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Paliperidone Palmitate in Morocco: A Practical Study

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Abstract **Original Research Article**

Schizophrenia can be effectively treated with the various antipsychotics on the market, but relapses, especially following poor compliance, can always recur and cause multiple complications. For this reason, long-acting antipsychotics have been developed. In Morocco, we only have paliperidone palmitate in its two monthly and quarterly forms. Objective: To describe the experience of Arrazi Hospital in Salé in the introduction of long-acting antipsychotics. Materials and methods: A retrospective descriptive and analytical study of 45 patients hospitalized and followed at Arrazi hospital in Salé, over a period between June 2020 and May 2023. The PANSS scale and the CGI clinical global impression scale were used. Results: The median age was 31 years, 88.9% were male, 86.7% had no occupation, 84.4% of participants had schizophrenia. 35.6% of patients had been hospitalized for between 5 and 10 years, and 35.6% for between 10 and 20 years. 84.4% of patients smoked, 80% used cannabis, and 15.56% had attempted suicide. The mean duration of treatment with paliperidone was 9.51 months ± 7.65. There was a statistically significant difference ($p<0.001$) between PANSS scores at admission, at D30 and at last observation, and also a statistically significant difference between PANSS scores at admission, at D30 and at last observation. Conclusion: Today, several formulations of long-acting antipsychotics are available, of which only paliperidone palmitate is available in Morocco. These treatments have proven their effectiveness in ensuring good therapeutic compliance.

Keywords: schizophrenia, long-acting antipsychotic, paliperidone palmitate.

INTRODUCTION

Schizophrenia is a severe chronic illness characterized by profound disturbances in thinking and perception, the symptoms of which can be grouped into two main categories: "positive" symptoms such as delusions, hallucinations and disorganization, and "negative" symptoms such as blunted affect and alogia [1]. This pathology can be effectively treated with the various antipsychotics on the market, but relapses and acute reactivations can still occur, leading to hospitalization and poor results for maintenance treatment [2, 3]. This relapse problem can be effectively treated by antipsychotics, but poor or non-adherence to orally administered treatments will compromise the effects of the drugs, since it is one of the main risk factors for relapse in schizophrenia [4], affecting up to 42% of patients [5]. Intramuscular sustained-release formulations of antipsychotics have been developed to alleviate the problem of compliance [6]. Paliperidone palmitate is a 2nd-generation long-acting antipsychotic, it is the main metabolite of risperidone, which is indicated mainly in the maintenance treatment of schizophrenia and also schizoaffective disorder [7], especially to overcome the problem of therapeutic compliance. In this sense, since 2020, the Arrazi Hospital in Salé has instituted a program for the use of paliperidone palmitate for hospitalized patients. In this study, we describe the hospital's experience in using paliperidone palmitate in its monthly and quarterly forms.

STUDY METHODOLOGY

This is a retrospective descriptive and analytical study of 45 patients treated at Arrazi Hospital in Salé, based on a review of medical records. The study lasted from June 2020, corresponding to the start of paliperidone palmitate use at Arrazi Hospital, to May 2023. The study involved patients hospitalized and monitored at Arrazi Hospital in Salé.

Inclusion criteria

Patients hospitalized at Arrazi Hospital, treated with paliperidone palmitate. Patients treated at Arrazi Hospital in Salé with paliperidone palmitate.

Exclusion criteria

Patients on other long-acting neuroleptics available in Morocco.

Evaluation tools

Information was collected from the medical records using an evaluation form containing:

- Socio-demographic data,
- Level of education,
- Medical history,
- Previous treatments,
- Diagnosis and total duration of treatment,
- Duration of monthly and quarterly paliperidone palmitate treatment,
- Results of scales used
- Side effects
- Course of treatment.

The scales used:

- **Positive and Negative Symptoms Scale (PANSS)**

The PANSS is a 30-item tool rated from 1 (absent) to 7 (extreme) used to assess psychopathological symptoms in patients with psychotic disorders, particularly schizophrenia. It calculates scores for three main dimensions: positive symptoms (7 items), negative symptoms (7 items) and general psychopathology (16 items).

- **Clinical global impression (CGI) scale**

The CGI consists of 3 items: One of the main advantages of these items is their simplicity of use and their applicability to all forms of pathology, whether simple or co-morbid. The first two items are assessed on a 7-level response scale, while the third item is a composite score that takes into account both efficacy and side effects. We used only:

- Assessment of the current severity of the patient's mental disorder. (CGI- severity) CGI-S: to assess severity at D0 and at the last consultation
- Assessment of patients' overall improvement (CGI-improvement) CGI-C: to estimate patients' improvement at last visit.

DATA MANAGEMENT AND ANALYSIS

First, we described our sample according to various socio-demographic characteristics, clinical features and history, as well as therapeutic history. Quantitative variables were expressed as mean ± standard deviation, while qualitative variables were expressed as percentages. Next, we compared PANSS scores at D1, D30 and D90, and CGI scores at admission and last observation. Means were compared using Student's t-test (CGI: two independent quantitative variables with Gaussian distribution) and repeated measures ANOVA (PANSS: three matched quantitative variables with Gaussian distribution). In all statistical tests, the significance level was set at 0.05. Statistical analysis was performed using JAMOVI software.

RESULTS

Descriptive statistics

We recruited 45 patients during this period.

Socio-demographic characteristics

Table 1: Socio-demographic data

Socio-demographic characteristics		Percentage
Age (median)	31 years old	
Sex	Male	88,9%
	Female	11,1%
Marital status	Single	80%
	Married	17,8%
	Divorced	2,2%
Level of education	Never attended school	2,2%
	Primary	26,7%
	Secondary	53,3%
	higher	17,7%
Living area	Urban	88,9%
	rural	11,1%
Profession	No profession	86,7%
	Stable job	4,4%
	Day laborer	6,7%
	Student	2,2%

Pathology data

84.4% of participants in this study were treated with paliperidone palmitate for schizophrenia, 13.3% for schizoaffective disorder and only 2.2% for bipolar disorder. The duration of illness in our sample was less than 5 years in 11.1% of patients, between 5 and 10 years in 35.6%, between 10 and 20 years in 35.6% and more than 20 years in 17.8%. With regard to the number of hospitalizations, 33.3% of participants were hospitalized 2 times, 13.3% of patients were hospitalized 3 times and 11.1% for more than 15 times. In terms of antecedents, 8.89% of participants had no notable pathological antecedents, while tobacco use was present in 84.4% of patients and cannabis in 80%. 8.89% of patients (4) had

a medical history (1 case of UC, 1 case of diabetes, 1 case of hypertension and 1 case of dyslipidemia).

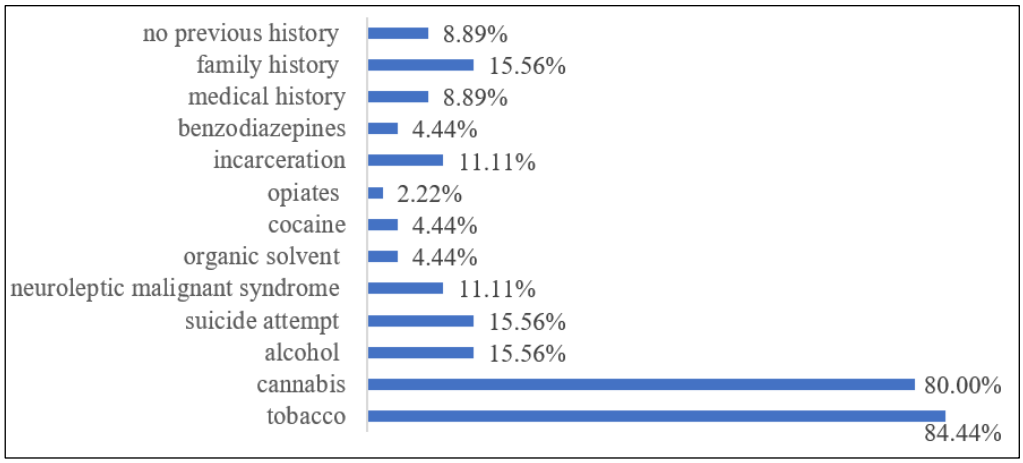

Figure 1: Distribution of patients by history

The time between the onset of illness and initiation of antipsychotic treatment was also studied, and the results were as follows: 51.1% of participants were started on treatment within one year of the onset of symptoms, 17.8% after 1 year, 6.7% after 2 years, 13.3% after 3 years, 2.2% after 4 years, and 4.4% after more than 5 years. Concerning treatment received prior to paliperidone palmitate. All patients in our sample had received risperidone, but prior to this, they had received several treatments, as described in Figure 2.

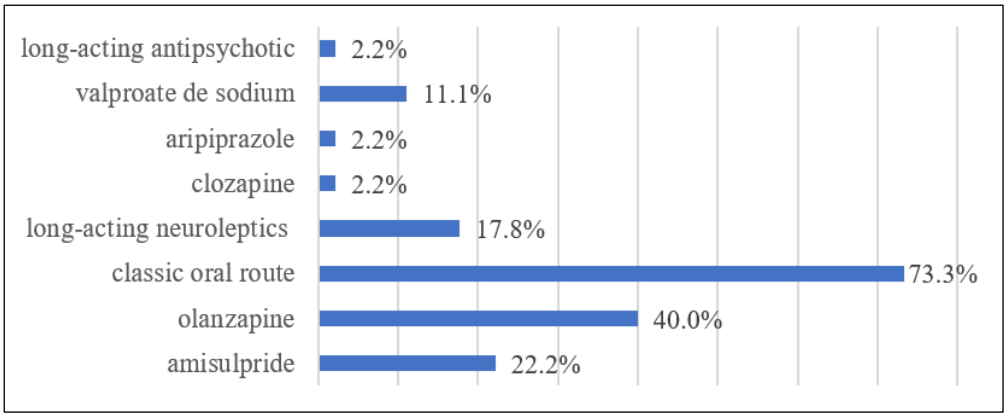

Figure 2: treatments received before paliperidone palmitates

The duration of paliperidone treatment ranged from 1 to 27 months, with an average of 9.51 ± 7.65 months. The PANSS was taken for our patients before treatment, after one month and after 3 months. PANSS values before treatment ranged from 50 to 116, with a mean of 86.7. After one month, PANSS values ranged from 44 to 95, with an average of 59.2, and after 3 months, PANSS varied from 32 to 90, with an average of 46.5.

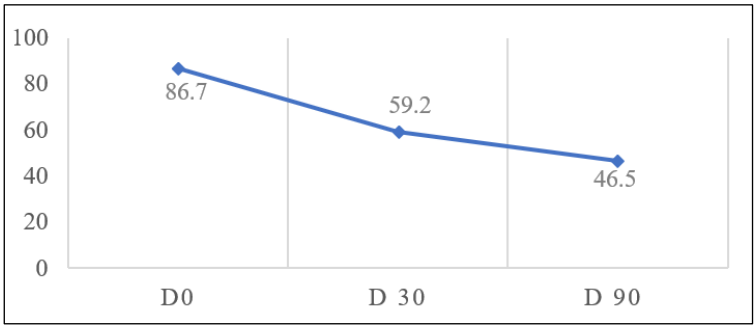

Figure 3: The evolution of PANSS

The severity of the disease was estimated using the CGI-S, which was taken before treatment and at the last consultation. Results obtained before treatment ranged from 4 to 7, with an average of 5.87. At the last consultation, the score varied between 4 and 7, with an average of 4.36.

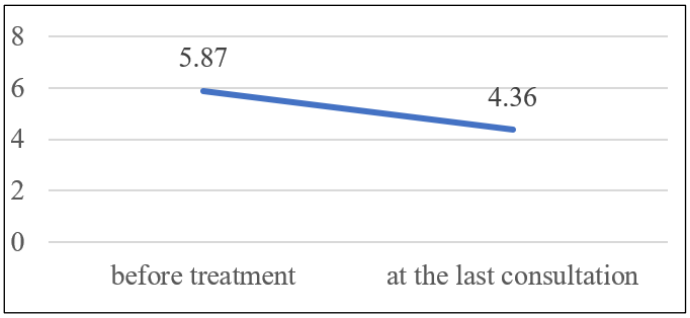

Figure 3: The evolution of CGI-S

For improvement, the CGI-C was used: before treatment, the scale value was 0 for all patients, whereas at the last consultation, the CGI-C value varied between 1 and 4, with an average of 2.42.

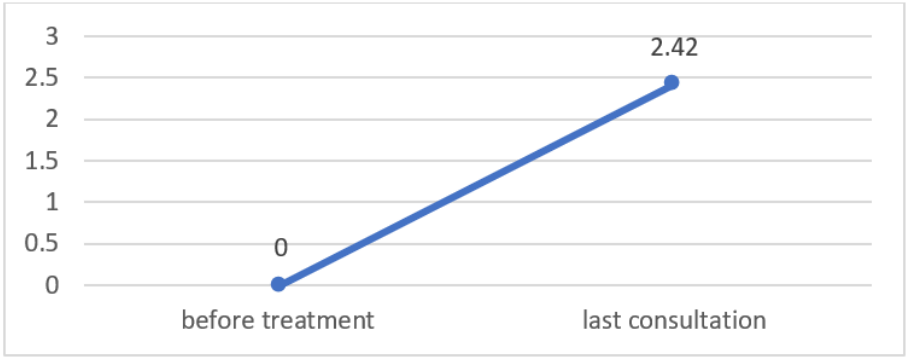

Figure 4: The evolution of the CGI-C

11.1% of study participants relapsed, 15.6% stopped treatment, and 8.9% lost sight of their condition 22.2% of patients were placed on long-acting paliperidone palmitate in its quarterly form, with an average treatment duration of 5.2 months. Side effects included somnolence in 4.4% of cases, and hyperprolactinemia leading to treatment discontinuation in 2.2% of cases. Pain at the injection site was reported by 13.3% of participants, and 2.2% reported nasopharyngitis.

Comparison of our sample according to PANSS score

In our sample (Table 2), there was a statistically significant difference ($p<0.001$) between PANSS scores at admission, at D30 and at D90. Indeed, the mean difference between the PANSS score at admission and at D30 was 25.7, while this difference was even greater between the score at admission and that at D90 (40.2). At the same time, there was a statistically significant difference between PANSS scores at D30 and D90 ($p<0.001$), with a mean difference of 12.7.

Table 2: Comparison of PANSS scores at D1, D30 and D90

	J1	J30	J90	p-value
PANSS[1]	86.7 ± 16	59.2±12	46.5 ± 12.7	<0.001

[1] : Mean ± standard deviation

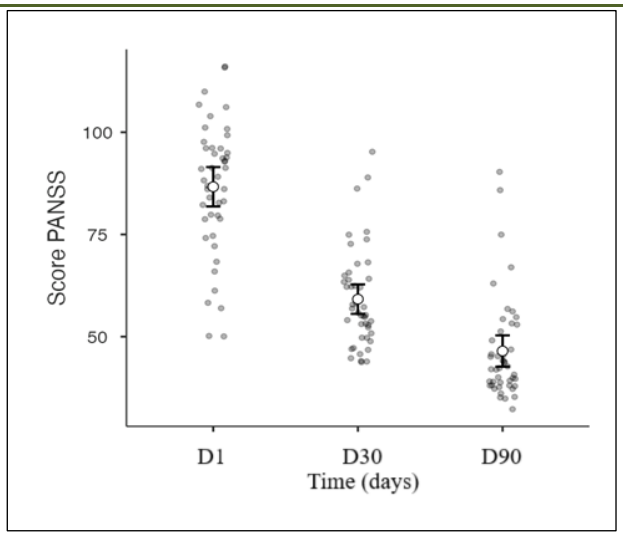

Figure 5: Evolution of PANSS score at D1, D30, and D90

Comparison of our sample according to CGI score

In our sample (Table 3), there was a statistically significant difference (p<0.001) between CGI-C scores at admission and at last observation. The mean difference was 2.41. Concerning CGI-S score, there was a statistically significant difference between admission and last observation (p<0.001) with a mean difference of 1.51.

Table 3: Comparison of CGI scores at admission and at last observation

	Admission	Last observation	p-value
CGI-C[1]	0	2.41 ± 0.658	<0.001
CGI-S[1]	5.87± 0.757	4.36± 0.679	<0.001

[1] : Mean ± standard deviation

DISCUSSION

Long-acting injectable antipsychotics have demonstrated their efficacy in psychiatry, however, their use in clinical practice remains limited. These drugs are mainly used to improve compliance in patients with schizophrenia, particularly those with severe symptoms, poor compliance, a history of frequent hospitalizations and unsatisfactory clinical outcomes [8]. Similarly, a Spanish study compared long-acting injectable antipsychotics with oral antipsychotics, revealing a lower risk of hospitalization in patients on injectable antipsychotics [9]. The efficacy of paliperidone in the treatment of schizophrenia has been the subject of a number of studies, such as the meta-analysis by Taro and colleagues, which objectiveizes the efficacy of paliperidone in its two forms, oral and depot injectable, compared with placebo in the treatment of schizophrenia, whether in its reactivation phase or maintenance [10]. Another study published in 2015 evaluated the efficacy of paliperidone palmitate compared with oral antipsychotics, especially during the early stages of the illness, and demonstrated the superior efficacy of the long-acting injectable antipsychotic compared with those administered orally in terms of time to relapse [8].

An Italian study published in 2019 concluded that paliperidone palmitate is a highly recommended therapeutic option for the short-term treatment of schizophrenia, given the changes induced by this treatment, notably the improvement in PANSS, CGI-S, CGI-C scores. With regard to its long-term use, the available data suggest that extended-release paliperidone not only maintains the improvements observed during the acute phases of treatment, but is also capable of inducing further improvements in both symptoms and personal and social functioning [11]. The present study showed an improvement in patients' PANSS, CGI-S and CGI-C scores after inclusion in the paliperidone palmitate program at Arrazi Hospital in Salé, and 11.1% of participants experienced at least one relapse during the study period. In the same vein, randomized double-blind clinical trials conducted over a period of 9 to 13 weeks have provided strong evidence for the efficacy of long-acting paliperidone palmitate versus 25 to 100 mg doses and placebo in improving acute symptoms of schizophrenia [12]. A review of 19 clinical trials controlled by placebo or an active comparator confirmed that patients on long-acting paliperidone injection showed significant improvement in psychotic symptoms, while exhibiting similar tolerability to treatment compared with the placebo group [13, 14]. Finally, the new formulation of paliperidone administered every 3 months (i.e., four times a year) also proved effective in prolonging the time to relapse in schizophrenic patients, compared with placebo administration [15].

In terms of side effects, quarterly paliperidone palmitate showed similar adverse effects to the monthly

formulation [16]. These included sleep disturbances, nasopharyngitis (the most common), injection-site skin reactions, extrapyramidal effects (particularly akathisia and Parkinsonism), weight gain, hyperprolactinemia and tachycardia [17, 18]. Previous studies have also reported that the adverse effects of antipsychotics (such as akathisia, sexual dysfunction and weight gain) often lead to non-adherence and drug resistance [19]. In our study 20% of participants had side effects, including 13.3% of patients with injection site pain. Demet Sağlam Aykut's study published in 2018, mentioned that patients treated with paliperidone palmitate reported fewer side effects than those on second-generation antipsychotics and that this reduction may lead to better adherence to treatment with paliperidone palmitate. It is therefore essential to promote the appropriate use of long-acting injectable antipsychotics in the management of schizophrenic patients, particularly those with compliance difficulties, in order to reduce the risk of hospitalization and improve clinical outcomes. In addition, it is important to consider the early use of these antipsychotics to improve therapeutic prospects in patients from the onset of the illness.

CONCLUSION

Non-adherence to treatment remains a major challenge in the management of patients suffering from schizophrenia. In the 1960s, the first depot antipsychotics were introduced to promote treatment adherence. However, their limited efficacy on negative symptoms and their tendency to cause extrapyramidal side effects led to restricted use. Today, several formulations of second-generation long-acting antipsychotics are available, of which only paliperidone palmitate is available in Morocco. This advance has considerably altered the treatment perspective, from a simple means of improving compliance to first-line drugs with proven efficacy and tolerability. Despite its advantages, the cost of paliperidone palmitate remains relatively high in Morocco and is not yet reimbursed by any insurance scheme, making it difficult for many patients to afford. However, it is important to note that first-generation antipsychotics are still prescribed, as not all second-generation molecules are available in Morocco. They represent an important therapeutic strategy not only for patients with a long disease course and poor compliance, but also for those in the early stages of the disease.

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