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The Role of Long-Acting Antipsychotics in Patients Suffering a Schizophrenia and Comorbid Drug Use The Case of Paliperidone Palmitate

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Abstract: The psychopharmacological treatment of psychotic dual disorders is a real challenge for the clinicians, due to the low level of adherence to the treatment in many cases. For this reason, in some recent guides (Cochrane, Nice) it had been proposed the use of Long-term antipsychotic treatment (LAI-APS) as a way to improve the adherence and increase the efficacy of the treatment. Paliperidone Palmitate is one the most recent LAI-APS, with very good results in the treatment of psychotic disorder, with low number of drop-outs due to the good tolerability to these effects. The authors carry-out a preliminary study comparing the tolerability and efficacy of this LAI-APS in two samples of schizophrenic patients, one of them with comorbid drug use. Our results shows that the treatment permits in both groups the decrease of dosage and/or number of concomitant oral antipsychotic treatment, decrease the number of psychiatric admissions and the use of drug, with no drop-out during a period of one years, comparing with the previous year. We conclude that Paliperidone Palmitate could be a useful treatment in the group of patients suffering psychotic disorder with comorbid drug use.

Keywords: Dual Disorders, Schizophrenia, Paliperidone Palmitate

1. Introduction

The «Dual Pathology» concept (or comorbidity) implies the coexistence of two disorders of Axis 1 of DSM at the same time. Regier et al., (1990) describe for first time the real magnitude of this disorder: 22,5% of patients presents some kind of comorbidity between psychiatric disorders and drug use (alcohol and cannabis mainly). More recent studies in this field (NESARC) (Hasin et al., 2015) have shown an increase in the prevalence of this pathology, specially in the case of the endogenous psychosis

Some theories have been proposed trying to explain this disorder:

1) Drug use is prior to the development of a psychotic disorder (amphetamine psychosis, cannabis abuse as risk factor to schizophrenia) (Van Os et al., 2002)

2) Psychotic disorder increase the risk of drug use (relief of side effects of psychotropic medications) (Dixon et al., 1999)

3) Bidirectionality (one disorder leads to the other and viceversa) (Ferdinand et al., 2005)

4) Common vulnerability (Chambers, 2001) (Common biologic vulnerability, caused by mesocorticolimbics

dopaminergic dysfunctions),

5) Self- medication hypothesis (Khanztian, 1985),

6) The two disorders are present at the same time and they are independents

The two more accepted theories are the Common vulnerability and the Self-medication Hypothesis, supported by an important number of publications.

We supposed that all the theories are present in a clinical setting and we consider which of them are correlated with our patients, with the aim to apply the more adequate treatment in every case.

1.1. Consequences of Drug Use in Clinical Outcomes

In general, the majority of the studies related to this field shows similar results: comorbid drug use in psychotic patients provokes an early onset of the disease (Veen et al., 2004), more time out of treatment (Green et al., 2004), an important increase of positive symptoms (Talamo et al., 2006), a higher level of behavioral disorders (Margolesse et al., 2004; Haddock et al., 2013), higher number of psychiatric admissions and longer duration (Wisdom JP et al., 2011) and decrease on the efficacy of antipsychotic treatments (decreasing adherence) (Large et al., 2014; Ameller and Gorwood., 2015).

1.2. Treatment

This is the major challenge in the case of these patients: to find a real effective treatment. Some proposals have been shown: for example, it´s necessary a multidisciplinary way of treatments, focusing in the abstinence of drug use as first target (Clarke et al., 2013; Marquez-Arrico et al. 2015)

Referred to psychopharmacological treatment, it seems clear that antipsychotic treatment is needed. But typical antipsychotic even may increase the level of drug use in these patients (haloperidol) (Samaha, 2014). In the other hand, Green et 2008 have demonstrated that clozapine, an atypical neuroleptic, decrease drug use in schizophrenic patients. So it may be supposed that this kind of neuroleptic is the best options (Sepede et al., 2014).

The review of some guides, as NICE (2011), Cochrane (2014) and WFSBP (2015), shows no evidence of effectivity of any psychopharmacological or psychological treatment in dual diagnosed patients.

In these guides, we may found some references, as for example, clozapine seems to be effective for the reduction of craving and substance intake in patients with dual diagnosis. In the same ways, some antipsychotic seems to be effective in patients with schizophrenia and alcohol use, and first generation antipsychotics (FGA) and second generation antipsychotics (SGA) show limited positive evidence in schizophrenics using cocaine, an inconsistent superiority of SGA over FGA in the reduction of craving and amount of drug use can be assumed, and due to the high non-compliance in dual diagnosis patients, the use of long-acting injectables could be useful.

1.3. Objectives

The main objective of the current research is to investigate the efficacy and tolerability of one of more recent LAI-APS, Paliperidone Palmitate, in a sample of schizophrenic patients with comorbid drug use.

We do a naturalistic prospective study. We employ the number of psychiatric admissions, dosage and number of another concomitant psychiatric treatment and number of subject using drug before and after the treatment as measurement of efficacy. The maintenance of the treatment and the number of drop-out during the period of study are two measures of tolerability.

2. Matherials and Methods

We carry out a study in a group of schizophrenic patients in two centers of the Navarra Mental Health Net among October de 2012 and Mars 2015

As inclusion criteria, we use the following:

1- Diagnosis of Psychotic disorder

2- Drug use at the same time

3- Receiving Paliperidone Palmitate as main psychopharmacological treatment

We record some clinical data:

1- Sociodemographic (age and sex)

2- Data of Psychotic disorder (age of onset of symptoms, number of psychiatric admissions, concomitant treatment)

3- Drug use history (mean substance of use)

To complete and corroborate the information, we have got additional information by families of the included patients of the sample.

As statistical method, we have employed the SSPS program. We employed the t-student and chi square test to compare the data pre and postreatment in both groups and in the comparison between groups.

3. Results

1. Our samples are constituted by 44 patients who meet the criteria of inclusion

2. Our data are similar than other studies: SCH+ are younger (32,9 v 41,1, p<0,05), mainly males (12), with a higher dosage of Paliperidone Palmitate and of concomitant antipsychotic treatment and higher number of psychiatric admissions. All these data are related to more severity of the disease. (Table 1)

Table 1. *General Data.*

ALL GROUP (N=44)	PRETR	POSTR	P value
AGE	28,7+ 7,5 years		
PALIPERIDONE DOSAGE(mg)	99,43 MG		
DIAGNOSIS	31 Schizophrenia, 6 Schizoaffective		
CONCOMITANT TREAT	38	14	P< 0,01
ANTIPSYCHOTIC CONC (Mg Risperidone)	6,41	0,61	P< 0,001
DRUG USE	NO 21	NO 12	P< 0,05
PSYCHIATRIC ADMISSIONS	0,86	0,22	P< 0,001
SIDE EFFECTS (YES)	29	15	P< 0,01

PRET: Pretreatment, POSTR: Posttreatment

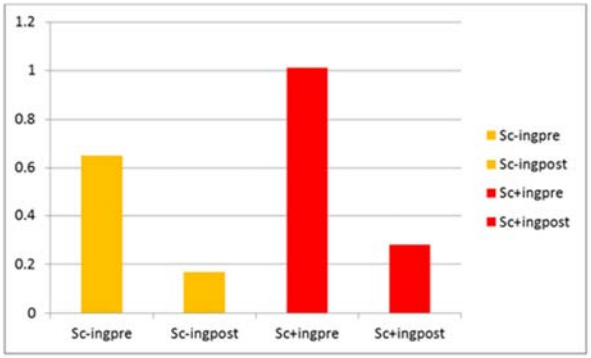
3. In the comparative study between pre and postreatment

data, we observe a significant decrease in all the variables intergroups and intragroups. (table 2 and 3, Fig. 1, 2, 3,4, 5 and 6)

4. However, in the comparison inter groups, it disappears the significance in psychiatric admissions (Fig. 1), the dosage of antipsychotic treatment (Fig. 2) and concomitant treatment (table 4, Fig. 3)

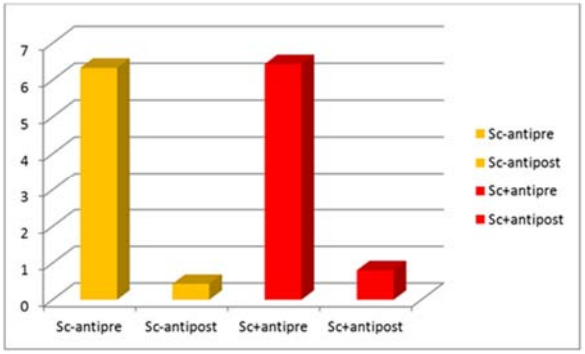
5. We also observe a decrease in the number of patients in SCH+ groups with comorbid drug use (table 4)

6. We think it´s very interesting the fact that SC+ group present a low and significant level in number of side effects to antipsychotic treatment, even before the beginning of Paliperidone Palmitate. This fact is maintained at the end of the research.



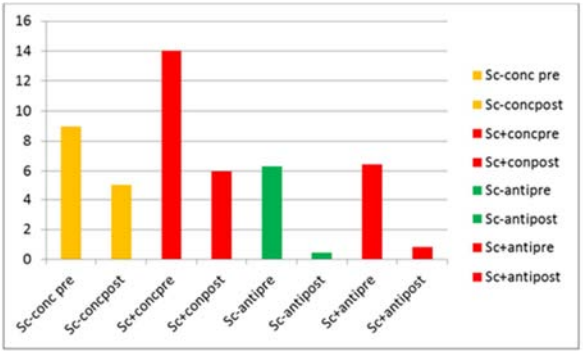
Sc- Schizophrenia without drug use; Sc+: Schizophrenia with drug use

Figure 1. *Psychiatric admissions.*



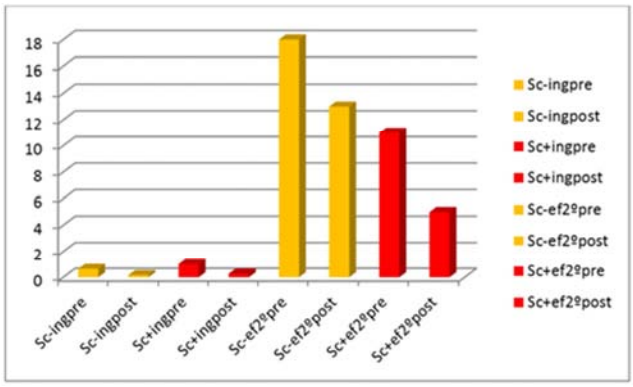
Sc- Schizophrenia without drug use; Sc+: Schizophrenia with drug use

Figure 2. *Antipsychotic dosage (Mg Risperidone).*



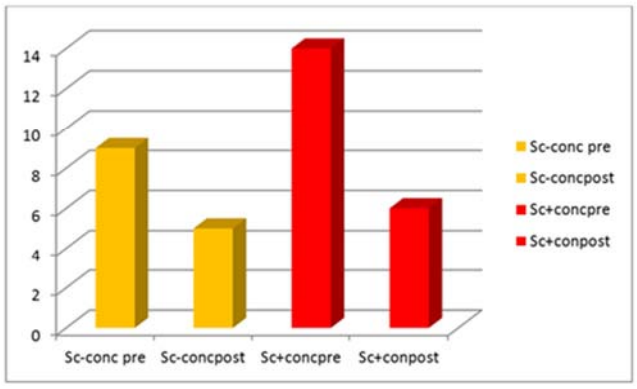
Sc- Schizophrenia without drug use; Sc+: Schizophrenia with drug use

Figure 3. *Concomitant Treatment pre and post Paliperidone Palmitate.*



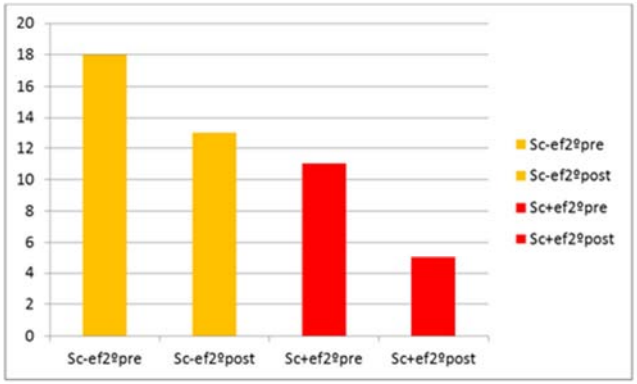
Sc- Schizophrenia without drug use; Sc+: Schizophrenia with drug use

Figure 4. *Psychiatric Admissions and Side effects pre and post Paliperidone Palmitate.*



Sc- Schizophrenia without drug use; Sc+: Schizophrenia with drug use

Figure 5. *Concomitant treatment (yes).*



Sc- Schizophrenia without drug use; Sc+: Schizophrenia with drug use

Figure 6. *Side effects.*

Table 2. *Comparison between the groups of patients (pretreatment).*

GROUP	SCH- (N=23)	SCH+ (N=21)	P value Pret
Concomitant tret	9	14	P< 0,05
Antipsychotic tto (Mg Risperidone)	6,33	6,43	NS
Psychiatric admissions	0,65	1,01	P< 0,01
Side effects	18	11	P< 0,01
Paliperidone (mg)	87,69 mg	116,66 mg	p< 0,05

SCH-: schizophrenics without drug use; SCH +: Schizophrenic with drug use

Table 3. *Comparison between the groups of patients (postreatment).*

GROUP	SCH- Group	SCH+ Group	P value
Concomitant treat	5	6	NS
Antipsychotic tto (Mg Risperidone)	0,43	0,80	P<0,05
Psychiatric admiss	0,17	0,28	NS
Side effects	13	5	P< 0,01
Paliperidone (mg)	87,69 mg	116,66 mg	p< 0,05

SCH-: schizophrenics without drug use; SCH +: Schizophrenic with drug use

Table 4. *Comparison between the groups of patients (pre and postreatment).*

GROUP	SCH- (N=23)A		SCH+ (N=21)B			
	Pretto	Postto	Pretto	Postto	P value Pre	P value Post
Concom treats	9	5	14	6	P< 0,05	NS
Antipsy tto (Mg Risperidone)	6,33	0,43	6,43	0,80	NS	NS
Psych adm	0,65	0,17	1,01	0,28	P< 0,01	NS
Side effects	18	13	11	5	P< 0,01	P< 0,01
Drug use (YES)	21	12	P< 0,05			

SCH-: schizophrenics without drug use; SCH +: Schizophrenic with drug use

4. Discussion

Our data shown that Palmitate Paliperidone, as main psychopharmacological treatment, is a useful alternative to get a good and prolonged response in the group of schizophrenic patients with comorbid drug use, getting a decrease of psychiatric admissions, the number and/or dosage of another psychopharmacological concomitant treatment, with no drop outs during one year of follow up.

We can´t compare our data with previous reports because we have made a systematic search in Medline, including "dual diagnosis, Psychosis and Long-acting paliperidone", so we may suppose that´s the first research that shown the efficacy of Paliperidone palmitate.

A previous report (Rubio et al., 2006), comparing the efficacy of two long-acting antipsychotic treatment, zuclopentixol and long-acting risperidone, shows a better results with the second one, suggesting more efficacy and tolerance with atypical antipsychotic in comorbid schizophrenic patients, according the conclusions of Sepede et al (2014).

This hypothesis was proposed by another group (Koola et al., 2014), wich opinion was based in the increase of adherence to psychopharmacological treatment, one of the main reasons for worse prognosis in this kind of psychiatric patients (Ameller and Gorwood, 2015). In our sample we observe no drop-out among the patients; for this reason, we suppose paliperidone palmitate is very well tolerated and it increase the adherence, with better outcome in our group. It also permits the reduction of the dosage of concomitant psychopharmacological treatment and it could be reasons which explain the decrease of drug use.

5. Conclusions

Our data support that Paliperidone Palmitate is a safety and effective treatment for patients suffering a psychotic disorder, with or without comorbid drug use, getting the abstinence in a half of the sample.

Paliperidone palmitate also decreases the number of psychiatric admissions, the dosage of another antipsychotics and the use of another non antipsychotic treatment.

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