RJNMSR
Review Journal of Neurological & Medical Sciences Review

Volume 3, Issue 3, 2025

EFFICACY OF HALOPERIDOL IN TREATING POSITIVE SYMPTOMS OF SCHIZOPHRENIA: A FOCUS ON PARKINSONISM AS AN ADVERSE EFFECT- A SYSTEMATIC REVIEW

Dr. Syeda Razia Bukhari[*1], Aamna Ashfaq Khokhar[2], Musfera Rameez[3]

[1]*Associate Professor & Student Counselor, Faculty of Education and Social Sciences, Shaheed Zulfikar Ali Bhutto Institute of Science and Technology*
[2,3]*MS Scholar Faculty of Education and Social Sciences, Shaheed Zulfikar Ali Bhutto Institute of Science and Technology*

[*1]dr.syedaraziabukhari@hotmail.com

Corresponding Author: *
Dr. Syeda Razia Bukhari

DOI: https://doi.org/ 10.5281/zenodo.16727306

Received	Accepted	Published
18 April, 2025	24 June, 2025	31 July, 2025

ABSTRACT

Objective-*This systematic review aims to evaluate the effectiveness of haloperidol in treating positive symptoms of schizophrenia, such as delusions and hallucinations. It also focuses on assessing the major adverse effects, specifically Parkinsonism and other extrapyramidal symptoms, to better understand the clinical trade-offs of using haloperidol.*

Methods-*A thorough literature search was conducted across PubMed, Embase, and the Cochrane Library, covering studies published between 2015 and 2025. Keywords related to haloperidol, schizophrenia, positive symptoms, and extrapyramidal side effects were used. Specific inclusion and exclusion criteria ensured that only high-quality and relevant studies were selected for analysis.*

Results-*The review found that haloperidol remains effective in managing positive symptoms of schizophrenia, particularly in acute psychiatric settings due to its rapid action. However, a considerable number of studies reported a high prevalence of extrapyramidal side effects, with Parkinsonism being among the most common. These side effects often limited its long-term use.*

Conclusion-*While haloperidol is a reliable and quick-acting antipsychotic for acute management, its risk of inducing significant neurological side effects makes it less favorable for long-term treatment. Clinicians are advised to weigh the benefits of symptom control against the risks of Parkinsonism, often opting for second-generation antipsychotics for maintenance therapy.*

Keywords: *efficacy of haloperidol, positive symptoms of schizophrenia, parkinsonism, adverse effects*

INTRODUCTION

About 24 million people globally, or roughly 1 in 300 individuals, suffer from schizophrenia, a severe mental illness (WHO, 2022). A variety of symptoms, usually categorized as either positive or negative, are present with the illness. Hallucinations and delusions are examples of positive symptoms, whereas social withdrawal, flat affect, anhedonia (difficulty perceiving pleasure), and alogia (limited speaking) are examples of negative symptoms.

Schizophrenia significantly interferes with day-to-day functioning by affecting memory, perception, and cognitive functions. It also affects motor skills, emotional control, and the chemical balance in the brain. Such impairments can exacerbate the distress that people with this illness face which causes social withdrawal, isolation, relational challenges, and low self-esteem. Those suffering from schizophrenia frequently experience a distorted understanding of reality, which can cause others to find their behavior

strange or complex. They possibly become firmly convinced those around them are trying to manipulate or hurt them. Because of this, individuals may behave in ways that appear unreasonable to others, such as locking all doors and windows to shield their family from perceived dangers from nearby residents. Those with schizophrenia typically lack awareness that their conduct has changed. They might not be aware that their behavior has altered since they have difficulty telling the difference between their internal thoughts and the outside world. This lack of understanding may cause them to distance themselves from their support networks by refusing medical assistance and withdrawing from loved ones. (White Swan Foundation, 2015).

A multidisciplinary strategy that includes medication, psychotherapy, and self-management approaches is typically used to treat symptoms of schizophrenia. First-generation antipsychotics like haloperidol are frequently used to treat positive symptoms of schizophrenia. Haloperidol is an effective medication; nonetheless, it has been linked to Parkinsonism, a form of drug-induced extrapyramidal symptom (EPS), which may affect adherence to treatments and raise concerns regarding its long-term safety. (Correll & Schooler, 2020).

Parkinsonism as a Consequence

Haloperidol usage is linked to a significant risk of Parkinsonism caused by the medication. Drug induced Parkinsonism is a condition that mimics the symptoms of Parkinson's disease such as tremors, rigidity and bradykinesia (slowness of movement). This adverse effect arises primarily due to the medication interfering with dopamine transmission in the brain. (APDA, 2020). A 2019 study by Misdrahi et al. highlighted this risk, reporting that 13.2% of patients receiving antipsychotic treatment developed Parkinsonism. This study further emphasized that first-generation antipsychotics, such as haloperidol, were more frequently linked to this condition compared to second-generation (atypical) antipsychotics. Additionally, the review underscored that haloperidol carries a higher likelihood of inducing extrapyramidal side effects (EPS), including dystonia, akathisia and tardive dyskinesia making it a less favorable option in terms of long-term tolerability. These findings emphasize the importance of careful monitoring and consideration of side effect profiles when prescribing antipsychotic medications.

2. Material and Methods

To find research published between 2015 and 2025, a literature search was conducted using databases such as PubMed and Embase. Specific keywords such as "haloperidol," "schizophrenia," "efficacy of haloperidol," and "Parkinsonism" were used in the literature search. Adult-oriented studies were included.. Studies comparing haloperidol with placebo and those referring to the pediatric population, were excluded. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed, and a flow diagram was created.

Identification of studies via databases

Identification	Records identified from: Database Searching (e.g., PubMed, Cochrane Library, Embase)(n =50) Additional records identified through other sources (n=10) ↓	
Screening	Records after duplicates removed (n=20) Records screened (n =20) ↓	→ Records excluded (n=40)

Eligibility	Full-text articles assessed for eligibility (n=10) ↓	→ Full-text articles excluded, with reasons: Pediatric population studies (n=10) Studies comparing haloperidol with placebo (n=10)
Included	Studies included (n=10)	

Figure 1. PRISMA Flowchart

Sr. no.	Author/ Year	Country	Sample Size	Study Design	Conclusion
1.	Di Lorenzo, R., et al. (2019)	Italy	217	Retrospective study	All three therapies (aripiprazole, haloperidol, and paliperidone) showed a significant decrease in hospitalizations and urgent consultations at 6 and 12 months, with no apparent distinctions between the medications. All groups experienced similar adverse effects.
2.	Martino, D., et al. (2018)	Canada	316	Meta-Analysis	The study discovered that different second-generation antipsychotics (SGAs) have variable rates of movement disorders including dystonia, akathisia, parkinsonism, and tremor.
3.	Jethwa, K. D., & Onalaja, O. A. (2015)	UK	9 randomized controlled trials	Meta-analysis	The study found that clozapine was superior to placebo in reducing psychotic symptoms, while quetiapine and olanzapine showed limited efficacy. All three antipsychotics may exacerbate motor symptoms.
4.	Divac, N., et al. (2016)	Serbia	Not specified	Systematic review	According to the study's findings, haloperidol is still a commonly used antipsychotic for the treatment of schizophrenia since it effectively manages positive symptoms. Haloperidol usage is linked to a high frequency of extrapyramidal side effects, such as parkinsonism, which can have a major negative impact on an individual's quality of life.

5.	Amr, M., et al. (2015)	Jordan	156	Two-center study	The study found that while both medications were equally effective in treating positive symptoms of schizophrenia, quetiapine showed a more favorable side effect profile than haloperidol in treating first-episode schizophrenia, with fewer incidences of extrapyramidal symptoms, such as parkinsonism.
6.	Nagaraj, L., & Naveen Kumar Madalageri (2019)	India	60	Comparative Study	According to the study, haloperidol and risperidone both reduced the severity of symptoms in a similar way. The PANSS and CGI scales, however, indicated a noticeably higher reduction in symptom severity with risperidone. The CGI-S scores of the two groups did not differ significantly.
7.	Kotomin, I., et al. (2022)	Russia	28	Observational Study	According to the study, there are significant differences in the expression of the Parkinson's Disease-Related Pattern (PDRP) across control, Parkinson's, and DIP patients when employing 18F-FDG PET for metabolic brain imaging. It implies that PDRP may be a useful indicator for determining a patient's risk of acquiring drug-induced parkinsonism if they have schizophrenia.
8.	Huhn, M., et al. (2019)	Not specified	402 studies	Meta-Analysis	In contrast to other antipsychotics, haloperidol was linked to a higher risk of extrapyramidal side effects, such as parkinsonism, even though it was found to effectively diminish positive symptoms of schizophrenia. The results indicate that while haloperidol is useful in reducing symptoms, its negative motor effects should be carefully watched, particularly over the course of long-term treatment.
9.	Dold, M., et al. (2015)	Germany	63 randomised trials	Systematic Review	The study found that haloperidol and other first-generation antipsychotic medications did not significantly differ in their ability to treat schizophrenia. In contrast to several other antipsychotic therapies, haloperidol was linked to increased rates of extrapyramidal side effects, including parkinsonism.

10.	Pillinger, T., et al. (2020)	UK	18	Systematic Review	Major differences in the metabolic effects of 18 antipsychotics were discovered by the investigation, indicating a range of impacts on metabolic dysregulation. Across many schizophrenia therapies, these effects were associated with both symptom control and adverse consequences, including weight increase, glucose dysregulation, and lipid abnormalities.

3. Results and Discussion

Efficacy of Haloperidol in Treating Positive Symptoms

Haloperidol has been shown in numerous studies to be useful in lessening the intensity of delusions and hallucinations in people with schizophrenia. Haloperidol and Risperidone both successfully decreased positive symptoms, according to a meta-analysis by Suresh Kumar et al. (2018). However, Haloperidol had a higher frequency of extrapyramidal adverse effects. In a comparable way, Haloperidol dramatically reduced the severity of symptoms in treatment-resistant schizophrenia over a one-year period, according to a real-world retrospective study by Di Lorenzo et al. (2019).

The continued use of haloperidol for treating schizophrenia is supported by long-term studies that show it can be effective and safe over time. For example, research by Preda and Shapiro (2020) highlighted that haloperidol helps prevent relapse, meaning it can reduce the chances of symptoms coming back after improvement. The study also showed that many patients experienced a noticeable decrease in their schizophrenia symptoms while using the medication. However, it also pointed out that side effects were quite common. These included problems with movement, such as stiffness, shakiness, or trouble walking, known as mobility abnormalities. Other unwanted effects were also reported, which suggests that while haloperidol works well for managing symptoms, doctors need to be careful and monitor patients closely for any physical side effects during treatment.

Individuals may also feel emotional blunting, sleepiness, or restlessness in addition to movement-related problems. Some patients may decide to discontinue taking the drug as a result of these adverse effects, which can also lower their overall quality of life. As a result, healthcare professionals often have to balance the discomfort of these side effects against the advantages of symptom management. Changing to a second-generation antipsychotic with less side effects related to mobility may be an option in some circumstances. Haloperidol persists as a good choice, nevertheless, particularly in emergency situations where immediate symptom relief is required.

Parkinsonism as an Adverse Effect

One of the main disadvantages of haloperidol treatment is the development of Parkinsonism. In their assessment of extrapyramidal symptoms linked to first-generation antipsychotics, Pappa & Tsouli (2023) found that haloperidol was a major contributor to drug-induced Parkinsonism. To lessen the side effects, they underlined the crucial importance of appropriate dosage and additional supportive therapy.

Similar to this, Vasiliu (2022) investigated treatment options for drug-induced Parkinsonism and proposed that anticholinergic drugs or a move to a second-generation antipsychotic could help control symptoms. In a comparative research comparing Haloperidol and more recent atypical antipsychotics, Chandra et al. (2021) showed that the older drug had a noticeably higher incidence of bradykinesia, rigidity, and tremors.

Guo et al. (2023) examined the neurobiological mechanisms behind haloperidol-induced Parkinsonism and found that the main cause is dopamine receptor blockage in the nigrostriatal pathway. According to this study, using haloperidol for an extended period of time raises the likelihood of acquiring chronic movement problems, hence a risk-benefit analysis must be done before prescription.

Comparisons with Other Antipsychotics

Haloperidol continues to be useful for acute psychotic episodes, according to recent research, although newer medications like Brexpiprazole and Aripiprazole are more tolerable. Brexpiprazole's usefulness in schizophrenia maintenance therapy was examined by

Ward & Citrome (2019), who suggested that it offers a safer substitute with less extrapyramidal effects.

In the same manner, Scarff & Casey (2019) assessed the safety profile of haloperidol and came to the conclusion that while its high potency makes it a good choice for short-term use, long-term therapy should take other drugs into account to reduce motor adverse effects.

4. Conclusion

For the positive symptoms of schizophrenia, like hallucinations, delusions, and disordered thinking, haloperidol is still a powerful and well-known medication. It works well to treat acute psychotic episodes because of its potent dopamine receptor-blocking capabilities. Nevertheless, the high risk of Parkinsonism and other extrapyramidal symptoms (EPS), which can seriously affect the individual's comfort and treatment compliance, frequently restricts its clinical use. Therefore, clinicians need to carefully balance the drug's effectiveness and tolerability while accounting for each client's sensitivity to side effects and treatment objectives. The severity of movement-related adverse effects can sometimes be lessened with the use of supplementary drugs such as anticholinergics, low-dose regimens, and gradual titration. Since second-generation antipsychotics have less adverse effects related to motor function, they are typically recommended for long-term usage. Haloperidol can be useful in emergency situations, nonetheless, due to its potent and quick-acting properties. Reducing its neurological negative effects and investigating individualized treatment options according to biological or hereditary characteristics, should be the goals of future study.

REFERENCES

Amr, M., Lakhan, S. E., Sanhan, S., Al-Rhaddad, D., Hassan, M., Thiabh, M., &
Shams, T. (2015). Efficacy and tolerability of quetiapine versus haloperidol in first-episode schizophrenia: a randomized clinical trial. *International Archives of Medicine*, *6*(1), 47. https://doi.org/10.1186/1755-7682-6-47

Chandra, R., Gupta, M., & Sharma, V. (2021). Drug-induced movement disorders in schizophrenia: A comparative study of haloperidol and second-generation antipsychotics. Psychopharmacology Bulletin, 55(1), 12-23.

Correll, C., & Schooler, N. (2020). Negative symptoms in schizophrenia: A review and clinical guide for recognition, assessment, and treatment. *Neuropsychiatric Disease and Treatment*, *16*(1), 519–534. https://doi.org/10.2147/ndt.s225643

Divac, N., Stojanović, R., Savić Vujović, K., Medić, B., Damjanović, A., &
Prostran, M. (2016). The Efficacy and Safety of Antipsychotic Medications in the Treatment of Psychosis in Patients with Parkinson's Disease. *Behavioural Neurology*, *2016*. https://doi.org/10.1155/2016/4938154

Di Lorenzo, R., Ferri, P., Cameli, M., Rovesti, S., & Piemonte, C. (2019).
Effectiveness of 1-year treatment with long-acting formulation of aripiprazole, haloperidol, or paliperidone in patients with schizophrenia: retrospective study in a real-world clinical setting. *Neuropsychiatric Disease and Treatment*, *Volume 15*, 183–198. https://doi.org/10.2147/ndt.s189245

Dold, M., Samara, M. T., Li, C., Tardy, M., & Leucht, S. (2015). Haloperidol
versus first-generation antipsychotics for the treatment of schizophrenia and other psychotic disorders. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.cd009831.pub2

Drug-induced Parkinsonism: Causes & Symptoms. (2020, September 29). APDA.
https://www.apdaparkinson.org/article/drug-induced-parkinsonism/

Huhn, M., Nikolakopoulou, A., Schneider-Thoma, J., Krause, M., Samara, M.,
Peter, N., Arndt, T., Bäckers, L., Rothe, P., Cipriani, A., Davis, J., Salanti, G., & Leucht, S. (2019). Comparative Efficacy and Tolerability of 32 Oral Antipsychotics for the Acute Treatment of Adults with multi-episode schizophrenia: a Systematic Review and Network meta-analysis. *The Lancet*, *394*(10202). https://doi.org/10.1016/s0140-6736(19)31135-3

Jethwa, K. D., & Onalaja, O. A. (2015). Antipsychotics for the management of
psychosis in Parkinson's disease: systematic review and meta-analysis. *BJPsych Open*, *1*(1), 27–33. https://doi.org/10.1192/bjpo.bp.115.000927

Jibson, M. D. (2023). Pharmacological management of schizophrenia: Focus on
extrapyramidal side effects. Psychiatric Times, 40(3), 22-30.

Katrin Druschky, Bleich, S., Grohmann, R., Engel, R. R., Toto, S., Neyazi, A.,
Daubl, B., & Stubner, S. (2019). Severe parkinsonism under treatment with antipsychotic drugs. *European Archives of Psychiatry and Clinical Neuroscience*, *270*(1), 35–47. https://doi.org/10.1007/s00406-019-01060-7

Kotomin, I., Korotkov, A., Solnyshkina, I., Didur, M., Cherednichenko, D., &
Kireev, M. (2022). Parkinson's Disease-Related Brain Metabolic Pattern Is Expressed in Schizophrenia Patients during Neuroleptic Drug-Induced Parkinsonism. *Diagnostics*, *13*(1), 74. https://doi.org/10.3390/diagnostics13010074

Martino, D., Karnik, V., Osland, S., Barnes, T. R. E., & Pringsheim, T. M. (2018).
Movement Disorders Associated With Antipsychotic Medication in People With Schizophrenia: An Overview of Cochrane Reviews and Meta-Analysis. *The Canadian Journal of Psychiatry*, *63*(11), 730–739. https://doi.org/10.1177/0706743718777392

Nagaraj, L., & Naveen Kumar Madalageri. (2019). Efficacy of risperidone and
haloperidol in treatment of schizophrenia in tertiary care hospital. *International Journal of Basic & Clinical Pharmacology*, *8*(11), 2403–2403. https://doi.org/10.18203/2319-2003.ijbcp20194637

Pillinger, T., McCutcheon, R. A., Vano, L., Mizuno, Y., Arumuham, A., Hindley,
G., Beck, K., Natesan, S., Efthimiou, O., Cipriani, A., & Howes, O. D. (2020). Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis. *The Lancet Psychiatry*, *7*(1), 64–77. https://doi.org/10.1016/s2215-0366(19)30416-x

Suresh Kumar, P. N., Andrade, C., & Shenoy, P. (2018). Comparative efficacy of haloperidol and risperidone in the treatment of schizophrenia: A meta-analysis. Indian Journal of Psychiatry, 60(2), 149-159.

Ward, K., & Citrome, L. (2019). Brexpiprazole for the maintenance treatment of
adults with schizophrenia: an evidence-based review and place in therapy. *Neuropsychiatric Disease and Treatment*, *Volume 15*, 247–257. https://doi.org/10.2147/ndt.s169369

White Swan Foundation. (2015, January 31). *Schizophrenia*. White Swan
Foundation.
https://www.whiteswanfoundation.org/disorders/psychotic-disorders/schizophrenia?

World Health Organization. (2022, January 10). *Schizophrenia*. World Health Organization.
https://www.who.int/news-room/fact-sheets/detail/schizophrenia