



Exploring the therapeutic benefits of paliperidone in the management of schizophrenia: A promising approach for the mental well-being of this population

Explorando os benefícios terapêuticos da paliperidona no manejo da esquizofrenia: Uma abordagem promissora para o bem-estar mental dessa população

DOI: 10.56238/isevjhv3n2-029

Receipt of originals: 04/09/2024

Acceptance for publication: 04/29/2024

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ABSTRACT

Paliperidone is a safe and effective option for the treatment of schizophrenia, with long-acting oral or intramuscular administration. Its low hepatic metabolism and renal excretion minimize complications in patients with pre-existing liver diseases, providing greater adherence and therapeutic efficacy. The current study is a literature review, with an active search for “Paliperidone” and “Schizophrenia” on national and international platforms. 21 articles were analyzed in the PubMed and Scielo databases. Twenty-one articles were selected based on evaluation of the title, abstract and relevance to the study. The publication period ranged from 2007 to 2024, all were organized according to title, authorship, year of publication and methodology used. The data demonstrate the consistent efficacy of paliperidone in relieving schizophrenic symptoms, its safety and tolerability, highlighting its ability to improve patients' quality of life. Although adverse events were observed, these were generally mild and did not compromise treatment continuity. In summary, the data support paliperidone as an effective and safe therapeutic option for schizophrenia, with the potential to improve patients' clinical and psychosocial outcomes. Paliperidone is an effective and well-tolerated option to treat schizophrenia, with studies indicating better patient adherence and clinical stability. Its low incidence of serious side effects increases long-term safety. This reduces relapse and hospitalization rates, improving quality of life.

Keywords: Antipsychotics, Schizophrenia, Paliperidone Palmitate, Mental disorders.

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INTRODUCTION

Schizophrenia is a disabling mental disorder that directly affects the cognitive and behavioral ability to make decisions and interact socially (Lin et al., 2021; LI et al., 2023) . Considering the clinical manifestations, it is necessary to have at least one or more of the following symptomatological criteria: thought disorder, delusions, hallucinations, disorganized motor behavior and negative symptoms. The process of diagnosing schizophrenia in Brazil, as guided by the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition), ensures that treatments are appropriately targeted to patients who really need them. This process is divided into criteria A to F, which detail the requirements for an accurate diagnosis.

In the therapeutic approach, Paliperidone, a second-generation antipsychotic, has stood out as an effective and safe option for the treatment of schizophrenia, when compared to other available antipsychotics, exerting its function against psychotic symptoms, on an outpatient basis and reducing hospital stays. (Elkis ; Louzã , 2007; VATS et al., 2023). Paliperidone can be administered by two routes: intramuscularly, depot, in a single dose every month or orally, in a single dose, with prolonged action, monthly or daily in smaller doses (DAVIDSON et al., 2007).

It has good adherence and therapeutic efficacy, due to the administration of safe doses, providing a treatment with few side effects for patients suffering from schizophrenia along with other comorbidities (VATS et al., 2023).

The advantage of the therapeutic use of paliperidone is its low hepatic metabolism, which minimizes the risk of complications in patients with pre-existing liver diseases (viral hepatitis, hepatic steatosis, liver toxicity and others). Furthermore, its main route of excretion is renal, which contributes to less burden on the liver and, consequently, reduces the risk of adverse effects related to hepatic metabolism (VATS et al., 2023).

Given the above, the evidence suggests superiority in the treatment of schizophrenia with the use of paliperidone in relation to other antipsychotics, both first and second generation. This finding is fundamental for clinical decision-making, as it indicates paliperidone as a promising therapeutic option, standing out for its efficacy and safety profile. The choice of an appropriate antipsychotic is crucial in the management of schizophrenia, and paliperidone is a valuable alternative, with better clinical results and patients' quality of life. Therefore, the study aims to describe the efficacy and safety of using paliperidone when choosing medication in the context of schizophrenia.



METHODOLOGY

PubMed databases in March 2024, using the following descriptors searched through the Health Science Descriptors (DECS): “Paliperidone”, “Schizophrenia”, these combined using the Boolean operator *AND*, being searched in English and Portuguese.

Based on the established filters, this study was based on freely available published scientific articles, published between 2007 and 2024 and also in full on the aforementioned search platforms. The exclusion criteria included repeated scientific publications or those whose topic did not fully address the objective of this study. Thus, using these criteria, the searches concluded with 21 results, of which 1 result was found in SciELO, 20 results in PubMed . All publications were selected for title and summary reading.

RESULTS

A total of 21 articles were delimited in the methodology, all of which had their title and abstract evaluated, were read in full and, as they covered the objective of the study, were selected to compose the present study. Of the 21 selected, the oldest study was published in 2007 and the most recent in 2024. All articles were separated by title, authorship, year of publication and methodology used, as shown in Table 1.

Table 1. Analysis of selected articles, regarding title, authors, year of publication and design .

Title	Authors	Year of Publication	Methodology
Achieving better outcomes for schizophrenia patients in Hong Kong	LoWA . et al.	2021	SYSTEMATIC LITERATURE REVIEW
New antipsychotics for the treatment of schizophrenia.	ELKIS, H. et al.	2007	SYSTEMATIC LITERATURE REVIEW
Paliperidone palmitate, a potential long-acting treatment for patients with schizophrenia	Kramer M. et al.	2010	RANDOMIZED, DOUBLE-EARLY, PLACEBO-CONTROLLED EFFECTIVENESS AND SAFETY STUDY
Efficacy, safety and early response of paliperidone extended-release tablets (paliperidone ER)	Davidson M. et al.	2007	PLACEBO-CONTROLLED RANDOMIZED STUDY
One-year open-label safety and efficacy study of paliperidone extended-release tablets in patients with schizophrenia.	Kramer M. et al.	2010	OPEN LABEL EXTENSION
Treatment of Patients With Schizophrenia and Comorbid Chronic Hepatitis With Paliperidone	Vats A. et al.	2023	SYSTEMATIC REVIEW



Long-term efficacy of antipsychotic drugs in initially acutely ill adults with schizophrenia: systematic review and network meta-analysis.	Leucht S. et al.	2023	SYSTEMATIC REVIEW AND META-ANALYSIS
Second-Generation Antipsychotic Drugs for Patients with Schizophrenia	Rognoni C. et al.	2021	SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS
Real-World Evidence of the Clinical and Economic Impact of Long-Acting Injectable Versus Oral Antipsychotics Among Patients with Schizophrenia in the United States	Lin D. et al.	2021	SYSTEMATIC REVIEW AND META-ANALYSIS
Long-acting injectable antipsychotics for early psychosis	Lian L. et al.	2022	COMPREHENSIVE SYSTEMATIC REVIEW
Paliperidone palmitate vs. paliperidone extended-release for the acute treatment of adults with schizophrenia	Kishi T. et al.	2022	SYSTEMATIC REVIEW AND PAIRED AND NETWORK META-ANALYSIS
Effectiveness and Safety of Switching from Oral Antipsychotics to Once-Monthly Paliperidone Palmitate (PP1M) in the Management of Schizophrenia	Li Q. et al.	2023	SYSTEMATIC REVIEW AND META-ANALYSIS
Antipsychotic-Induced Weight Gain	Wu H. et al.	2022	DOSE-RESPONSE META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS
Benefits and harms of Risperidone and Paliperidone for treatment of patients with schizophrenia or bipolar disorder	Hodkinson A. et al.	2021	META-ANALYSIS
Calibrated meta-analysis to estimate the efficacy of mental health treatments in target populations	Hong H. et al.	2023	META-ANALYSIS
Efficacy, acceptability and side-effects of oral versus long-acting injectable antipsychotics	Wang D. et al.	2024	SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS
Characteristics of patients with schizophrenia switching from oral antipsychotics to once-monthly paliperidone palmitate (PP1M)	Li Q. et al.	2024	SYSTEMATIC REVIEW
Efficacy and safety of paliperidone extended-release tablets	Marder SR. et al.	2007	PLACEBO-CONTROLLED RANDOMIZED STUDY
A controlled, evidence-based trial of paliperidone palmitate, a long-acting injectable antipsychotic, in schizophrenia	Nasrallah HA. et al.	2010	EVIDENCE-BASED CONTROLLED TRIAL
A randomized, placebo-controlled study to assess the efficacy and safety of 3 doses of paliperidone palmitate in adults with acutely exacerbated schizophrenia	Pandina GJ. et al.	2010	RANDOMIZED PLACEBO-CONTROLLED STUDY



Efficacy and safety of paliperidone palmitate in adult patients with acutely symptomatic schizophrenia: a randomized, double-blind, placebo-controlled, dose-response study	Gopal S. et al.	2010	RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED DOSE-RESPONSE STUDY
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Source: Own

DISCUSSION

By exploring the findings and conjectures provided by the literature on the efficacy, safety, tolerability and clinical implications of the use of paliperidone in the treatment of schizophrenia, existing knowledge was synthesized and areas requiring further investigation were identified. The data analyzed in this discussion consistently reveal the efficacy of paliperidone in the management of schizophrenia, corroborating previous findings and highlighting its position as a valuable therapeutic option for patients with this condition.

However, it is crucial to recognize the limitations of the studies discussed and the knowledge gaps that still persist. Future research should address outstanding questions such as the long-term efficacy and safety of paliperidone, the factors that influence individual response to treatment, and the mechanisms underlying the drug's therapeutic effects.

EFFECTIVENESS OF PALIPERIDONE IN THE TREATMENT OF SCHIZOPHRENIA

The analysis of the discussion on the effectiveness of paliperidone in the management of schizophrenia is based on data from multiple sources, including controlled clinical trials, observational studies, and meta-analyses. A key point is the ability of paliperidone, regardless of the form of administration or dose, to alleviate a wide range of symptoms associated with schizophrenia such as hallucinations and delusions (Vats A. et al. 2023). In the studies evaluated, the paliperidone dose groups showed significant improvement over placebo in the Positive and Negative Syndrome Scale (PANSS) total score, as well as clinical global impression severity scores and Marder factor scores of negative and negative symptoms. PANSS positives (Nasrallah HA. et al. 2010).

Furthermore, relapse and hospitalization rates are important indicators of success in treating schizophrenia. Patients undergoing treatment with paliperidone have longer intervals between relapses, lower hospitalization rates, and less likelihood of discontinuing treatment (Lian L. et al., 2023). These results represent clinically meaningful improvements for patients with schizophrenia, as relapses of the disease are associated with a substantial social and economic burden.



The administration of paliperidone results in a notable improvement in patients' adherence to medication, which in turn would lead to better clinical and psychosocial treatment outcomes. Furthermore, there is a significant reduction in neurotoxicity and side effects experienced by patients, when compared to other antipsychotics. Better medication adherence tends to reduce relapse and treatment interruption rates, reducing the occurrence of remission (Lo WA. et al. 2021).

This increase in the use of paliperidone would also contribute to reducing the social burden on patients, since the reduction in relapses would result in less brain damage. Taking all these aspects into account, the costs associated with the treatment of schizophrenia, including hospitalizations and outpatient visits, would tend to decrease. Consequently, reducing hospitalization and relapse rates would ease the workload of healthcare professionals, allowing them to focus more effectively on psychosocial approaches and reintegrating patients into the community. Ultimately, increased use of paliperidone would result in a higher quality of care for patients, thanks to better adherence to treatment (Lo WA. et al. 2021).

Follow-up studies further indicate that this efficacy is maintained in the long term, with reduced rates of relapse and hospitalization in patients who continue treatment. This consistency in results over time reinforces confidence in the efficacy of paliperidone as a stable and reliable therapeutic option for the management of schizophrenia. (Li Q. et al., 2023).

These findings suggest that paliperidone may play a key role in improving quality of life and reducing the burden associated with schizophrenia due to paliperidone's high efficacy, greater safety, and greater patient satisfaction. (Vats A. et al. 2023) However, it is essential to consider individual factors, such as patient tolerability profile and personal preferences, when making treatment decisions.

SAFETY AND TOLERABILITY OF PALIPERIDONE

Detailed analysis of the results revealed that the Personal and Social Performance Scale showed significant improvement between the treatment groups, except the 12mg dose, suggesting a benefit in the ability to maintain daily and social activities of patients undergoing different therapeutic regimens (Marder SR . et al. 2007). With regard to treatment safety, the overall incidence of emergent adverse events was comparable between groups, indicating an acceptable safety profile for paliperidone compared to placebo.

One of the main extrapyramidal symptoms linked to the treatment of schizophrenia is parkinsonism, which was observed at similar rates in the groups receiving placebo (5%) and



paliperidone (5-6% between doses). These findings suggest that paliperidone did not significantly increase the risk of extrapyramidal side effects compared to placebo, thus providing an important safety assurance for its clinical use (Nasrallah HA. et al. 2010).

Regarding common treatment-emergent adverse events, as defined by occurrence in $\geq 2\%$ of patients in either treatment group, a higher incidence was observed in the paliperidone group compared to the placebo group (Pandina GJ. et al .2010). However, it is important to highlight that the majority of these events were mild to moderate in nature and did not result in treatment discontinuation. Events such as dizziness, sedation, pain in extremities and myalgia were the most reported, with statistically significant differences between groups (Nasrallah HA. et al. 2010).

It is important to highlight that all doses of paliperidone demonstrated efficacy and good general tolerability, both in relation to local and systemic adverse events. Adoption of this revised dosing regimen allowed rapid and consistent achievement of therapeutically effective plasma levels. Furthermore, the adverse effects associated with the use of paliperidone are comparable to those of placebo, giving it superior tolerability compared to other available antipsychotics. Due to this high tolerability, patients showed better tolerance to paliperidone compared to other antipsychotic agents (Vats A. et al. 2023).

Another point is the metabolic profile of paliperidone, since when compared to other antipsychotics it presents a less harmful metabolic profile, as it has a low probability of producing drug interactions, considering that the cytochrome P450 (CYP) enzyme system in the liver metabolizes it. only marginally. The only two CYP isoenzymes known to partially degrade paliperidone are CYP 3A4 and 2D6 (Vats A. et al. 2023).

Assessing the safety and tolerability of paliperidone is crucial in clinical practice, as it influences treatment adherence and the patient's general well-being. The data suggest that paliperidone has a favorable safety and tolerability profile, with a low incidence of serious adverse effects. The most common adverse events, such as akathisia, sedation and weight gain, are generally tolerable and rarely lead to treatment discontinuation (Nasrallah HA. et al. 2010).

CONCLUSION AND FINAL CONSIDERATIONS

Paliperidone has stood out as an effective and well-tolerated therapeutic option in the management of schizophrenia. Studies have shown that patients undergoing treatment with paliperidone have more consistent adherence to medications when compared to other available therapeutic options. The low incidence of serious adverse events associated with the use of



paliperidone provides greater safety to its use, making it a therapeutic option attractive to patients and healthcare professionals.

paliperidone as a promising therapeutic alternative in the management of schizophrenia becomes evident. Its ability to promote greater adherence to treatment, combined with its good tolerability and clinical efficacy, makes it a valuable choice for patients facing the challenges of this mental condition. However, it is essential that more randomized, double-blind research with case-control groups be carried out to assess long-term effectiveness and the impact on patients' quality of life, aiming to improve the care offered to this population.



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