

ASSESSING THE CRITICAL ISSUES OF ATYPICAL ANTIPSYCHOTICS IN SCHIZOPHRENIC INPATIENTS

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SUMMARY

Antipsychotics are effective in reducing positive and disorganization symptoms of schizophrenia. Although SGAs initially all were believed to be more efficacious and tolerable than FGAs, several data show that the SGAs are no more effective than FGAs. In clinical practice, frequent switching of antipsychotic medications is widespread for lack of efficacy, adverse side effects, and partial or not-compliance response. This study suggested that most clinically stable inpatients with schizophrenia maintain their remission states after being switched to another atypical antipsychotic; but that at the end (after 20 years) of the observation period of our study, 11.54% of the patients assumed again typical antipsychotics (haloperidol).

Key words: *schizophrenic spectrum – atypical antipsychotics – switching therapy*

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BACKGROUND

Schizophrenia is a debilitating disease, ranked among the top 20 causes of disability worldwide (Vos 2010). Numerous studies have demonstrated more efficacy, tolerability of atypical than typical antipsychotics in schizophrenic patients. Evidence suggests that although second-generation atypical antipsychotics (SGAs) have a similar efficacy to first-generation typical antipsychotic agents (FGAs), they are more favourable in terms of tolerability, especially about extrapyramidal symptoms (Murray 2017). However, the question of which antipsychotic drug should be preferred for treatment of the disease is controversial. Despite their proven efficacy and tolerability, in many patients clinicians switch several antipsychotic treatments due to the lack of therapeutic response (Kane 2012, Barak 2012). Meta-analyses generally do not support efficacy differences among the other atypical antipsychotics compared with the older typical agents. Some studies emphasise that the differences in efficacy among drugs were small, and smaller overall than those for side-effects (Keating 2017, Leucht 2013). Antipsychotics differ substantially in side-effects, and small but robust differences were seen in efficacy. Adverse effects have a significant impact on quality of life and adherence to medication and residual symptoms have an impact on quality of life too (Haro 2014). In daily clinical practice, frequent switching of antipsychotic medications is widespread for this aim. There are several reasons for switching, including a partial or complete lack of efficacy, adverse side effects, and partial or not-compliance with medication (Correl 2011). Many physicians begin to switch antipsychotics with the original intention to discontinue the drug, but, eventually, continue with more drugs.

However, owing to the diverse receptor profile of antipsychotics, it may be observed many adverse events when switching medications and clinicians should be cautious and closely monitor patients for potential adverse events during the switch (Su 2012). Several new atypical antipsychotics are now available; increasing clinical experience can provide study to long-time (Citrome 2012). We performed this study to determine the maintenance, effectiveness and tolerability of antipsychotics demonstrated in a 20-years study comparing atypical vs typical antipsychotics in schizophrenic in/outpatients.

OBJECTIVE AND METHOD

The aim of our observational study has been to determine the maintenance, effectiveness and tolerability of antipsychotics in a 20-years period, comparing atypical (SGAs) vs typical (FGAs) antipsychotics in schizophrenic in/outpatients. This study has been the extension of our previous switching studies (Franza 2012, Franza 2006).

Observational study in 78 inpatients with schizophrenia or schizoaffective disorder (DSM-IV and subsequently DSM-IV-TR and DSM 5) was observed for the first time in 1996 in Neuropsychiatric Centre "Villa dei Pini", Avellino, Italy. Subsequently, those patients were evaluated clinically until 2016 in an observational 'clinical routine' setting and in practice office. Data were collected for effectiveness, remission, side effects, and compared to switching among antipsychotics (from haloperidol to clozapine/risperidone/olanzapine/quetiapine/aripiprazole and/or back). At baseline all 78 inpatients took haloperidol.

Table 1. Epidemiological characteristics in 78 patients

	Total	Female	Male
Patients	78	30	48
Mean Age (years)	31.18	33.27	27.83
± DS	±11.34	±10.68	±13.36
at baseline			
Mean Education (years)	9.42	8.23	10.77
± DS	± 4.55	±3.33	±4.65
Mean Number Admission (years)	6.21	5.90	6.40
± DS	±1.91	±2.07	±1.77

Retrospectively, we evaluated also data collected during the period of observation in routine clinical setting. Some biological parameters such as blood arterial pressure, lipidic and glucidic profile, liver enzymes, complete blood count, electrocardiogram and body weight (and body mass index) were collected, too.

Data were analyzed regularly and highlighted at the following times: baseline (T0); 1 year (T1); 5 years (T2); 10 years (T3); 15 years (T4); 20 years (T5) during every clinical control visit in relation to antipsychotic therapy. The rating scales administered were the following: Positive and Negative Syndrome Scale (PANSS) (Kay 1989); Brief Psychiatric Rating Scale; (BPRS) (Overall 1962), Quality of Life Index (QLi); (Ferrans 1985). Partial data were obtained with the Scale for the Assessment of Positive Symptoms (SAPS)(Andreasen

1984) and the Scale for Assessment of Negative Symptoms (SANS) (Andreasen 1983).

These scales were administered to each patient during hospitalization or outpatient control.

The overall analysis consisted of the comparison of the upper bound of the 95% confidence interval (CI) baseline and at the end of the study of mean other scales of evaluation (PANSS: completed data; SAPS; SANS: partial data; Quality Life Index). [EZAnalyze© ver.3.0].

RESULTS

We have observed discontinuity with substitution of initial treatment with typical antipsychotic (haloperidol) and beginning a new pharmacological treatment with atypical antipsychotics or possible return to a treatment with typical antipsychotics (oral or long-acting medication). In each patient's interview, we have recorded the following items appraised for every atypical used age; number of admissions/year; therapeutic compliance (family investigation); social operation; scholastic and/or working activity; poli-drugs abuse. Furthermore, we have recorded the preceding switch treatment with typical to atypical. Table 1 shows the epidemiological data concerning the patients that have assumed atypical antipsychotics. Timetable (Figure 1) reports the summary of antipsychotics switching about observational 20-year-study.

Table 2. PANSS EZAnalyze Results Report - Paired T- Test of T (haloperidol)

PANSS	T0 Mean Haloperidol	Tn	T5 Mean	N Pairs:	Mean Difference	SE of Diff.	Eta Squared	with T5	or Tn vs	T5
								T-Score	P	
Haloperidol	128.818		77.636	11	51.182	10.295	0.692	4.971	0.001	
Clozapine	124.370		82.815	27	41.556	2.483	0.912	16.735	0.000	
Risperidone	120.478		92.173	23	28.304	7.061	0.411	4.009	0.001	
Olanzapine	115.000		90.913	23	24.087	4.698	0.533	5.127	0.000	
Quetiapine	109.250		89.750	20	19.500	4.228	0.515	4.612	0.000	
Aripiprazole	115.375		88.688	32	26.688	4.186	0.560	6.376	0.000	

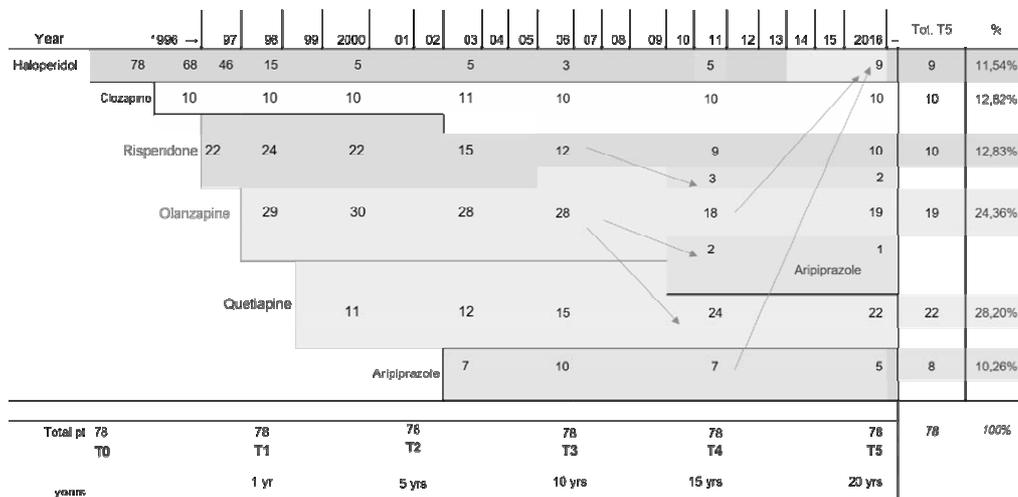


Figure 1. Timetable: switching antipsychotics 136 schizophrenic patients from 1996 to 2016

Table 2 reports the results to PANSS for any atypical treatment in each patient who has continued the initial therapy for all the period of observation and the rates of discontinuous therapy after the switch from typical antipsychotic (haloperidol).

At the baseline their mean ages, gender distribution, baseline PANSS Scale scores were collected. In the clozapine group, the remission rates were higher than in the other groups and the 28.84% of patients that have started the treatment with risperidone and 42.85% with quetiapine have interrupted the therapy, and with the necessity of the assumption of a typical antipsychotic (haloperidol; haloperidol depot). A consistent number of patients (11.54%), who have suspended the “first” therapy with haloperidol, have assumed again the therapy with haloperidol at the end of the observation period. Outcome was good in 28.4%, intermediate in 50,1% and poor in 21%. Other parameter data will be presented in another study, which is currently being processed.

CONCLUSIONS

Antipsychotics are effective in both treating the acute psychotic episode and preventing relapses. In addition, both FGAs and SGAs are effective in reducing positive and disorganization symptoms. Although SGAs were all initially believed to be more efficacious and tolerable than FGAs, several data show that the SGAs are no more effective than FGAs (Lieberman 2005). Antipsychotic medications cause a range of neurologic, metabolic, cardiovascular, gastrointestinal, hematologic, genitourinary, musculoskeletal, endocrine, and other side effects. In contrast to their broadly similar efficacy, antipsychotics differ markedly in their adverse effect profiles (Tandon 2014). Our study suggests that most clinically stable schizophrenic inpatients maintain their remission states after being switched to atypical antipsychotics. Therefore, it's interesting to note that at the end of the period of observation (20 years: III Switching), 11.54% of the patients have assumed again typical antipsychotics, long-acting or oral, and the 51,18% have reported satisfactory and better therapeutic efficacy than previous pharmacological treatments with antipsychotics of second generation. Therefore, guidelines are important for switching drugs nevertheless few ones are being developed (Poo 2015). When switching patients from one antipsychotic to another, a good clinical judgment and a conservative approach can be used to balance the risk of clinical exacerbation with that of increased adverse effects. It is not currently possible to predict which antipsychotic may be optimal for a given patient. To achieve optimal therapy for schizophrenia, clinicians must balance efficacy, risks, and benefits of treatments in a way that is customized for the needs and vulnerabilities of the individual patient (Tandon 2014).

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