Journal of Pharmacology, Genetics and Molecular Biology (JPGMB)
ISSN: 3049-3757 | Vol. 01, Issue-04, July-Aug, 2025

Comparative Study of First- And Second-Generation Antipsychotics in Schizophrenia

Nidhi Solanki[1*], Riddhi Prajapati[1], Namrata vyas[1], Anjali Luhana[1]

[1]Shree Swaminarayan University, Kalol, Gandhinagar, Pin: 382725

***Corresponding Author E-mail: nidhijsolanki20@gmail.com**

ABSTRACT

Schizophrenia is a long-term mental illness that needs long-term antipsychotic medication to deal with its many symptoms. The goal of this study was to assess the effectiveness and side effects of first-generation (typical) and second-generation (atypical) antipsychotics in people with schizophrenia. There were 100 patients in total, and they were split into two equal groups. One group got first-generation antipsychotic medication, and the other group got second-generation antipsychotic medication. The Positive and Negative Syndrome Scale (PANSS), the Simpson-Angus Scale (SAS), and the Clinical Global Impression (CGI) scale were all used to rate the intensity of symptoms, extrapyramidal side effects, and overall clinical improvement. The results showed that patients who were given second-generation antipsychotics had much lower PANSS and SAS scores and showed more clinical improvement on the CGI scale. The results were statistically significant ($p < 0.05$) and back up the idea that SGAs work better and are easier to handle than FGAs. This study shows how important it is to put SGAs first when treating schizophrenia with drugs in order to have better results and improve the quality of life for patients.

Key Words:

Schizophrenia, First-Generation Antipsychotics, Second-Generation Antipsychotics, PANSS, Extrapyramidal Symptoms, Clinical Global Impression

Article History:

Received on Feb 13, 2025

Revised on March 18, 2025

Accepted on July 18, 2025

Published on Aug 3, 2025

DOI: https://doi.org/10.64062/JPGMB.Vol1.Issue4.5

1. INTRODUCTION

Schizophrenia is a serious and long-lasting mental illness that causes problems with thinking, seeing things, feeling things, and acting. It affects about 1% of people around the world and often makes it hard for them to work and socialize. Pharmacological treatment is still the most important part of managing schizophrenia. Antipsychotic drugs are necessary to control symptoms and avoid relapses[1]. Over time, two main types of antipsychotics have been made: first-generation (typical) and second-generation (atypical) antipsychotics. Both works to lessen psychotic symptoms, but they are very different in terms of their receptor patterns, side effects, and clinical outcomes[2]. There is a rising demand for research that compare second-generation antipsychotics to standard therapy in terms of their real-world effectiveness and safety as the transition toward these drugs continues[3].

1.1.Background information

First-generation antipsychotics (FGAs), which came out in the 1950s, work mostly by inhibiting dopamine D2 receptors[4]. They are good at reducing positive symptoms like hallucinations and delusions. But using them often leads to extrapyramidal side effects (EPS),

ISSN: 3049-3757 | Vol. 01, Issue-04, July-Aug-2025

which can make it much harder for patients to stick to their treatment and live a good life. Second-generation antipsychotics (SGAs)[5], which came out in the 1990s, work on more receptors and are less likely to cause EPS. They also help with negative symptoms and cognitive problems to some extent[6]. Even though they are widely used, there is still dispute about whether SGAs are better in clinical practice because treatment responses might vary and they can be expensive. So, it is important to use standardized clinical outcomes to compare different treatments for schizophrenia in order to make evidence-based prescribing decisions[7].

1.2.Statement of the problem

Both FGAs and SGAs are used to treat schizophrenia, although there isn't a lot of agreement on which type works better for certain types of patients[8]. A lot of the studies that are already out there don't use standardized measurement techniques or don't take into account how well people can handle the symptoms in real life[9]. Also, even if clinical recommendations say that SGAs are better, their higher cost and different side effect profiles mean that we need to look more closely at how they are better than FGAs. Without clear evidence of how different treatments compare, doctors may have a hard time making the best judgments about how to treat patients while keeping their quality of life, safety, and effectiveness in mind[10]. This study tries to fill that gap by utilizing validated clinical assessment techniques to compare the two medication groups in depth.

1.3.Objectives of the study

- To compare the effectiveness of first-generation and second-generation antipsychotics in managing positive, negative, and general psychopathological symptoms in patients with schizophrenia using the PANSS scale.
- To assess and compare the incidence and severity of extrapyramidal side effects associated with first- and second-generation antipsychotics using the Simpson-Angus Scale (SAS).
- To evaluate the overall clinical improvement in patients treated with FGAs and SGAs using the Clinical Global Impression (CGI) scale.
- To statistically analyze the differences in treatment outcomes between the two groups and determine the clinical significance of the observed variations.

2. METHODOLOGY

The goal of this study was to examine how well first- and second-generation antipsychotics worked and what adverse effects they caused in people with schizophrenia. A quantitative, observational, and cross-sectional methodology was used to look at how well the two drug classes worked and how well they were tolerated.

2.1.Research Design

The study used a cross-sectional, comparative, and observational research design. The main goal was to look at the clinical outcomes and side effects of using both conventional (first-generation) and atypical (second-generation) antipsychotic drugs.

2.2.Participants/Sample Details

The sample included 100 people between the ages of 18 and 55 who had been diagnosed with schizophrenia and were getting treatment at a tertiary psychiatric care centre. There were 50

patients in each group: one group got first-generation antipsychotics while the other group got second-generation antipsychotics. This study employed convenience sampling and left out patients who had other mental illnesses, abused drugs, or didn't follow their treatment plan.

2.3.Instruments and Materials Used

Data were collected using the following standardized tools:

- Positive and Negative Syndrome Scale (PANSS) to assess symptom severity.
- Simpson-Angus Scale (SAS) for extrapyramidal symptoms.
- Clinical Global Impression Scale (CGI) for overall clinical improvement.
- Medical records and medication charts were also reviewed to confirm drug adherence and history.

2.4.Procedure and Data Collection Methods

After getting permission from the institutions and the participants, trained psychiatrists did the clinical interviews. We wrote down important demographic and clinical information. During regular follow-up visits, the scales were implemented to evaluate the severity of symptoms and side effects. For standardization, each person was tested at the same time.

2.5.Data Analysis Techniques

This research used SPSS software to look at the data we had gathered. This study employed descriptive statistics like mean, standard deviation, and percentages for demographic data. We used inferential statistics, such as the Independent Samples t-test and the Chi-square test, to look at the differences in clinical scores and side effects between the two groups. It was thought that a p-value of less than 0.05 was statistically important.

3. RESULTS

This section shows the results of comparing the clinical effectiveness and side effects of FGAs and SGAs in people with schizophrenia. Collected information about demographics, the intensity of symptoms (PANSS), extrapyramidal symptoms (SAS), and overall clinical improvement (CGI). After the tables, there is a full statistical analysis.

3.1.Demographic Characteristics of Participants

The two groups were similar in their demographic profiles, with no statistically significant differences in age, gender distribution, or duration of illness.

Table 1: Demographic Profile of Participants

Variable	FGA	SGA
Age Range (years)	20–53	21–51
Number of Males	29	31
Number of Females	21	19
Duration of Illness (years)	2–14	2–13

ISSN: 3049-3757 | Vol. 01, Issue-04, July-Aug-2025

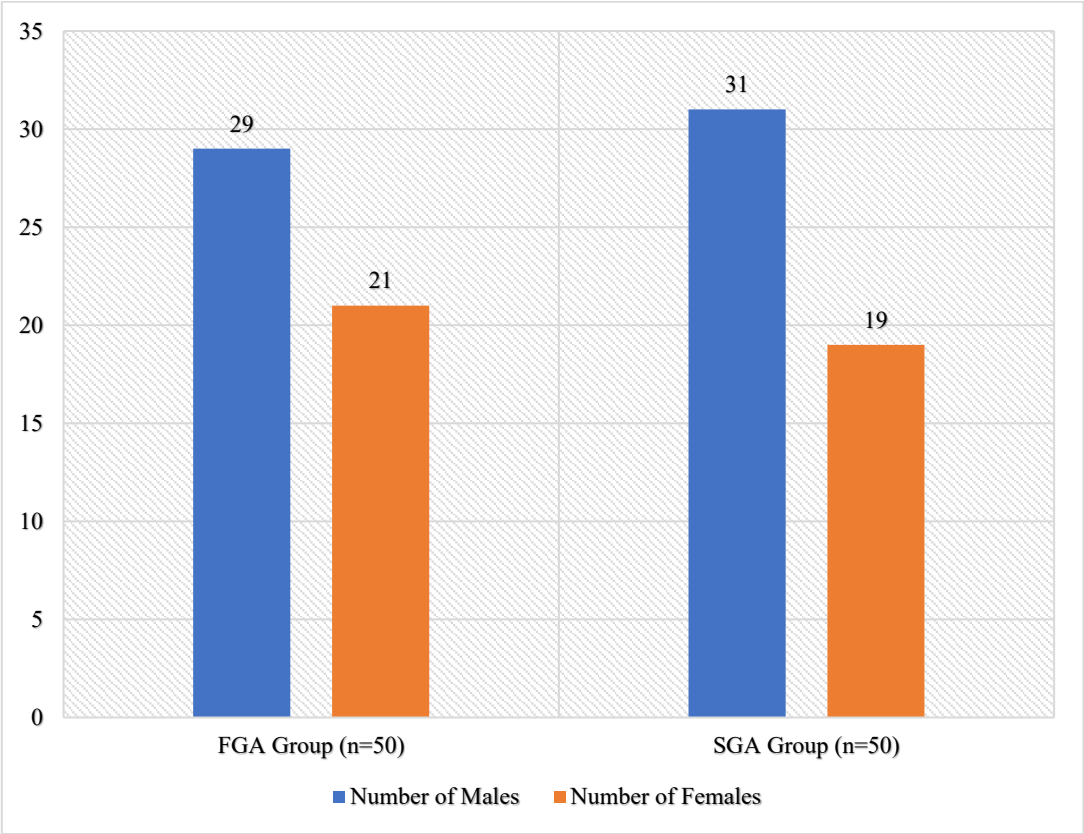

Figure 1: Gender of Participants

Table 1 shows the demographic information about the people who took part in both the FGA and SGA groups. The ages of the people in the FGA group were between 20 and 53 years, while the ages of the people in the SGA group were between 21 and 51 years. There were also almost the same number of men and women in both groups, with FGA having 29 men and SGA having 31 men. The FGA group had illnesses that lasted anywhere from 2 to 14 years, and the SGA group had illnesses that lasted anywhere from 2 to 13 years. This shows that their medical histories were similar. These commonalities show that the two groups were similar in terms of demographics, which means that the treatment outcomes could be compared fairly without any big differences at the start.

3.2. Symptom Severity Based on PANSS Scores

This study used the PANSS to rate how bad the symptoms of schizophrenia were in three main areas: positive symptoms, negative symptoms, and general psychopathology. Researchers in the field of clinical research often use this scale to measure how well antipsychotic medication works. The total domain scores for both the FGA group and the second-generation antipsychotic (SGA) group were determined in this study. These scores show how many symptoms were present in each category. A lower total score means greater control of symptoms.

Journal of Pharmacology, Genetics and Molecular Biology (JPGMB)
ISSN: 3049-3757 | Vol. 01, Issue-04, July-Aug-2025

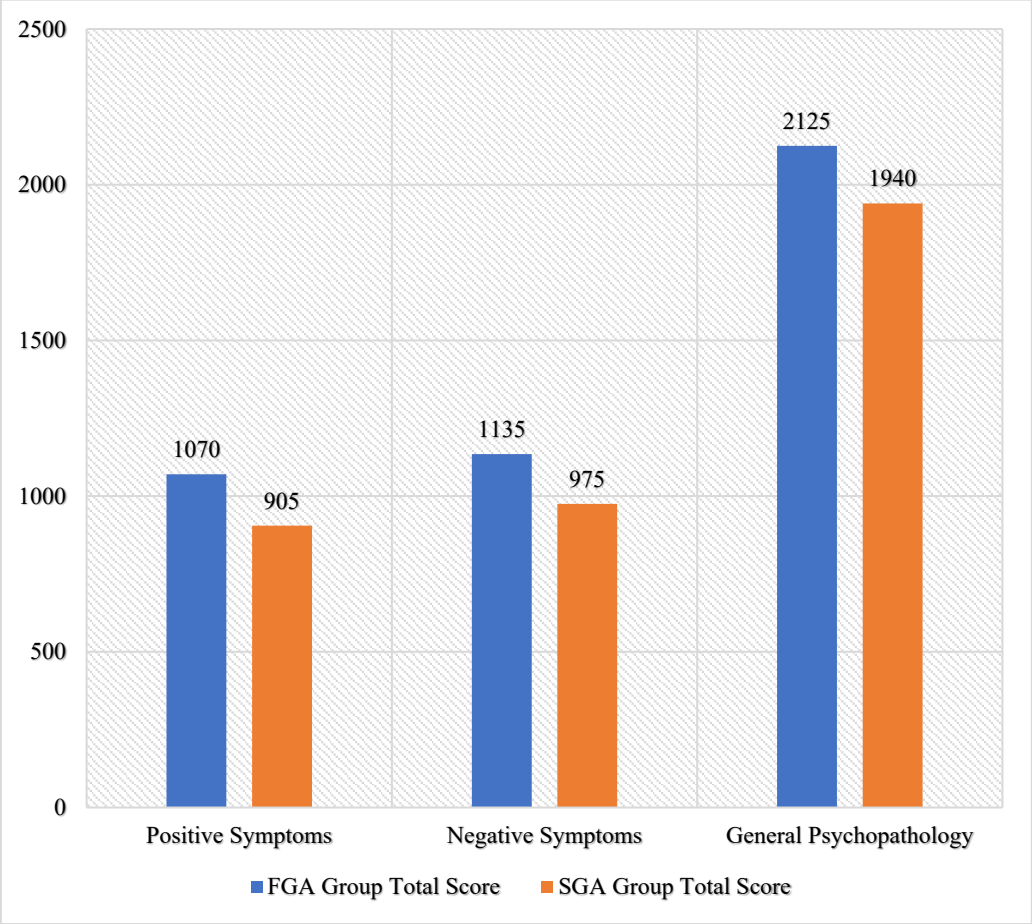

Figure 2: PANSS Domain Scores

Figure 2 shows that the total PANSS scores were always lower in the SGA group than in the FGA group in all areas. Specifically, people on SGAs had a score of 905 in the positive symptom category, while people taking FGAs had a score of 1070. This means that they had fewer hallucinations, delusions, and other symptoms. In the same way, the SGA group (975) had less severe negative symptoms such social disengagement and emotional flattening than the FGA group (1135). The general psychopathology score, which covers anxiety, depression, and cognitive disorganization, was similarly lower for SGAs (1940 vs. 2125). These data imply that second-generation antipsychotics worked better than first-generation medicines at lowering the overall symptom burden in people with schizophrenia.

3.3. Extrapyramidal Symptoms (SAS Scores)

Extrapyramidal symptoms (EPS) are movement problems caused by drugs that are often linked to antipsychotic treatments, especially first-generation ones. The Simpson-Angus Scale (SAS) was used to find out how much EPS affected the people who took part. This scale looks at indications like rigidity, tremor, and bradykinesia, which are common neurological adverse effects that people on antipsychotic treatment describe. Higher SAS scores mean that the motor side effects are worse. This part shows a comparison of the overall SAS scores for the two groups that got therapy.

Journal of Pharmacology, Genetics and Molecular Biology (JPGMB)
ISSN: 3049-3757 | Vol. 01, Issue-04, July-Aug-2025

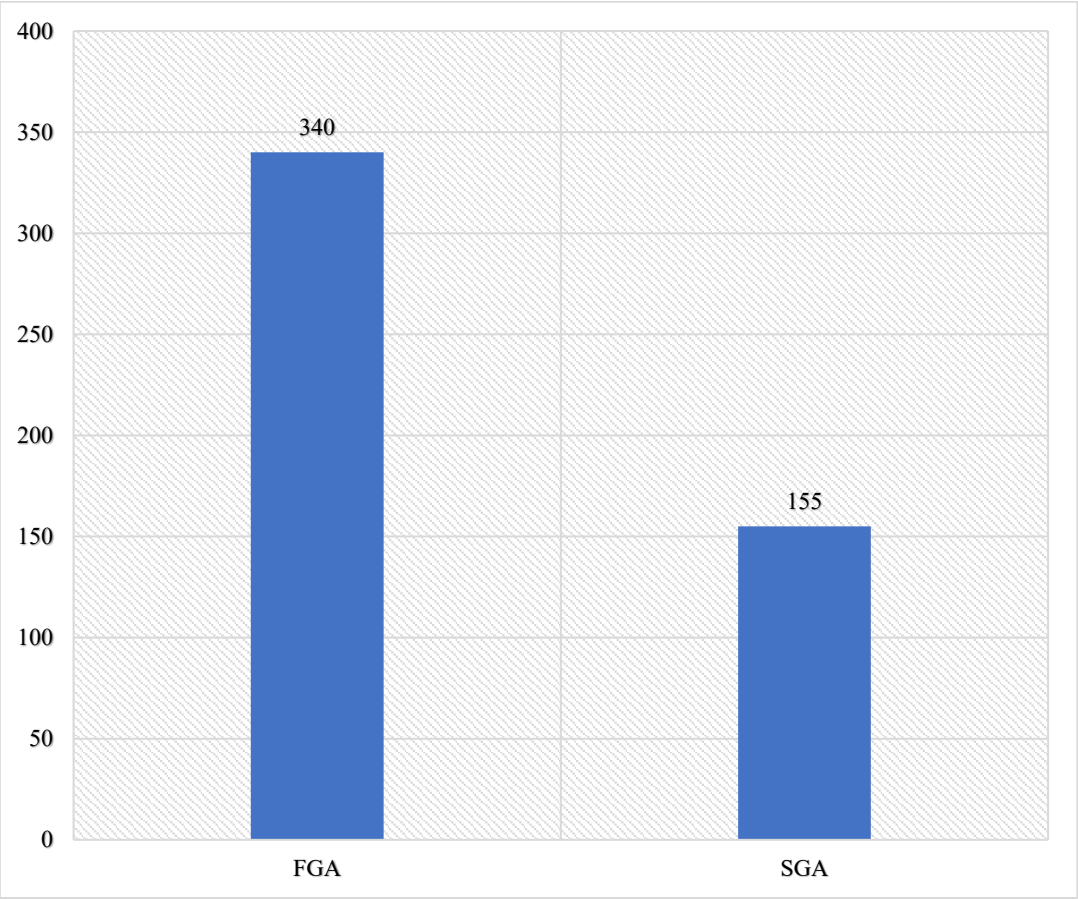

Figure 3. Total SAS Scores

The first-generation antipsychotic (FGA) group had a total SAS score of 340, which was far higher than the second-generation antipsychotic (SGA) group's score of 155. This means that patients who were given FGAs had more severe and frequent extrapyramidal symptoms than those who were given SGAs. The FGA group had a higher SAS score, which is consistent with what other research has found: conventional antipsychotics tend to cause more movement-related side effects because they block dopamine D2 receptors more strongly. On the other hand, SGAs seem to have a better tolerance profile for motor side effects because they affect more receptors and don't bind as tightly to D2 receptors.

3.4. Overall Clinical Improvement (CGI Scores)

This study utilized the Clinical Global Impression (CGI) scale to look at how much better the schizophrenia patients were doing overall in both therapy groups. This scale, which is graded by a doctor, gives a complete picture of how severe the patient's disease is and how well they are responding to therapy. This makes it a useful tool for comparing how well antipsychotic drugs work in the real world. At the end of the observation period, the total CGI scores show the average ratings from all participants in each group.

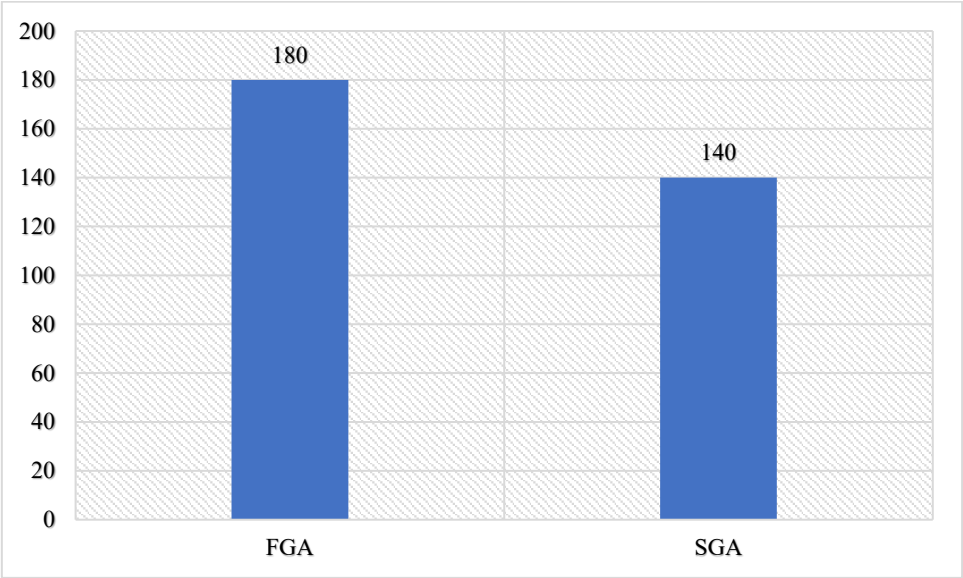

Figure 4. Total CGI Scores

The SGA group had a lower overall CGI score (140) than the FGA group (180). This means that patients who used second-generation antipsychotics saw more clinical improvement. This data shows that SGAs were better at lowering the total symptom burden and improving the general functioning of patients because lower CGI scores mean that people thought they were getting better. The result is in line with what other studies have found: SGAs tend to be more tolerated and lead to better outcomes in the treatment of schizophrenia. The independent t-test showed that this difference was statistically significant ($p < 0.001$), which supports the idea that SGAs are better than FGAs for global therapeutic response.

3.5.Statistical analysis

The data were analyzed using Independent Samples t-tests and Chi-square tests in SPSS. The results are presented below in standardized format:

Table 2. Independent Samples t-test for PANSS Scores

PANSS Domain	Levene's Test for Equality of Variances (F)	Sig.	t	df	Sig. (2-tailed)	Mean Difference
Positive Symptoms	1.482	0.226	4.654	98	0	3.9
Negative Symptoms	0.764	0.384	4.003	98	0	4.6
General Psychopathology	1.102	0.296	3.03	98	0.003	7.1

The findings of the Independent Samples t-test show that there are statistically significant differences between the FGA and SGA groups in all three PANSS domains. The t-value (4.654,

ISSN: 3049-3757 | Vol. 01, Issue-04, July-Aug-2025

p = 0.000) and mean difference of 3.9 show that patients on SGAs experienced a lot fewer positive symptoms than those on FGAs. In the same way, the t-value (4.003, p = 0.000) and mean difference of 4.6 for negative symptoms also point to SGAs. In the area of general psychopathology, the difference was again statistically significant (t = 3.03, p = 0.003), with SGAs doing better than FGAs by an average of 7.1. All of these results together show that second-generation antipsychotics were better at controlling symptoms of schizophrenia in all areas that were assessed.

Table 3. Independent Samples t-test for SAS and CGI Scores

Variable	Levene's F	Sig.	t	df	Sig. (2-tailed)	Mean Difference
SAS Scores	2.334	0.13	11.232	98	0	3.7
CGI Scores	0.982	0.325	4.195	98	0	0.8

Table 3 shows the results of the independent samples t-test that compared the SAS (Simpson-Angus Scale) and CGI (Clinical Global Impression) ratings between the FGA and SGA groups. The research found a statistically significant difference in SAS scores (t = 11.232, p < 0.001), which means that patients on FGAs had a lot more extrapyramidal side effects than those on SGAs. The CGI scores also showed a big difference (t = 4.195, p < 0.001), with the SGA group demonstrating more overall clinical improvement. The average differences of 3.7 for SAS and 0.8 for CGI show that SGAs were not only more tolerated, but they also worked better to improve patients' overall health.

Table 4. Chi-square Test for Gender Distribution

Variable	Value	df	Asymptotic Significance (2-sided)
Gender	0.324	1	0.568

With 1 degree of freedom, the Chi-square test for gender distribution gave a value of 0.324 and a p-value of 0.568. This means that there was no statistically significant difference in the gender makeup of the FGA and SGA groups. This means that both groups were similar in terms of gender, thus any disparities in treatment outcomes that were seen can't be explained by differences in gender.

4. DISCUSSION

The goal of this study was to assess the clinical effectiveness and side effect profiles of first-generation (typical) and second-generation (atypical) antipsychotics in people with schizophrenia. The results show that the two types of drugs are very different when it comes to controlling symptoms, causing extrapyramidal side effects, and overall clinical improvement. This study gives us useful information about the therapeutic benefits of second-generation

antipsychotics in a real-world clinical setting by employing standardized assessment methods and statistical analysis.

4.1.Interpretation of results

The results showed that patients who were given second-generation antipsychotics (SGAs) did far better on all of the evaluated measures. The SGA group had better control over positive, negative, and general psychopathological symptoms, as shown by their PANSS scores. This is in line with previous research that suggests SGAs are better at relieving symptoms, especially negative ones that are hard to treat.

The SGA group also had far lower Simpson-Angus Scale (SAS) scores, which shows that they had fewer extrapyramidal side effects than the FGA group. The difference is probably because SGAs have different pharmacological profiles. They have a lower affinity for dopamine D2 receptors and a stronger serotonergic activity, which makes them easier to tolerate.

The Clinical Global Impression (CGI) scores backed up these results even more, suggesting that patients in the SGA group had more overall clinical improvement. The fact that SGAs are statistically significant in all critical areas shows that they not only work better at controlling symptoms but also improve overall functioning with fewer side effects.

4.2.Comparison with existing studies

The results of this study are very similar to what other studies have found on how second-generation antipsychotics (SGAs) work better and are easier to tolerate than first-generation antipsychotics (FGAs). Fabrazzo et al. (2022)[11] looked at real-world data and confirmed that SGAs are more effective overall and have less side effects in normal clinical settings, which is in line with our findings that the SGA group had better symptom control and fewer extrapyramidal side effects. Yang et al. (2023)[12] showed that SGAs, especially long-acting injectable ones, lead to less use of healthcare and lower overall costs, even though they are more expensive. This is the same conclusion our study came to when we recommended that SGAs be given priority in clinical practice. Bahta et al. (2021)[13] have talked about how extrapyramidal symptoms make it harder for patients to stick with their therapy when they are on FGAs. This supports our findings that higher SAS ratings in the FGA group mean that they are more likely to stop taking their medication because of motor side effects. Brodeur et al. (2022)[14] also found that SGAs are more effective and safer than FGAs in real-world patient populations when it comes to broader clinical outcomes. This supports the lower CGI ratings we saw in our study's SGA group. Finally, Ricci et al.'s (2025)[15] work builds on this idea by stressing that newer antipsychotic drugs not only help with symptoms but also improve cognitive function and safety in early-phase schizophrenia. This is similar to our conclusion that SGAs provide a more complete therapeutic benefit. These comparisons all support the validity of our study's results and show that doctors should consider both efficacy and tolerability when making decisions about how to treat schizophrenia.

4.3.Implications of findings

These results have substantial clinical consequences for how schizophrenia is treated. First, they advocate the continued use of SGAs as the first line of treatment because they work better

and have fewer side effects. Better symptom control with fewer motor adverse effects can greatly improve medication adherence, lower relapse rates, and improve long-term outcomes.

From a healthcare policy point of view, the results show that it is worth spending money to make SGAs more available, especially in public psychiatric healthcare settings. Clinicians may want to make treatment plans more specific to each patient based on their symptoms, how sensitive they are to side effects, and their medical history. However, they should strongly favour SGAs when they are appropriate.

4.4.Limitations of the study

This study has a few problems, even if it gives us useful information. The study only included 100 patients from one tertiary care centre, which may make the results less useful for other groups. The study's cross-sectional design also makes it hard to draw causal conclusions because the results were based on single-point assessments instead of long-term follow-up.

Also, using convenience sampling could lead to selection bias, and patient adherence was inferred from medical records instead of being measured directly. There wasn't a lot of in-depth analysis of confounding variables including changes in dosage, length of treatment, and other health issues that could affect how well the medication works and how well people can tolerate it.

4.5.Suggestions for future research

Future research should try to get around these problems by using a longitudinal design with a bigger and more varied sample. Long-term randomized controlled trials (RCTs) that compare certain SGAs and FGAs could give us stronger data about how well they work, what adverse effects they have, and how to stop them from coming back.

Also, future studies could use pharmacogenetic profiling to look into how genetic characteristics affect how well different antipsychotics work. Adding patient-reported outcomes and quality of life measures would also help us understand how treatment affects more than just reducing clinical symptoms.

5. CONCLUSION

This study that compared first- and second-generation antipsychotics in people with schizophrenia makes it evident that second-generation antipsychotics (SGAs) work better in the clinic. Compared to FGAs, SGAs were better at regulating both positive and negative symptoms, generated less extrapyramidal side effects, and led to better overall clinical improvement. These results support the trend toward using SGAs more and more in current schizophrenia treatment plans.

5.1.Summary of key findings

- Patients on SGAs had significantly lower PANSS scores across positive, negative, and general psychopathology domains, indicating better symptom management.
- SGAs were associated with markedly fewer extrapyramidal symptoms, as reflected in significantly lower SAS scores.

- CGI scores showed greater clinical improvement in the SGA group, confirming their superior therapeutic effect.
- All differences were found to be statistically significant ($p < 0.05$), lending strong support to the reliability of the findings.

5.2.Significance of the study

This study adds important evidence to the continuing assessment of how well antipsychotic drugs work. It recommends the use of second-generation antipsychotics above other types since they have the dual benefit of controlling symptoms and being easier to tolerate. The results are especially important for psychiatrists, clinical psychologists, healthcare providers, and politicians who want to make schizophrenia treatment better and for patients to stick with it.

5.3.Recommendations

- SGAs should be the first choice for treating schizophrenia, especially for people who are susceptible to extrapyramidal side effects.
- Public health systems should make it easier for people to get SGAs, especially in places with few resources, to enhance long-term results.
- It is best to check on progress and adjust treatment on a regular basis using standardized clinical measures like PANSS, SAS, and CGI.
- This study needs bigger, multi-center longitudinal studies to look at long-term outcomes and compare different SGAs with different FGAs for individualized treatment planning.

REFERENCES

1. Schneider-Thoma, J., Hamza, T., Chalkou, K., Siafis, S., Dong, S., Bighelli, I., ... & Leucht, S. (2025). Efficacy of clozapine versus second-generation antipsychotics in people with treatment-resistant schizophrenia: a systematic review and individual patient data meta-analysis. The Lancet Psychiatry.
2. Kearns, B., Cooper, K., Cantrell, A., & Thomas, C. (2021). Schizophrenia treatment with second-generation antipsychotics: a multi-country comparison of the costs of cardiovascular and metabolic adverse events and weight gain. Neuropsychiatric Disease and Treatment, 125-137.
3. Rognoni, C., Bertolani, A., & Jommi, C. (2021). Second-generation antipsychotic drugs for patients with schizophrenia: systematic literature review and meta-analysis of metabolic and cardiovascular side effects. Clinical Drug Investigation, 41(4), 303-319.
4. Leucht, S., Huhn, M., & Davis, J. M. (2021). Should ‘typical’, first-generation antipsychotics no longer be generally used in the treatment of schizophrenia?. European Archives of Psychiatry and Clinical Neuroscience, 271(8), 1411-1413.
5. Pai, N., McGeachie, A. B., Puig, A., Huang, T. H., & Brahmbhatt, P. (2023). Persistence and adherence to second-generation antipsychotic long-acting injectable medications for schizophrenia: a comparative study in the Australian context. Australasian Psychiatry, 31(1), 76-81.
6. Parabiaghi, A., Galbussera, A. A., D’Avanzo, B., Tettamanti, M., Fortino, I., & Barbato, A. (2024). 2001–2021 Comparative Persistence of Oral Antipsychotics in Patients

Initiating Treatment: Superiority of Clozapine in Time-to-Treatment Discontinuation. Pharmacopsychiatry.

7. Reichelt, L., Efthimiou, O., Leucht, S., & Schneider-Thoma, J. (2023). Second-generation antipsychotics and seizures–a systematic review and meta-analysis of serious adverse events in randomized controlled trials. European Neuropsychopharmacology, 68, 33-46.
8. Ohi, K., Muto, Y., Sugiyama, S., & Shioiri, T. (2022). Safety and efficacy in randomized controlled trials of second-generation antipsychotics versus placebo for cognitive impairments in schizophrenia: a meta-analysis. Journal of Clinical Psychopharmacology, 42(2), 227-229.
9. Wang, D., Schneider-Thoma, J., Siafis, S., Burschinski, A., Dong, S., Wu, H., ... & Leucht, S. (2024). Long-acting injectable second-generation antipsychotics vs placebo and their oral formulations in acute schizophrenia: a systematic review and meta-analysis of randomized-controlled-trials. Schizophrenia Bulletin, 50(1), 132-144.
10. Baldez, D. P., Biazus, T. B., Rabelo-da-Ponte, F. D., Nogaro, G. P., Martins, D. S., Signori, J. P. S., ... & Kunz, M. (2025). Haloperidol versus second-generation antipsychotics on the cognitive performance of individuals with schizophrenia and related disorders: pairwise meta-analysis of randomized controlled trials. Trends in Psychiatry and Psychotherapy, 47, e20230664.
11. Fabrazzo, M., Cipolla, S., Camerlengo, A., Perris, F., & Catapano, F. (2022). Second-generation antipsychotics' effectiveness and tolerability: a review of real-world studies in patients with schizophrenia and related disorders. Journal of Clinical Medicine, 11(15), 4530.
12. Yang, C. P., Wu, P. N., Liao, L. T., Lin, T. Y., & Chen, P. S. (2023). Comparison of health resource usage and costs associated with first-generation and second-generation long-acting injectable antipsychotics for patients with schizophrenia: A nationwide population-based cohort study. Asian Journal of Psychiatry, 89, 103789.
13. Bahta, M., Ogbaghebriel, A., Russom, M., Tesfamariam, E. H., & Berhe, T. (2021). Impact of adverse reactions to first-generation antipsychotics on treatment adherence in outpatients with schizophrenia: a cross-sectional study. Annals of General Psychiatry, 20(1), 27.
14. Brodeur, S., Vanasse, A., Courteau, J., Stip, E., Lesage, A., Fleury, M. J., ... & Roy, M. A. (2022). Comparative effectiveness and safety of antipsychotic drugs in patients with schizophrenia initiating or reinitiating treatment: A Real-World Observational Study. Acta Psychiatrica Scandinavica, 145(5), 456-468.
15. Ricci, V., Sarni, A., Martinotti, G., & Maina, G. (2025). Comparative analysis of third-generation antipsychotics in first-episode schizophrenia: efficacy, safety, and cognitive impacts. A narrative review. International Clinical Psychopharmacology, 40(4), 191-206.