Long-acting (LA) neuroleptics in comparision. A naturalistic and retrospective study on 109 patients of a Mental Health Center

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Abstract

In this naturalistic and retrospective study, we analyzed many variables, 35 specifically, in order to see if and in what percentage patients who make or have made use of SGA have improved their lives in the sense of greater recovery and/or quality of life and if you have reduced the expenditure for admissions, in the sense of the number of total days, both in SPDC and psychiatric structures accredited in the region of Lazio.

KEY WORDS: adherence, compliance, efficacy, cost effectiveness, FGA and SGA Neuroleptics.

Introduction

Current scientific knowledge on and in relation to the use of long-acting neuroleptic antipsychotic drugs (1-6) shows evidence on the overall improvement of patients' clinical conditions, both in terms of compliance and adherence, with a greater possibility of functional recovery, both personal and social of the subjects treated. It is also true that such investigations, like some randomized studies (7, 8), are mostly carried out by comparing patients who take therapy with the same drugs but by oral means, leaving brackets, a whole series of variables that surely can influence research results. Another variable to consider is that linked to future medium and long-term follow-up, where it will be understood if the extrapyramidal effects (9) are really minor and if the metabolic syndrome (10) is not even increasing. The various meta-analyzes (11-13) help us in part to analyze the critical variables, but we think we need to further expand what is already present in the literature to get a more comprehensive picture of the problem.
The main purpose of this work is therefore to want to study and analyze if it is true that the use of "Atypical" Neuroleptics (SGA) compared to the classic first-generation Depot (FGA), is really more effective and that these reduce health care, especially with respect to the use of drugs, in the clinical management of psychotic patients.

Materials and Methods

In order to analyze what has been explained, a grid of and with 35 variables (Table 1), listed below, has been developed *ad hoc*, then analyzed using the Chi Square Test.

Sample

- Sample: consisting of 109 subjects, all with a diagnosis of psychosis
- Gender: F = 41 (37.6%) and M = 68 (62.4%)
- Age: 21-75 (Average 47.6); F 21-75 (Average 50.7); M 21-75 (Average 45.7)
- Observation period: second semester 2014 - all 2015 - first hundred days of 2016, all patients belonging to a Mental Health Center (MHC) in Rome (ex B), with a catchment area of about 250,000 inhabitants
- Enrollment: the first prescription of Depot/LA, between 01.02.1995 and 02.10.2015.

The prescribed drugs were as follows (Table 2):

- ALO-D = 63 (3 switch to PAL-D)
- ARI-D = 3
- FLU-D = 15
- PAL-D = 21 (1 switch to ALO-D)
- RIS-D = 6 (1 switch to PAL-D)
- ZUC-D = 1

The period or time of use is described below:

- <1 year = 23 (21.1%)
- 1-3 years = 35 (32.1%)
- 3-5 years = 23 (21.1%)
- > 5 years = 28 (25.7%)

Statistical significance was calculated with paired samples test (Tables 4-6).
The first data refer to the resources and the latter to the results.
The values are for all referred to the last year compared to the previous year for the resources and final towards the previous year, for the outcomes.

Table 1 - Variables.

1	Gender (M/F)
2	Age
3	General Physician
4	Beginning Of Prescription
5	End Of Prescription
6	Drug
7	Total Milligrams Prescribed In The Period (Including Induction)
8	Previous Drug
9	Reason for the Switch
10	Total Recovery In Spdc 6 Months Before The Period Of Observation
11	Total Recovery's Days In Spdc 6 Months Before The Period Of Observation
12	Total Recovery In Spdc 6 In The Period Of Observation
13	Total Recovery's Days In Spdc 6 In The Period Of Observation
14	Total Recovery In CDC 6 Months Before The Period Of Observation
15	Total Recovery's Days In CDC 6 In The Period Of Observation
16	Visits Of The Psychiatrist 6 Months Before The Period Of Observation
17	Visits Of The Psychiatrist In The Period Of Observation
18	Visits Of The Psychologist 6 Months Before The Period Of Observation
19	Visits Of The Psychologist In The Period Of Observation
20	Visits Of The Nurse 6 Months Before The Period Of Observation
21	Visits Of The Nurse In The Period Of Observation
22	Visits Of The Social Worker 6 Months Before The Period Of Observation
23	Visits Of The Social Worker In The Period Of Observation
24	Other Drugs 6 Months Before The Period Of Observation
25	Other Drugs In The Period Of Observation
26	Initial Global Evaluation Of Operation (VGF)
27	Final Global Evaluation Of Operation (VGF)
28	Initial HoNOS
29	Final HoNOS
30	Initial QTc
31	Final QTc
32	Initial BMI Body Mass Index
33	Final BMI Body Mass Index
34	ESP Extrapyramidal Symptoms (yes/no)
35	PRL Prolactin (yes/no)

Results

From the data collected with the study, with all its limitations, at the moment it does not seem to clearly emerge a significant difference between SGA and FGA. It should be noted that in the sample there were no subjects treated with olanzapine and with perfenazine in depot formulation. The complexity and the heterogeneity of many of the variables analyzed does not allow to evaluate with precision and correctness the efficacy (1) and the cost effectiveness (14) (cost-effectiveness analysis = CEA, method of evaluation of public investment projects) of different neuroleptics. To tell the truth, to look at the numerical results, in terms of statistical significance, particularly for the resources used and studied even more than the outcomes, data seem to emerge slightly in favor of the SGA compared to the FGA. The P-factor, i.e. the probability which represents the significance level of a test, usually has a probability level of 0.05 (5%) or 0.01 (1%). This probability represents a quantitative estimate of the probability or not that the

Table 2 - Drugs' list.

Drugs	Cases
Total Patients	109
ALO	0
ALO-D (haloperidol depot)	60
ALO-D/PAL-D	3
AMI	0
ARI	0
ARI-D (aripiprazole depot)	3
ASE	0
BRO	0
CLOR	0
CLOZ	0
DIP	0
FLU-D (fluphenazine depot)	15
LEVM	0
LEVS	0
OLA	0
OLA-D (olanzapine depot)	0
PAL	0
PAL-D (paliperidone depot)	20
PAL-D/ALO-D	1
PER	0
PER-D (perphenazine depot)	0
PRO	0
QUE	0
RIS	0
RIS-D (risperidone depot)	5
RIS-D/PAL-D	1
TIO	0
TRI	0
ZUC-D (zuclopentixol depot)	1

observed differences are due to chance or not. It's like saying, the risk of misinterpreting the result of the research.
Below is the legend concerning the reasons for the change of drug (switch) (Table 3).
Below are listed the results of the statistical evaluations with the descriptive and meaningful tests of the differences in the use of resources (admissions, visits, etc.) and in the outcomes (scales VGF, HONOS, etc.), plus two non-comparable variables, the Prolactin and extrapyramidal symptoms.

Resources

The admissions data is as follows:
- 25 *vs* 48 (p-value <0.05)
- -47.9%

The days of hospitalization in SPDC (psychiatric service of diagnosis and treatment):
- 304 *vs* 448 (do not sign)
- -32.1%

Inpatient days in the CDC (approved nursing home):
- 267 *vs* 302 (do not sign)
- -11.6%

Psychiatric visits:
- 989 *vs* 1296 (p-value <0.01)
- -23.7%

Psychological visits:
- 242 *vs* 488 (p-value <0.01)
- -49.6%

Nursing visits:
- 558 *vs* 744 (p-value <0.01)
- -25.0%

Social worker visits:
- 163 *vs* 342 (p-value <0.01)
- -52.3%

Outcomes

VGF (global evaluation of operation) mean:
- 45.89 *vs* 43.01 (p-value <0.01)
- +2.9

HoNOS (outcome evaluation scale: Health of the Nation Outcome Scales) media:
- 19.23 *vs* 20.02 (p-value <0.01)
- -0.75

Table 3 - Reason of drugs' switch.

Reason for the switch	Cases
Total	**92**
1 - Poor/Reduced Or No Clinical And/Or Symptomatological Efficacy	41
2 - Comparison Of Important Side Effects	8
3 - Request Of Patient And / Or Of Caregivers, To Improve Compliance	22
4 - Simplification Of The Recruiting Scheme	20
5 - Reduction Of Costs Of Drugs	1
6 - Other	0

Table 4 - Statistics for paired samples.

		Average	N	Standard Deviation (SD)	Standard Error Average
Couple 1	R_SPDC_pre	,4404	109	,87592	,08390
	R_SPDC_post	,2294	109	,42236	,04045
Couple 2	GD_SPDC_pre	4,1101	109	8,70434	,83372
	GD_SPDC_post	2,7890	109	6,14949	,58901
Couple 3	GD_CDC_pre	2,7706	109	8,48051	,81229
	GD_CDC_post	2,4495	109	6,71163	,64286
Couple 4	VIS_PSI_pre	11,8899	109	5,14843	,49313
	VIS_PSI_post	9,0734	109	4,66608	,44693
Couple 5	VIS_PSICO_pre	4,4771	109	5,99938	,57464
	VIS_PSICO_post	2,2202	109	2,82305	,27040
Couple 6	VIS_INF_pre	6,8257	109	7,03542	,67387
	VIS_INF_post	5,1193	109	6,51739	,62425
Couple 7	VIS_AS_pre	3,1376	109	3,32629	,31860
	VIS_AS_post	1,4954	109	1,82890	,17518
Couple 8	VGF_pre	42,8257	109	6,59383	,63157
	VGF_post	45,5596	109	7,57974	,72601
Couple 9	HONOS_pre	19,9450	109	3,48498	,33380
	HONOS_post	19,2385	109	4,48846	,42992
Couple 10	QTc_pre	,3992	109	,04378	,00419
	QTc_post	,4071	109	,04520	,00433
Couple 11	BMI_pre	23,9174	109	4,19684	,40198
	BMI_post	24,5229	109	4,29814	,41169

Table 5 - Correlations for paired samples.

		N	Correlation	Statistical significance
Couple 1	R_SPDC_pre and R_SPDC_post	109	,325	,001
Couple 2	GD_SPDC_pre and GD_SPDC_post	109	,307	,001
Couple 3	GD_CDC_pre and GD_CDC_post	109	,700	,000
Couple 4	VIS_PSI_pre and VIS_PSI_post	109	,659	,000
Couple 5	VIS_PSICO_pre and VIS_PSICO_post	109	,538	,000
Couple 6	VIS_INF_pre and VIS_INF_post	109	,903	,000
Couple 7	VIS_AS_pre and VIS_AS_post	109	,336	,000
Couple 8	VGF_pre and VGF_post	109	,557	,000
Couple 9	HONOS_pre and HONOS_post	109	,859	,000
Couple 10	QTc_pre and QTc_post	109	,640	,000
Couple 11	BMI_pre and BMI_post	109	,920	,000

QTc (value extrapolated from the ECG trace) mean:
• 0.41 *vs* 0.40 (p-value <0.05)
• +0.1

BMI (body mass index) average:
• 24.53 *vs* 23.93 (p-value <0.01)
• +0.6 / + 2.5%

In addition, the data related to other studied variables are also reported, very little assessable by their nature, such as:
• Extrapyramidal symptoms: 40/109
• PRL (prolactin): 14/109

A note of caution we feel at this point to add it to you.

Table 6 - Paired samples test.

		Couple differences					T	Df	Significance (2-tail)
		Average	SD	Standard Error Average	Confidence Interval at 95%				
					Lower	Upper			
Couple 1	R_SPDC_pre - R_SPDC_post	,21101	,83968	,08043	,05159	,37043	2,624	108	,010
Couple 2	GD_SPDC_pre - GD_SPDC_post	1,32110	8,98443	,86055	-,38466	3,02687	1,535	108	,128
Couple 3	GD_CDC_pre - GD_CDC_post	,32110	6,10992	,58522	-,83892	1,48112	,549	108	,584
Couple 4	VIS_PSI_pre - VIS_PSI_post	2,81651	4,07832	,39063	2,04221	3,59081	7,210	108	,000
Couple 5	VIS_PSICO_pre - VIS_PSICO_post	2,25688	5,07244	,48585	1,29384	3,21992	4,645	108	,000
Couple 6	VIS_INF_pre - VIS_INF_post	1,70642	3,03468	,29067	1,13026	2,28258	5,871	108	,000
Couple 7	VIS_AS_pre - VIS_AS_post	1,64220	3,21318	,30777	1,03216	2,25225	5,336	108	,000
Couple 8	VGF_pre - VGF_post	-2,73394	6,72563	,64420	-4,01086	-1,45703	-4,244	108	,000
Couple 9	HONOS_pre - HONOS_post	,70642	2,33056	,22323	,26395	1,14890	3,165	108	,002
Couple 10	QTc_pre - QTc_post	-,00784	,03780	,00362	-,01502	-,00067	-2,167	108	,032
Couple 11	BMI_pre - BMI_post	-,60550	1,70521	,16333	-,92925	-,28176	-3,707	108	,000

Discussion

We can say that perhaps more variables are needed, studied for longer times, with a more selected population of psychotic patients, but even more it would be better to enter the specifics of some variables, such as the number of SPDC and CDC admissions.

There are patients who have been treated with LA (long-acting) for a year and others for much longer: this makes the desired effect "distorted", that is to say underestimated, because it is presumable that patients in therapy for a long time are now "stabilized". As to say that after a long period of stable care, with good compliance and also adherence, the weight that one or the other drug has is reduced; furthermore, it is also obvious that all the other psycho-social variables come into play, which can at least disguise the different value of efficacy (1, 3) of the drugs used, if not actually covered.

On the other hand, doing this statistical evaluation, only on those patients who entered therapy in the last year or three years, would have reduced the whole sample too much.

Therefore, we have preferred to leave the data for what it is, in order to propose it like a possible object of study and reflection, for those who want it, in a future that we hope is coming soon and brings more certain results.

The sustainability of health care expenditure and in particular that for the management and assistance of patients with psychiatric disorders, seems to us more and more timely and not to be underestimated, in order not to have to fight public administrators with subjective and impressionistic opinions, but with real and measurable data.

Only a correct analysis of our daily clinical action will allow us to feel really free to prescribe this or that drug, this or that psychological support or even that rehabilitation, knowing with sufficient certainty that you are doing the best for that person, in that moment and also in the interest of the community.

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