia, thought disorder, and depression/anxiety subscores compared with those maintained on FGAs (N = 262). Switched individuals were more likely to live independently; had fewer previous psychiatric admissions, shorter

Table 2. Comparison Between Patients Maintained on FGA Regimen and Those Switched to SGA or to Polypharmacy (FGA + SGA)

Patient/Illness Characteristic	N	Maintained on FGA, %	Switched From FGA to SGA, %	Switched From FGA to FGA + SGA, %	p Value	Case-Mixed p Value[b]
Total	414	63.3	21.2	15.5		
Female	412	39.2	52.0	45.3	< .05	
Independent living (alone, original or new family)	402	77.7	85.5	85.3	< .01	
Involuntary admission	409	39.8	34.9	31.7	NS	
> 6 previous admissions	345	46.9	20.8	24.6	< .001	
First episode	402	3.5	12.1	7.9	< .05	
Work in competitive setting	372	7.6	25.0	18.5	.002	
Self-harming behavior history	413	30.5	24.0	30.2	< .05	
Substance abuse comorbidity	414	21.8	15.9	12.5	< .05	
Early response[a]	414	8.9	10.2	6.3	NS	
		Mean (SD)	Mean (SD)	Mean (SD)		
Age, y	412	41.5 (12.5)	37.9 (12.4)	35.6 (10.2)	.001	
Age at illness onset, y	356	27.6 (14.3)	29.1 (14.4)	26.9 (16.9)	NS	
Illness duration, y	414	14.7 (11.4)	8.8 (10.1)	13.9 (10.8)	< .001	
Length of hospital stay, d	407	30.7 (36.4)	60.0 (38.9)	51.8 (41.4)	< .001	< .001
Admission scores						
GAF	409	36.0 (16.1)	31.0 (14.2)	32.9 (4.8)	< .05	
PANSS						
Total	405	86.2 (27.1)	92.6 (22.6)	90.1 (24.4)	< .05	
Paranoia	409	8.2 (4.6)	9.6 (5.0)	8.9 (4.6)	< .05	
Discharge scores						
GAF score	389	50.2 (16.0)	60.4 (17.2)	54.7 (17.1)	< .001	< .001
PANSS						
Total	399	61.7 (24.6)	54.3 (20.7)	62.9 (26.6)	< .05	< .05
Positive	399	12.7 (6.1)	10.6 (4.3)	12.6 (6.7)	< .05	< .05
Schizophrenia	392	18.8 (8.5)	15.7 (6.2)	19.0 (9.3)	< .01	< .05
Paranoia	399	5.5 (3.3)	4.6 (2.4)	5.7 (3.7)	< .05	.05
Thought disorder	393	7.8 (3.7)	6.4 (2.8)	7.4 (3.6)	< .05	NS
Change in PANSS subscores from admission to discharge						
Total decrease	393	24.6 (22.6)	38.2 (23.8)	26.8 (25.2)	< .001	< .05
Positive decrease	393	8.4 (8.3)	12.8 (8.4)	9.9 (8.8)	< .001	< .05
Schizophrenia decrease	389	10.1 (10.6)	16.7 (11.4)	12.1 (11.2)	< .001	< .05
Thought disorder decrease	393	4.2 (4.5)	6.9 (4.8)	5.1 (5.6)	< .001	NS
Change in GAF score from admission to discharge	389	14.0 (18.2)	29.5 (21.5)	22.1 (24.8)	< .001	< .001

[a]Early response is defined as PANSS total score decrease by more than 10% in the first week of treatment.
[b]Case-mix model controlled for sex, age, age at illness onset, duration of illness, number of previous hospital stays, PANSS total score, PANSS thought disorder subscore, and concurrent substance disorder. Analyses of change in PANSS and GAF scores from admission to discharge also included adjustment for total score at admission.
Abbreviations: FGA = first-generation antipsychotic, GAF = Global Assessment of Functioning, NS = not significant, PANSS = Positive and Negative Syndrome Scale, SGA = second-generation antipsychotic.

illness duration, and fewer substance comorbidities; and were more likely to work in a competitive setting and to be undergoing treatment for the first time due to a psychotic disorder (Table 2).

At discharge in patients switched from FGAs to SGAs, GAF score increase and total PANSS decrease achieved during the hospital stay were significantly stronger than in those patients treated with FGAs alone. The decrease in the positive, negative, schizophrenia, thought disorder, and anxiety/depression subscores of the PANSS was significantly stronger in switched patients than in those maintained on FGAs. The total anxiety/depression subscore value was equal among switched and maintained patients. Controlling for the case-mix variables sex, age, age at illness onset, duration of illness, number of previous hospital stays, PANSS thought disorder subscore, concurrent substance disorder, and PANSS total score at admission, the more favorable disease course with regard to PANSS and GAF total scores and the PANSS subscore in switched patients remained significant. Remarkably, length of stay of switched patients was twice as high as that of those patients maintained on FGAs.

Switch From First-Generation Antipsychotic to Polypharmacy Versus Maintained Treatment

Patients switched to antipsychotic polypharmacy were younger than those maintained on FGAs and had fewer previous psychiatric hospitalizations (Table 2). Illness duration was comparable with those taking FGAs. There was less substance abuse comorbidity compared with monotherapy patients (FGAs or SGAs). The PANSS total score, the schizophrenia subscore, and the paranoia

Table 3. Logistic Regression Evaluating the Relationship Between Switching From FGA to SGA Monotherapy and Patient and Clinical Characteristics[a]

Variable	Parameter Estimate	Adjusted Odds Ratio	Confidence Interval
Female	0.43	1.52	0.74 to 3.12
First episode	0.55	1.70	0.37 to 7.91
Disease duration > 10 years	–0.94*	0.38	0.17 to 0.84
> 6 previous hospital stays	–1.28**	0.24	0.09 to 0.62
Involuntary admission	–0.67*	0.57	0.27 to 0.98
Work in competitive setting	0.28	1.29	0.47 to 3.55
Independent living	0.04	1.25	0.42 to 3.68
Positive subtype	–0.01	0.92	0.44 to 1.91
Thought disorder	0.73*	1.77	1.13 to 3.59
Hospital A[b,c]	–1.80**	0.54	0.24 to 0.83
Hospital B[b]	–1.11	0.63	0.17 to 1.31
Hospital C[b]	–1.42*	0.86	0.31 to 0.96
Hospital D[b,c]	0.83	15.80	0.27 to 23.1
Hospital E[b]	–0.60	2.40	0.64 to 5.25
Hospital F[b]	0.42	2.00	0.81 to 3.12
Substance disorder	–0.13	0.52	0.31 to 1.86

[a]Controlling for sex, age, age at illness onset, duration of illness, number of previous hospital stays, PANSS total score, PANSS thought disorder subscore, and concurrent substance disorder.
[b]Reference category was hospital G.
[c]University hospital.
*Significant at $p < .05$.
**Significant at $p < .01$.
Abbreviations: FGA = first-generation antipsychotic, SGA = second-generation antipsychotic.

subscore at admission as well as at discharge did not differ significantly from the values of those maintained on FGAs. However, although PANSS and GAF admission scores were comparable with the group of patients switched from FGAs to SGAs, the increases in GAF and reductions in PANSS scores achieved during the hospital stay were significantly smaller for the polypharmacy group. Taking into account differences in case-mix did not change the significance results with the exception of the PANSS thought disorder subscore.

Factors Associated With Switching

As shown in the logistic regression model in Table 3, among those patients initially treated with an FGA, patients with multiple previous psychiatric hospital stays, a longer disease duration, or involuntary admission were less likely to be switched from FGAs to SGAs. However, those patients with a thought disorder had a higher probability of being switched. We also found a significant hospital effect, in which being treated in hospital A or C was related with a lower probability of being prescribed an SGA at discharge after initial FGA treatment. These differences remained significant when case-mix variables and, particularly, when length of stay were controlled for. With the exception of thought disorder, the majority of variables associated with switching from FGA to SGA treatment thus point to a less chronic disease course and the practices of the treating institution or legal admission status. This finding suggests that these factors were at least as important as clinical ones. Age, first episode state, total PANSS score, PANSS subscores, and social functioning did not contribute to discriminating between switched and maintained patients. There was no interaction between thought disorder and any other patient or institutional characteristics pointing to an independent effect on pharmacotherapy decisions. However, there was a strong interaction between duration of disease and number of previous hospital stays. This was accounted for by reporting adjusted ORs in the multivariate analysis. Excluding hospital effects, the regression model assigned 79% of cases in the sample correctly to the switching groups.

There was only 1 significant predictor for a switch to antipsychotic polypharmacy (FGA plus SGA) in patients initially treated with FGAs. Individuals with multiple previous psychiatric hospitalizations had a lower probability of being switched to polypharmacy (adjusted OR = 0.29, CI = 0.12 to 0.72). We found no clinical or demographic variables associated with switching from SGA to FGA monotherapy or from SGA to antipsychotic polypharmacy.

Excluding patients with a hospital stay of fewer than 7 days did not change our results significantly. Demographic and clinical variables within the different treatment groups had values comparable with the whole group, with the exception that GAF scores at admission did not vary significantly between the groups. The disease course in the group of patients switched from FGA to SGA monotherapy remained more favorable. Whereas in the regression model, patient and institutional factors retained their statistical influence on switching from FGAs to SGAs, the presence of a thought disorder was no more discriminative between these 2 groups. Thus, with the exception of extremely short-term patients, the patient, hospital, and disease course factors and not the evaluated clinical factors were associated with switching from SGA to FGA.

DISCUSSION

SGAs are used increasingly as first-line treatment in schizophrenia because randomized controlled trials have shown similar or superior efficacy compared with FGAs in improving symptoms and preventing relapses.[7,8] However, in practice, the decision of which patients to switch from FGAs to SGAs is more difficult to ground in solid scientific evidence. Furthermore, little is known from naturalistic studies regarding which patients are currently more likely to be switched to SGA drugs and which factors in clinical settings contribute to this change. Therefore, evaluating these factors would be an important contribution in understanding nonadherence to current guidelines and targeting quality improvement efforts in hospitals.

The main finding of our naturalistic study is that the decision to switch from an FGA regimen to an SGA regimen is strongly associated with institutional factors as

well as the disease course and the psychiatric care system utilization. We could not show that in acute psychosis clinical factors play a decisive role in the decision to switch antipsychotic treatment. The most powerful individual factors associated with continuation of FGA treatment versus switching to SGA monotherapy were a high number of previous psychiatric hospital stays and a long disease duration.

Two explanations for our findings are possible. As 1 major indication for switching is a lack of or incomplete response to FGA treatment,[24] the group of patients maintained on FGAs could consist mainly of chronic schizophrenics with multiple relapses and low treatment adherence but a history of a certain response to FGA treatment. At the time of the study, there was no depot formulation available for SGA drugs. Therefore, would-be depot patients could not be switched to SGA monotherapy. Another explanation could be the lack of psychiatrists' confidence in atypical drugs to control symptoms in chronic patients. It remains unclear why, for a considerable number of patients in which FGAs have shown low effectiveness, clinicians did not employ alternatives but continued with unsuccessful treatment efforts. The high hospitalization rate in FGA-maintained individuals in our sample hints at limited effectiveness of previous antipsychotic treatments in a substantial amount of cases.

We were able to replicate some results of our previous study from 1997 to 1998 concerning a preference of initial SGA treatment in younger people with shorter illness duration and lower admission schizophrenia and higher anxiety/depression PANSS subscores.[25] However, in the present study, age and first-episode status were not more significant predictors for a medication change, although the mean age was lower and there were more first-episode patients in the group switched to SGA monotherapy than in the FGA-maintained group. In both studies, length of stay did not depend on the initial antipsychotic treatment regimen but on switching conditions. Switched patients had the most prolonged length of stay.

The remarkable impact of hospital practice on the decision to switch antipsychotics replicates the findings from U.S. studies that local institutional cultures exert a powerful influence on medical treatment norms.[26] Controlling for important case-mix variables, the different patient characteristics could not explain the variations in switching behavior between hospitals. We found no evidence that cost considerations accounted for hospital variations. University (hospitals A and D) or state affiliation (hospitals A, B, and C in 1 state and hospitals D, E, F, and G in another state) did not have an observable impact on switching decisions. At the time the study was carried out, there was no considerable budgetary pressure on inpatient medication costs in Germany. However, we could not evaluate other potential cost drivers for prescription habits.

An important finding is the lower switching rate among involuntarily admitted patients that is not sufficiently explained by case-mix differences. Studies have shown that the risk of compulsory admission increases with the number of previous psychiatric hospitalizations.[27] Patients with compulsory admissions have been described to have lower insight,[28] thus contributing to a lower probability to be switched to an SGA drug. The preference of FGA treatment for patients in involuntary settings, but also in the chronically ill, may be explained by the notion that FGAs are more sedative than SGAs. Agitation, aggression, and suicidality are common features of involuntarily admitted patients for which clinicians may appreciate rapid sedation. Furthermore, depot formulations for SGAs are rarely available, thus driving the preference of some clinicians toward FGAs for patients in locked units. With an increasing number of studies showing comparable short-term effectiveness of SGAs and FGAs in the treatment of agitation,[29,30] the association between legal admission status and the propensity to use an SGA may become weaker.

Our study has certain limitations. First, outcome assessment took place only during the inpatient hospital stay. Treatment adherence after discharge, relapse prevention, and other long-term effects could not be assessed. Second, with a naturalistic design, we were only able to give descriptive information that did not allow a consideration of the causality issues. With regard to the better disease course in patients switched from FGAs to SGAs, only prospective controlled trials can evaluate if those patients currently maintained on FGAs could benefit in similar ways from a switch to SGA monotherapy. Increasing evidence from cohort studies[11] and some controlled studies[9,10] is available, but further controlled trials are needed. Third, we cannot exclude a medication-independent time effect contributing to the better outcome of switched patients, as length of stay in individuals switched to SGA monotherapy was twice as high as that of FGA-maintained patients. However, patients switched from FGA to FGA/SGA-combination treatment had lengths of stay comparable with those switched to SGA monotherapy, but symptom scores were similar to those maintained on FGAs. This finding suggests that the observed better disease course after switching is not merely a time effect confounding our results.

More research under naturalistic conditions is necessary in order to ground guideline recommendations concerning the conditions and the adequate time for a change in the antipsychotic medication regimen in solid science. In order to understand the variations in antipsychotic switching patterns, evidence points to a strong influence of staff, legal, and institutional characteristics that have to be taken into account for optimizing mental health care. Local guideline implementation tools should address clinical setting factors in addition to clinical indicators.

Drug names: aripiprazole (Abilify), chlorpromazine (Sonazine, Thorazine, and others), clozapine (Fazaclo, Clozaril, and others), fluphenazine (Permitil, Prolixin, and others), haloperidol (Haldol and others), olanzapine (Zyprexa), perazine (Compazine and others), perphenazine (Trilafon and others), pimozide (Orap), quetiapine (Seroquel), risperidone (Risperdal), trifluoperazine (Stelazine and others).

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