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Original Article

Schizophrenic patient's preference for long-acting injectable antipsychotics in Saudi Arabia

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ABSTRACT

Objectives: Gaining insight into patients' preferences for long-acting injectable (LAI) antipsychotics could aid in mitigating potential barriers to the utilization of LAI in patients with schizophrenia.

Methodology: A cross-sectional descriptive study was conducted among schizophrenic patients in Saudi Arabia between June 2023 and October 2023. An analysis was conducted on the responses obtained from the Medication Preference Questionnaire.

Results: There was a subtle trend toward favouring oral antipsychotics over LAIs. Patients on oral antipsychotics commonly favoured the following outcomes: "I don't have to worry about taking medicines" (77%), "I can get back to my favourite activity" (71%), and "I feel symptoms will not come back" (65%). Most patients favoured gluteal injections over deltoid injections for the following reasons: easier use (90%), improved symptom relief (73%), lesser side effects (73%), and reduced pain (73%). Overall, 65% of patients favoured the dose once per month as opposed to three times per month (18%) or daily (17%). The common reasons cited by patients who favoured a 1-monthly dose were "less medication-related conflict" (97%) and "dislike to taking too much medication at once (93%)."

Conclusion: This study unveiled the presence of a subtle differentiation between LAI antipsychotics and oral antipsychotics in terms of their relative desirability, with a slight inclination toward an increased preference for oral medications. Patients with schizophrenia favoured the gluteal injection over the deltoid injection on account of its greater ease of use, efficacy in symptom relief, absence of adverse effects, and reduced discomfort. Furthermore, patients exhibited a greater inclination towards monthly LAI in comparison to 3-monthly LAI and oral pill antipsychotics.

Keywords: Antipsychotics, schizophrenic, long-acting injectable, preference, injection.

INTRODUCTION

Schizophrenia is a chronic mental disorder characterized by substantial impairments in the execution of routine activities.^[1] It may affect the personal, familial, social, occupational, and educational functions of

the patient. Moreover, psychosis, encompassing hallucinations, and delusions, is the most prevalent symptom of schizophrenia that warrants antipsychotic treatment; according to global statistics, the prevalence of schizophrenia is estimated to be around 24 million individuals, or 1 in 300 people (0.32%).^[1] The prevalence of schizophrenia among inpatients in Saudi Arabia stands at 55.8%, while it is observed among outpatients at 28.9%.^[2] In Saudi Arabia, the treatment of schizophrenia heavily favors the use of typical antipsychotics, which are prescribed at rates three times higher than atypical antipsychotics.^[1] This preference is reflected in the frequent use of combination therapies, where patients often receive two or more antipsychotics, contrary to guidelines that recommend monotherapy when possible.^[1] High doses of medications such as haloperidol, olanzapine, and paliperidone are common, frequently exceeding recommended daily amounts.^[1] This highlights the necessity for careful monitoring to achieve optimal therapeutic outcomes while minimizing adverse effects.^[1]

A recent meta-analysis highlighted that specific personal traits and aspects related to medication played significant roles in predicting medication adherence among individuals with schizophrenia.^[3] Conversely, factors like having a supportive environment and maintaining positive attitudes were associated with better adherence.^[3] This underscores the importance of taking a holistic approach, considering various factors beyond medication alone, to effectively address challenges in medication adherence among individuals living with schizophrenia.^[3] In schizophrenia, medication nonadherence and subsequent relapses contribute to a deteriorating prognosis and symptomatology, thereby exacerbating the disease burden.^[4,5] Sustained antipsychotic therapy is thus a formidable objective in the management of schizophrenia. Long-acting injectable (LAI) antipsychotics decrease the risk of relapse and rehospitalization caused by treatment discontinuation, thereby reducing adherence demand by eliminating the need for daily dosing and maintaining stable therapeutic drug levels for extended intervals.^[5-7] LAI prescription rates in clinical practice are relatively low, ranging from 20% to 33%, in many Western countries, despite the advantages. Such rates are limited to patients who have previously demonstrated nonadherence with oral antipsychotics and those who prefer and are likely to accept LAIs.^[8-11] The discrepancy between the proportion of patients presently receiving LAI treatment and the nonadherence rate among patients diagnosed with schizophrenia (ranging from 40% to 80%) suggests that LAIs are underutilized.^[12]

The significance of patient-centric care in schizophrenia is underscored by the fact that patients' perceptions and attitudes are recognized as potential barriers to LAI usage and are critical determinants of medication adherence.^[13-15] The previous study identified several prominent barriers to the use of LAI antipsychotics.^[16] Negative patient attitudes, insufficient patient education, and logistical challenges such as transportation and cost emerged as the most significant obstacles.^[16] It was found in a population-based survey of patients with schizophrenia that the acceptance rate of LAI antipsychotics exceeded the rate of prescription.^[17] Additionally, a divergence in the evaluation of treatment objectives has been noted between patients and clinicians, which may influence the choice and continuation of treatment.^[18,19] Considering the diverse functional and symptomatic impacts of antipsychotic medications, it is prudent to comprehend the patient's treatment expectations and medication preferences to promote alignment with treatment objectives, foster patient participation, and streamline the use of LAIs in the treatment of schizophrenia.^[18] While numerous studies have examined the viewpoints of clinicians and caregivers, there is a scarcity of research in Saudi Arabia that specifically examines the perspective of patients with schizophrenia regarding the selection of LAIs or oral antipsychotic medications. Moreover, it's imperative to acknowledge the cultural diversity and distinctive sociocultural and religious influences within Saudi Arabia, recognizing their potential impact on patients' attitudes and preferences towards antipsychotic treatment. By delving into these nuances, the study seeks to provide valuable insights that

can guide the development of personalized and culturally sensitive treatment approaches. Gaining insight into patients' preferences regarding LAI versus oral antipsychotics (pills) has the potential to alleviate barriers to LAI utilization in schizophrenia treatment. Therefore, we aimed to identify whether patients with schizophrenia prefer LAI or oral antipsychotics in Saudi Arabia.

METHODS

Study design and setting

From June 2023 to October 2023, an anonymous electronic questionnaire was utilized to conduct a descriptive cross-sectional study at Eradh Psychiatric Hospital in Riyadh, Saudi Arabia.

Inclusion and exclusion criteria

Individuals who had received a diagnosis of schizophrenia were enrolled in our research. Adult patients, irrespective of gender, who met the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, DSM-IV criteria for schizophrenia and underwent a minimum of one depot injection during a one-year period while receiving psychiatric services from the medical home visit department at Eradh psychiatric hospital were invited to participate in this research. Similarly, we recruited patients who were on antipsychotic treatment or had been previously prescribed such medication. We excluded patients without schizophrenia (e.g., schizoaffective illness, bipolar disorder) and with allergies or contraindications to LAIs or oral antipsychotics.

Data collection

An invitation letter and consent form were utilized to obtain the consent. A self-administered Medication Preference Questionnaire (MPQ) was disseminated to gather information regarding schizophrenic patients' medication preferences for LAI antipsychotics, which was derived from a prior study²⁰. Concerning treatment preference, the initial section of the MPQ inquired about the significance of general treatment outcomes and objectives, such as symptoms, side effects, and general well-being. The responses were categorized as "Not Important," "Important," or "Not Sure." In the second section of the MPQ, patients were requested to specify explicit reasons (e.g., convenience and pain) influencing their preference for LAI medication or oral pills. Patients were asked to specify the factors (e.g., pain and comfort) influencing their preference for deltoid or gluteal injections in the third section of the MPQ. In the fourth section, patients were queried regarding their inclination towards dosage frequency (daily, monthly, or every three months) and the rationales behind their selection of monthly injections as opposed to three-monthly ones. The response options for sections 2, 3, and 4 were "Yes," "No," and "Not sure," respectively.

Ethical considerations

Due to the study's design, there were no adverse effects on patients or modifications to their treatment because of this research. De-identified data from this study have been compiled, rendering patient-specific information inaccessible, including date of birth, name, and address. This study was conducted in accordance with the tenets of the Helsinki Declaration and only after receiving authorization from the Institutional Review Board of the King Saud Medical City, Saudi Arabia (Approval number: H1RI-24-May23-01).

Sample size and statistical analysis

The sample size estimator for proportions was utilized to ascertain that a minimum of 269 patients was required to detect an anticipated 77% of patients who preferred LAIs over oral antipsychotics²⁰ with 5% absolute precision and 95% confidence. The data was entered into a Microsoft Excel database and analysed using Statistical Analysis Software version 24 (IBM Inc., Chicago, IL, USA). To evaluate the normality of continuous variables, the Kolmogorov-Smirnov test was applied. For continuous variables,

the descriptive statistics were presented as the mean and standard deviation (\pm SD); for categorical variables, the frequencies and percentages were utilized. The responses of patients to MPQ items were descriptively summarized.

RESULTS

From June 2023 to October 2023, 310 schizophrenic patients completed the MPQ. The average age of the patients was 46 (10.9%); females comprised the majority (52%) (Table 1).

Table 1: Demographics and Baseline Characteristics

The variables	Preference		Total n=310
	Oral medications	Injectable medications	
Male	65 (48.9)	85 (48.0)	150 (48.4)
Female	68 (51.1)	92 (52.0)	160 (51.6)
Age, mean (SD)	45 (11.69)	47 (10.45)	46 (10.99)
Number of admissions,	1.47 (1.61)	1.32 (1.46)	1.38 (1.53)

Preferred treatment based on goals and outcomes

The following outcomes were considered important by patients who favoured oral antipsychotics: "I don't have to worry about taking medicines" (77%); "I can get back to my favourite activity" (71%); "I feel symptoms will not come back" (65%) (Figure 1). The subsequent results were deemed significant by patients who favoured LAIs: "Make symptoms go away" (81%); "I don't have to worry about taking medicines" (69%); "I feel less confused" (65%); and "I have more control over my medicines" (64%) (Figure 1). Overall, outcomes related to patient empowerment (e.g., greater control over medicine), quality-of-life (e.g., no worry about taking medicine), and symptom improvement (e.g., resolution of symptoms) were regarded as important among schizophrenic patients who preferred LAIs and oral pills. However, there was a slight tendency toward a greater preference for oral medications.

Preference-based on personal experience

Most common reasons quoted for medication preference (LAI vs pills) were: More in control/don't have to think about medicines" (93% vs 79%), "pills/injections work better for my symptoms" (81% vs 55%), "less pain/sudden symptoms" (73% vs 73%), and "less embarrassed" (0% vs 78%) (Figure 2). The most common reason cited by patients who preferred oral pills was "LAIs/pills are easier for me" (100% vs 65%).

Preference-based on injection site

Most schizophrenic patients favoured gluteal (buttock) injections over deltoid (arm) injections for the following reasons: easier use (90%), improved symptom relief (73%), lesser side effect (73%), and reduced pain (73%), as shown in Figure 3. The reasons given by patients favouring deltoid injections were largely consistent: higher ease of use (70%), improved symptom management (70%), reduced pain (70%), and less embarrassment (70%).

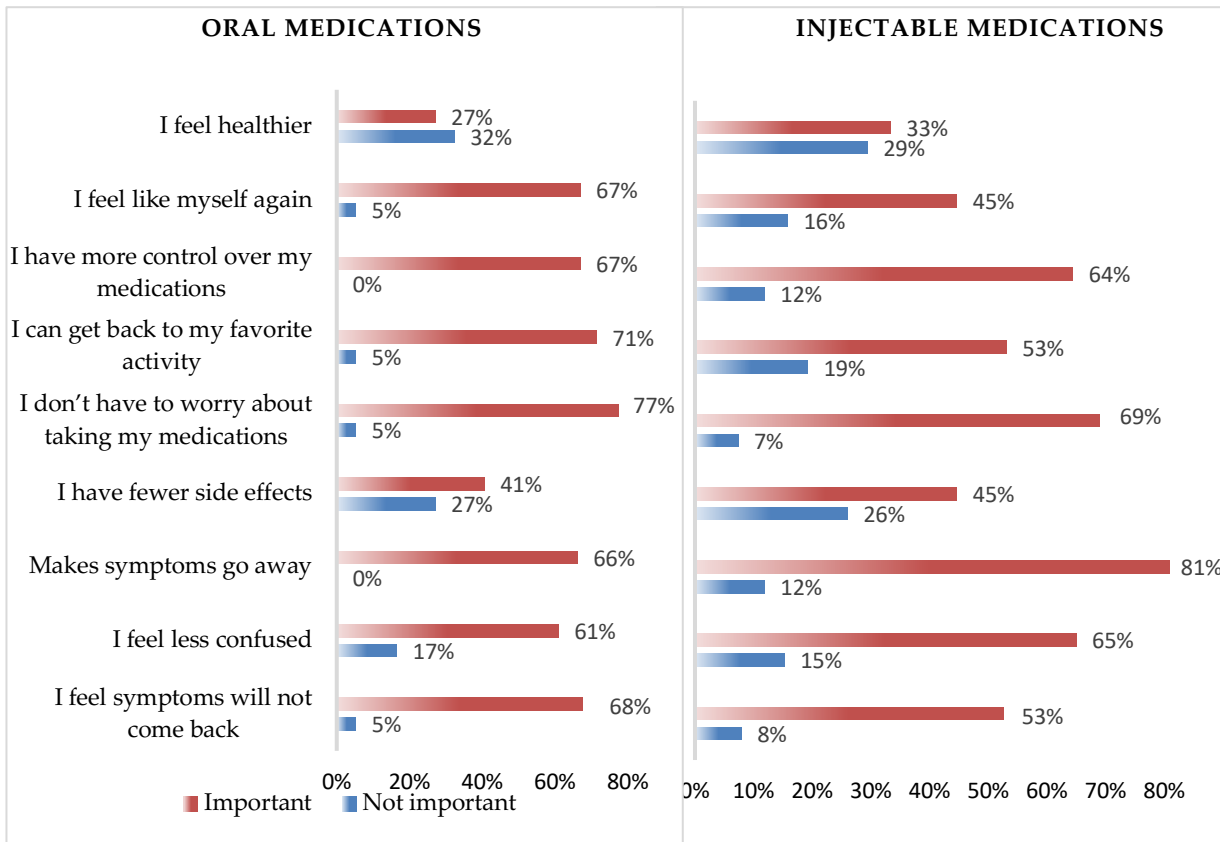


Figure 1: Treatment goals or outcomes reported as important or not important for medicine preference.

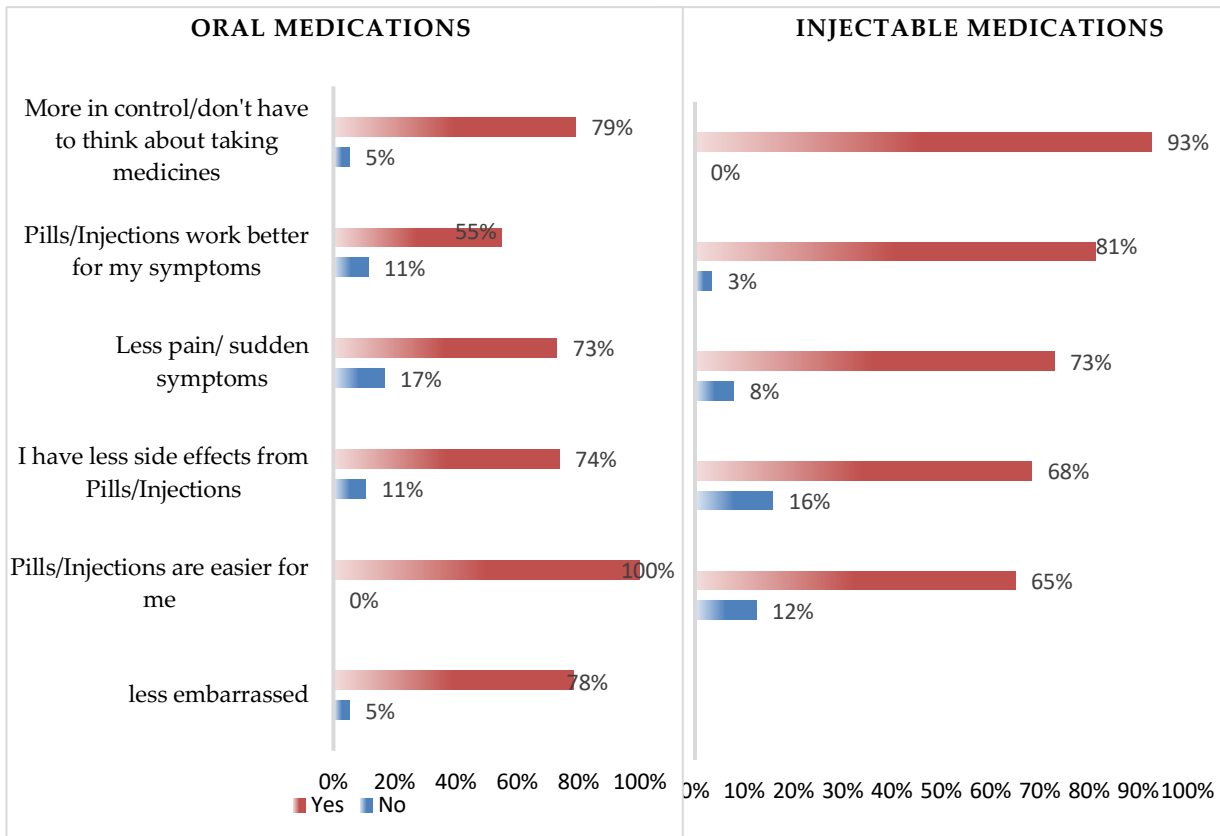


Figure 2: Cited reasons for choosing LAI over oral antipsychotics.

Overall, 65% of patients favoured the dose once per month as opposed to three times per month (18%) or daily (17%) (Figure 4). The most frequently cited reasons for favouring the three-monthly option were "fewer doctor visits" (80%) and "fewer injections are less painful" (84%). The reasons cited by patients who favoured a 1-monthly dose were "less medication-related conflict" (97%) and "dislike to taking too much medication at once" (93%).

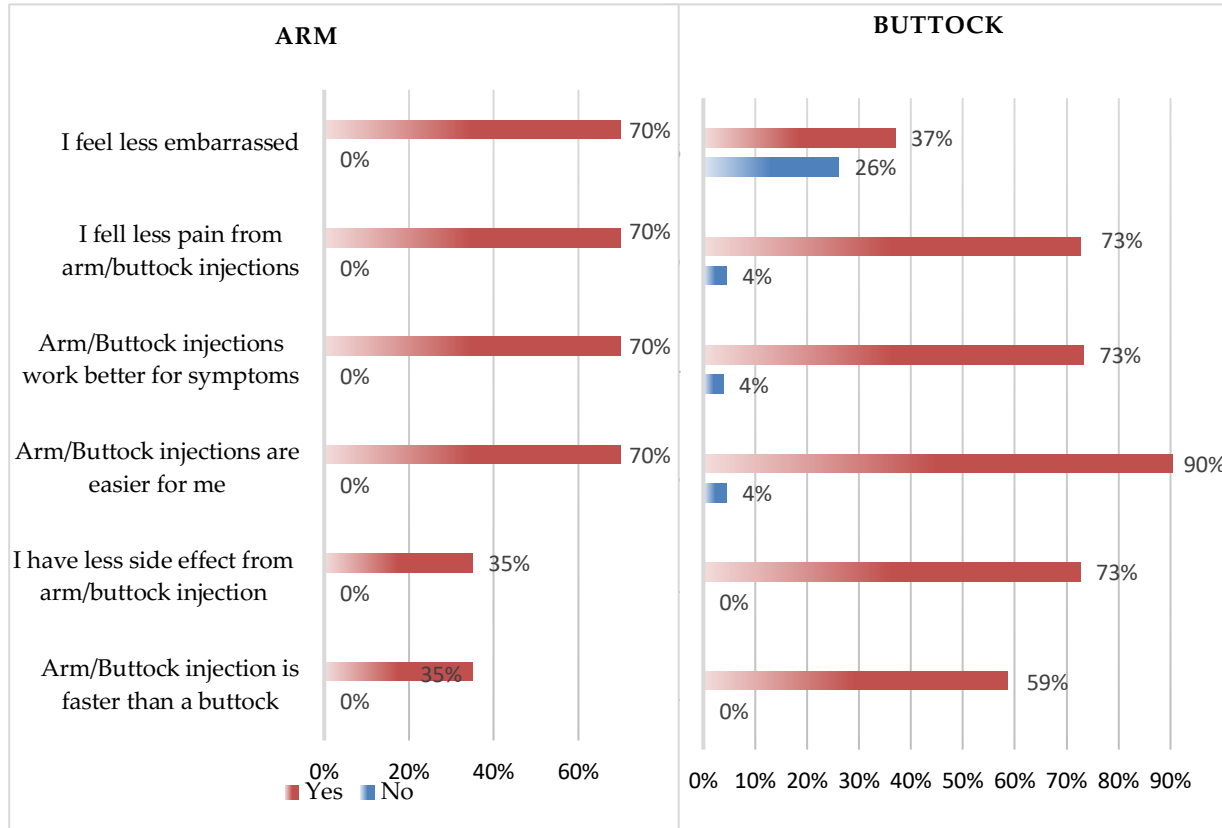


Figure 3: Cited reasons for injection-site preference: deltoid vs gluteal.

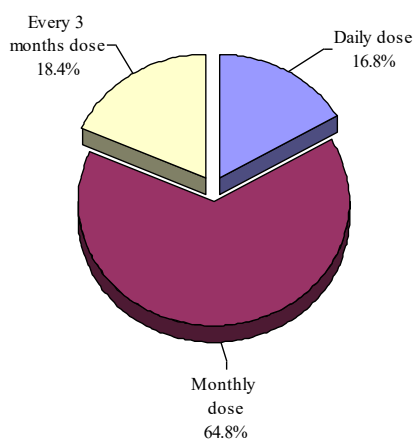


Figure 4: Medication preference based on dosing frequency and reasons for preference.

DISCUSSION

The findings obtained from this study offer valuable insights into patient's preference for LAI or oral antipsychotics (pills) as a treatment option for schizophrenia. The analysis emphasized the differentiation

of distinct components of treatment objectives that patients consider significant and anticipate attaining because of their treatment. In this study, patients diagnosed with schizophrenia exhibited a slightly favourable attitude towards oral antipsychotics over LAIs. Nonetheless, prior research indicated that LAIs were more preferred than oral tablets.^[20,21] Saudi Arabian cultural beliefs and norms may have an impact on the attitudes of patients towards methods of medication administration. For instance, cultural preferences for injectable medications may be influenced by concerns regarding injectability or the perceived lack of convenience or acceptability. The previous study suggests that cultural influences influence patients' medication administration method choices and perceptions as culture is linked to medicine method preference.^[22] Despite this relationship, the oral route is still the most preferred mode of medicine administration, followed by injection. However, oral route dominance differs among countries, showing how cultural influences affect patient drug route preferences.^[22]

Concerns regarding patient autonomy and quality of life were important for schizophrenic patients who opted for oral antipsychotics rather than LAIs. Priorities of most patients who were recruited and expressed a preference for oral pills included overall well-being, achievement of clinical objectives (such as symptom reduction), improved self-reliance (such as greater medication control), and functional enhancements (such as the ability to resume favourite hobbies or activities). These observations were consistent with the results obtained from a survey conducted among individuals diagnosed with recent-onset schizophrenia who acknowledged the significance of symptom relief and its impact on routine tasks and social engagements.^[18] On the contrary, psychiatrists recognize that the main motivations for using LAIs are symptom management, preventing relapse, and minimizing the severity of side effects, and frequently underestimate the significance of improvements in functional capacity, essential daily tasks, and the ability to work independently.^[19,23]

Even though fear of needles or injection discomfort is frequently cited by healthcare professionals as a significant barrier to LAI use, the percentages of participants in both groups (73% oral vs. 73% LAI) who preferred LAI over oral pill antipsychotics were comparable in this study.^[24,25] There is a need to delve deeper into the complex factors behind treatment decisions because of this finding. This study challenges the commonly accepted notion that patients' treatment decisions are primarily influenced by their concerns about injection pain. Instead, it emphasizes the importance of heeding patients' preferences.

Many participants mentioned that oral medications are more convenient, easier to control, and don't cause as many adverse effects. Additionally, many reported feeling less embarrassed when taking oral antipsychotics, suggesting that this method of drug delivery is widely preferred. Taking medication orally may be preferred for several reasons, including the fact that it is more comfortable, easier to self-administer, and gives the impression of more privacy. The prolonged time required to attain steady-state levels and the slow titration process are the primary drawbacks of LAI antipsychotics.^[26] This can be especially problematic for critically ill patients who require immediate dose adjustments. This frequently requires supplementary oral antipsychotic medication, which further complicates the treatment process. Further complicating the process is the protracted duration required to achieve sustained plasma levels, which frequently exceeds two months.^[26] Consequently, LAIs are generally initiated once patients have achieved a certain degree of stability with their existing medications. While more recent LAIs, like paliperidone palmitate, can attain therapeutic concentrations rapidly without the need for oral administration, olanzapine still occasionally causes uncommon severe adverse effects. Additional concerns encompass discomfort at the site of injection, the possibility of irritation due to drug leakage, and the restricted accessibility of LAI formulations for every oral antipsychotic.^[26]

A significant proportion of patients expressed a preference for gluteal (buttock) injections rather than deltoid (arm) injections due to their perceived advantages in terms of reduced pain, improved symptom

relief, and ease of use. A previous study indicated a marginal inclination towards buttock injections, except for patients who have undergone two to five episodes, in which case the deltoid muscle is marginally preferred.^[23] A prior review demonstrated that injection site tolerability was marginally higher for gluteal injections, whereas the incidence of adverse events related to the injection site (most frequently pain) was greater for deltoid injections compared to gluteal injections.^[27] However, this study's finding also contradicts previous investigations among schizophrenia patients who exhibited a preference for deltoid injections rather than gluteal injections.^[20,28] The diversity of findings suggests that patient preferences regarding a particular injection site may be influenced by a vast array of factors, including personal convenience, prior experiences, and the characteristics of the medicine being administered. The contrasting results underscore the importance of considering individual patient preferences and tailoring injection techniques to align with the unique needs and comfort levels of the cohort under investigation.

Extended dosing intervals of LAIs provide an objective means of monitoring adherence and facilitate administration.^[5] The lack of regular doctor visits and the resulting strained doctor-patient relationship, limitations on dose titration, and the potential for overlooking early indicators of adverse events or symptom exacerbation have all been identified as potential obstacles associated with LAIs.^[29]

In this study, patients preferred monthly injections over quarterly injections and daily oral pills. The significance of medication adherence and convenience in the management of psychiatric disorders is underscored by the patient's preference for monthly dosage over three-monthly injections and daily pills in our study. Monthly dosing ensures consistent drug ingestion without the inconvenience of daily administration, which is consistent with the notion of a predictable and manageable treatment regimen. This finding is consistent with the increasing need for patient-centered care, which entails tailoring treatment plans to enhance patient engagement and convenience. In this study, reduced doctor visits and decreased discomfort resulting from fewer injections were cited as common reasons influencing their decision. The cited reasons (e.g., less pain due to fewer injections and fewer doctor visits) that influenced their decision in the previous study were, however, consistent with our findings.²⁰ In contrast, patients who took part in the prior research exhibited a preference for quarterly injections as opposed to monthly injections and daily oral medication.^[20] It is noteworthy that prior data regarding patient inclination towards the frequency of LAI injections revealed a spectrum of preferences: 50% indicated a preference for every three months, 38% for every month, and 9% maintained no preference.^[20] The perceived advantages of once-monthly injections for patients centered on timing, such as "reduced frequency of visits to the clinic or doctor's office," "easier time management," and "obviation of the need to recollect daily medication administration."

The findings of our study corroborate the recent American Psychiatric Association guideline, which mentions LAI use briefly in relation to patient preference, dosing frequency, and injection site.³⁰ According to the guidelines, antipsychotics are advised for patients who have a history of compromised adherence or who prefer LAIs.^[30] It is recommended that international guidelines prioritize patient preference more heavily, as this will ultimately result in improved treatment outcomes, increased adherence, and enhanced treatment satisfaction.^[20] At the onset of treatment, clinicians ought to establish transparent channels of communication with patients and their caregivers to cultivate patient-centric management and enhance their understanding of patient's treatment preferences.^[20]

Clinical implications and directions future research

It is imperative that healthcare providers give utmost importance to patient education and counselling concerning the benefits and limitations of LAI and oral antipsychotic medications. This involves examining the advantages of LAIs, including their ease of use and improved alleviation of symptoms, in

addition to addressing apprehensions regarding irritation at the injection site and conflicts related to medication. The development of patient advocacy groups, healthcare providers, and policymakers must work in collaboration to establish comprehensive strategies that promote the acceptance of LAI antipsychotics and guarantee patient-centered treatment for those diagnosed with schizophrenia.

Qualitative interviews or focus groups could further investigate patient inclinations towards oral antipsychotics as opposed to LAI antipsychotics. Further research may be warranted to examine the underlying motivations for patients' preferences, the implications of healthcare provider recommendations, and the effects of cultural, social, and religious influences. By utilizing semi-structured interviews and focus groups, valuable insights can be obtained regarding patient experiences, which can then be utilized to develop antipsychotic treatment strategies that are more individualized, and patient-centered. A more comprehensive understanding of their decision-making processes may be obtained by analysing the various factors that influence their selections. Future research may also ascertain whether cultural or sociodemographic variables impact injection frequency preferences among schizophrenic patients.

Strengths and limitations

This study is the first of its kind that assessed the patient preference for LAIs via MPQ in Saudi Arabia. Moreover, it is important to note that this research was conducted exclusively at a single medical facility, thus precluding any comparisons with other healthcare institutions. The outcome will be more generalizable if a multicenter study comprising a representative sample of hospitals is conducted. Our use of descriptive analysis may not capture significant differences or relationships between variables as well as statistical tests. Additionally, self-reported patient preferences may add response biases and make the sample less representative of the population. These factors may affect our findings' generalizability.

CONCLUSION

This study unveiled the presence of a subtle differentiation between LAI antipsychotics and oral antipsychotics in terms of their relative desirability, with a slight inclination toward an increased preference for oral medications. Goals pertaining to patient empowerment, symptom improvement, and quality of life were prioritized by patients who selected LAI and oral antipsychotics. Patients with schizophrenia favoured the gluteal injection over the deltoid injection on account of its greater ease of use, efficacy in symptom relief, absence of adverse effects, and reduced discomfort. Furthermore, patients exhibited a greater inclination towards monthly LAI in comparison to 3-monthly LAI and oral pill antipsychotics. Similarly, fewer medication-related conflicts and a dislike of taking too much medication at once were commonly cited reasons for taking monthly LAI.

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Nil

Conflict of Interest

The authors declare no conflict of interest relevant to this article.

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