

Olanzapine Pamoate Use for Schizophrenia: Retrospective Records Based Study from a Tertiary Care Hospital

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ABSTRACT

Background: Little is known from India about the experience of using olanzapine long-acting antipsychotic injectables (LAI). In this background, this study aimed to evaluate the clinical profile of patients suffering from schizophrenia who were prescribed olanzapine LAI and to evaluate the usefulness and acceptability of olanzapine LAI among these patients. **Methods:** In this retrospective study, data of all the patients with schizophrenia receiving olanzapine pamoate, was extracted. **Results:** 40 patients (males-55%; mean [SD] age- 36.2 (12) years; mean duration of illness (SD) prior to depot-143.3 (115.9) months) were included in the study. Olanzapine LAI was invariably prescribed in patients with a past history of non-compliance. Data was available for a mean (SD) follow-up duration of 17 (10.8) months. The most frequently used dose of olanzapine LAI used was 300 mg every two weeks (55%). This was followed by 405 mg every four weeks in (32.5%). Mean Clinical Global Impression (CGI) Severity score prior to starting of olanzapine LAI was 5.8 (0.7), which reduced to 2.7 (1.1) at the time of last follow-up or the last use of olanzapine LAI, and this was a statistically significant improvement (paired t-test value = 16.41; $P < 0.001$). Only one (2.5%) patient experienced Post injection Delirium/Sedation Syndrome during the study period. Only one patient was hospitalized after starting depot olanzapine. **Conclusion:** Olanzapine LAI is mostly used in patients with a history of non-compliance. Olanzapine LAI is associated with a significant reduction in the severity of illness.

Key words: Depot, long-acting injectables, olanzapine

Key messages: Olanzapine LAI is mostly used in patients with a past history of poor compliance with oral antipsychotics. The use of Olanzapine LAI is associated with a significant reduction in psychopathology.


Schizophrenia is a severe mental illness, which usually starts in early-to-mid 20s and is associated with a high level of disability, social stigma, caregiver burden,

and premature mortality.^[1-6] Antipsychotics are the mainstay of the treatment of schizophrenia. However,

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medication non-adherence rates are high among patients with schizophrenia, with about half of the patients discontinuing the medications at some point in treatment.^[7] The largest pragmatic clinical trial in schizophrenia, the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study reported that 74% of the study population discontinued medication over a period of 18 months.^[8] Non-adherence among patients with schizophrenia is associated with serious consequences such as exacerbation of psychotic symptoms, increased aggression, poor prognosis,^[9-11] relapse, rehospitalization,^[12,13] suicide,^[14] and increased cost of care.^[13]

To overcome the issue of medication non-adherence, in the 1960s, long-acting antipsychotic injectable (LAIs) were introduced.^[15] The use of LAIs in patients with schizophrenia is recommended by various treatment guidelines.^[16-20] A systematic review and meta-analysis of 10 randomized controlled trials (RCTs) showed that use of LAIs is associated with a statistically significant reduction in relapse rates, with relative and absolute risk reductions of 30% and 10%, respectively (RR 0.70, CI 0.57-0.87, NNT 10, CI 6-25, $P = 0.0009$) and reduction in dropout due to inefficacy (RR 0.71, CI 0.57-0.89).^[21] Data from systematic reviews and meta-analyses also strongly support the superiority of LAIs in comparison to oral antipsychotics in terms of hospitalization rates and all-cause discontinuations.^[22,23] A nationwide cohort study from Finland reported that compared to those taking oral medications, patients receiving LAIs have significantly lower (one third) risk of rehospitalisation.^[24]

In the last two decades, various LAIs of second-generation antipsychotics have been marketed. The first second-generation antipsychotic depot of risperidone was introduced in 2003.^[25] Subsequently, many other depots of second-generation antipsychotics were introduced. Olanzapine pamoate was approved by the European Union for treatment of schizophrenia^[26] and by the Food and Drug Administration of the United States for treatment of schizophrenia in 2009. Available data suggest that oral olanzapine and olanzapine LAI have comparable efficacy in both acute as well as maintenance treatment of schizophrenia,^[27,28] with the side effect profile and safety profile of olanzapine LAI being comparable to those of oral olanzapine except for the higher incidence of Post injection Delirium/Sedation Syndrome (PDSS) with olanzapine LAIs.^[28,29]

Olanzapine LAI was launched in India in September 2015. There is a lack of data on the use of olanzapine LAI from India. So far, only three case reports have been published about PDSS from India,^[30-32] and no data is available from India about the long-term

experience and outcome with olanzapine LAI. In this background, the current study aimed to evaluate the clinical profile of patients suffering from schizophrenia who were prescribed olanzapine LAI and to evaluate the usefulness and acceptability of olanzapine LAI among these patients.

METHODOLOGY

This was a retrospective study in which treatment records of all the patients diagnosed with schizophrenia (as per the ICD-10 criteria) and started on olanzapine LAI were reviewed. The study was approved by the Ethics Committee of the institute. All the patients started on olanzapine LAI from 1st January 2016 to 31st January 2019 formed the study sample.

Data were retrieved for the sociodemographic variables and clinical variables such as history of past treatment, prior use and response to oral olanzapine, age of onset of the illness, duration of untreated psychosis, prior hospitalizations, issues related to treatment adherence, and Clinical Global Impression (CGI) severity and improvement scores (at the time of starting of LAI and at the time of receiving the last dose of LAI). Data were also extracted for any PDSS or other injection-related side effects and need for hospitalization. Scores on CGI severity were retrospectively generated for the patients, based on the available data on psychopathology in the treatment records, at the time of the starting of olanzapine pamoate and at the time of the last follow-up. Usefulness of olanzapine LAI was also specifically evaluated for the subgroup of patients who fulfilled the criteria of treatment resistant schizophrenia (TRS). TRS was defined as lack of response to 2 adequate trials of antipsychotics, in the chlorpromazine equivalent doses of 400 mg/day given for more than 6 weeks.

RESULTS

Data of 40 patients who were started on olanzapine pamoate were extracted. The demographic and clinical profile of the patients is shown in Table 1.

Use of olanzapine LAI

The mean duration of treatment with olanzapine LAI for the study sample was 17 months (SD = 10.8). The most frequent dose of olanzapine LAI used was 300 mg every two weeks (N = 22;55%), and this was followed by 405 mg every four weeks in 13 (32.5%) patients [Table 2]. In terms of Severity Rating, the mean CGI score prior to starting of olanzapine LAI was 5.8 (0.7), which reduced to 2.7 (1.1) at the time of last follow-up or last use of olanzapine LAI, and this improvement was statistically significant (paired t-test

Table 1: Demographic Profile of the study sample

| Variable | Mean (SD) Range/Frequency (%) |
|---|--|
| Age (in years) | 36.2 (12) (19-62) |
| Gender: Male/Female | 22 (55%)/18 (45%) |
| Education (in years) | 13.8 (3.9) (5-23) |
| Religion: Hindus/Non-Hindus | 34 (85%)/6 (15%) |
| Occupation: Unemployed/employed/House wife/Student | 18 (45%)/7 (17.5%)/10 (25%)/5 (12.5%) |
| Income: On paid wages/Not on paid wages | 7 (17.5%)/33 (82.5%) |
| Marital Status: Married/Single | 20 (50%)/20 (50%) |
| Family Type: Nuclear/Non-nuclear | 29 (72.5%)/11 (27.5%) |
| Locality: Urban/Rural | 29 (72.5%)/11 (27.5%) |
| Age of onset (in years) | 22.9 (6.5) (13-46) |
| Duration of untreated psychosis in months | 69.5 (72.6) (5-345) Median: 54 (IQR: 13.25-106.5) |
| Duration of illness prior to starting of Olanzapine LAI | 143.3 (115.9) (13-478) Median: 100.5 (IQR: 48.5-207.75) |
| Duration of Treatment prior to starting of Olanzapine LAI | 78.8 (89.1) (0-346) Median: 46.5 (IQR: 26.25-123) |
| Onset of Illness: Acute/Insidious | 0/40 (100%) |
| Course of illness: Episodic/Continuous course | 0/40 (100%) |
| Subtype of Schizophrenia: Paranoid/Undifferentiated/Simple | 26 (65%)/13 (32.5%)/1 (2.5%) |
| Comorbid Substance harmful use/dependence ¹ : Yes/No | 16 (40%)/24 (60%) |
| Comorbid physical illness ² : Absent/Present | 27 (67.5%)/13 (32.5%) |
| Comorbid Psychiatric Illness ³ : Absent/Present | 25 (62.5%)/15 (37.5%) |
| Past history of surreptitious use of antipsychotics: No/Yes | 22 (55%)/18 (45%) |

¹Comorbid substance dependence: Alcohol ($n=1$), Cannabis ($n=5$), Tobacco ($n=13$). Comorbid Harmful use of a substance: Alcohol ($n=1$), Cannabis ($n=1$), Tobacco ($n=13$). ²Comorbid Physical Illness: Hypertension ($n=6$), Hypothyroidism ($n=1$), Others ($n=10$). ³Comorbid Psychiatric Illness: Depression ($n=12$), Obsessive Compulsive Disorder ($n=2$), Paranoid Personality Disorder ($n=1$). SD – Standard deviation, IQR – Interquartile range, LAI – Long Acting Injectable

value = 16.41; $P < 0.001$). At the time of starting olanzapine LAI, almost all the patients were rated as severely/extremely ill, and at last assessment, most of the patients were rated as either mildly or moderately ill. There were significant reductions in the CGI severity score in patients with TRS (paired t-test value = 8.51; $P < 0.001$) and those without TRS (paired t-test value = 14.29; $P < 0.001$).

Mean number of hospitalizations per year of illness prior to the starting of olanzapine LAI was 0.076 (SD = 0.11), and after starting olanzapine LAI, at the time of assessment, it came down to 0.075 (0.11), with only one patient getting hospitalized during the period the study sample received olanzapine LAI [Table 3]. Only 1 (2.5%) patient experienced PDSS during the study period, but this did not lead to the stoppage of olanzapine LAI. There was no report of local injection site infection. At the last follow-up, it was found that in 9 (22.5%) patients, olanzapine LAI had been discontinued due to various reasons like patient reluctance ($n = 5$; 12.5%), lack of response ($n = 3$; 7.5%) and affordability issues ($n = 1$; 2.5%).

DISCUSSION

The main objective of the present study was to evaluate the clinical profile of patients with schizophrenia who

were prescribed olanzapine LAI and to evaluate the usefulness and acceptability of olanzapine LAI among these patients. The present study included data of 40 patients who were started on olanzapine LAI. The present study suggests that clinicians preferred to use olanzapine depot in patients with a past history of good response to olanzapine, but discontinued the same due to one or other reason. Additionally, the present study suggests that in about one-third of the patients, clinicians continued using oral antipsychotic medications along with olanzapine LAI. Furthermore, the current study also suggests that slightly more than one-third of the patients undergoing treatment with olanzapine LAI had TRS. The most common reason for the use of olanzapine LAI was found to be non-compliance with medications.

To summarize, it can be said that clinicians use olanzapine LAI in a subgroup of patients who have a history of non-compliance, are treatment-resistant, and are difficult to treat. In other words, it can be said that olanzapine LAI is not used as the first-line treatment for schizophrenia. These findings possibly suggest that there are barriers at the level of clinicians in prescribing olanzapine LAI to patients with first-episode schizophrenia or psychosis. A similar pattern has been pointed out in the existing literature regarding the use of long-acting depot antipsychotics in general.^[33]

Table 2: Treatment profile of use of Olanzapine Pamoate

| Variable | Mean (SD) Range/Frequency (%) |
|--|-------------------------------|
| Setting in which olanzapine LAI was started: Inpatient/Outpatient | 19 (47.5%)/21 (52.5%) |
| Trial of oral Olanzapine prior to olanzapine LAI: No/Yes | 7 (17.5%)/33 (82.5%) |
| Number of previous antipsychotic trials | 1.4 (1) (0-3) |
| Duration of treatment with oral olanzapine in months prior to depot | 9.5 (15.7) (0-66) |
| Duration of treatment with olanzapine Pamoate (in months) | 17 (10.8) (3-37) |
| Response to prior Oral Olanzapine: good | 33 (82.5%) |
| Number of lifetime relapses due to non-compliance prior to starting of olanzapine LAI | 2 (1.1) (0-5) |
| The dose of Olanzapine LAI used during the follow-up | |
| 210/2 Weeks | 1 |
| 405/4 Weeks | 13 |
| 300/2 Weeks | 22 |
| 300/4 Weeks | 4 |
| Olanzapine oral equivalent dose (mg) | 17.3 (3.4) (10-20) |
| Oral Antipsychotic co-prescription: No/Yes | 28 (70%)/12 (30%) |
| Oral Antipsychotic co-prescription along with olanzapine LAI: Olanzapine/Haloperidol/Clozapine | 10 (25%)/1 (2.5%)/1 (2.5%) |
| History of noncompliance: No/Yes | 1 (2.5%)/39 (97.5%) |
| Past History of side effects with antipsychotics: No/Yes | 29 (72.5%)/11 (27.5%) |
| Features of difficult to treat schizophrenia | |
| Inadequate response to conventional antipsychotics | 12 (30%) |
| Problems of adverse drug effects | 11 (27.5%) |
| Problems of compliance | 39 (97.5%) |
| Problems of comorbid medical conditions | 13 (32.5%) |
| Problems of comorbid psychiatric conditions | 15 (37.5%) |
| Treatment failure-relapse on adequate drug dosage | 20 (50%) |
| Does the patient fulfill the criteria of TRS | 15 (37.5%) |
| Reason for prescribing Olanzapine Pamoate: Noncompliance/Patient preference/History of good response in the past | 38 (95%)/1 (2.5%)/1 (2.5%) |
| 1-Non-compliance was operationalized as any episode of medication discontinuation or reduction in the doses to the less than the recommended doses, leading to relapse of symptoms | |

LAI – Long acting injectable; TRS – treatment resistant schizophrenia

Table 3: Outcome of olanzapine pamoate

| Variable | Before Olanzapine LAI Mean (SD)/Frequency (%) | After Olanzapine LAI Mean (SD)/Frequency (%) | Comparison Statistics |
|---|---|--|---|
| Number of lifetime hospitalizations per year of illness | 0.076 (0.11) (0-0.46) Median: 0.039 (IQR: 0-.11) | 0.075 (0.11) (0-0.40) Median: 0.043 (IQR: 0-0.10) | Wilcoxon signed-rank test: - 3.39 ($P=0.001$) |
| Clinical Global Impression severity score | 5.8 (0.7) (4-7) | 2.7 (1.1) (1-6) | T=16.41 ($P<0.001$) |
| Clinical Global Impression severity score Borderline mentally ill | | | |
| Mildly mentally ill | - | 2 (5%) | |
| Moderately mentally ill | - | 19 (47.5%) | |
| Markedly mentally ill | 1 (2.5%) | 12 (30.0%) | |
| Severely mentally ill | 12 (30%) | 3 (7.5%) | |
| Extremely mentally ill | 23 (57.5%) | 3 (7.5%) | |
| PDSS | 4 (10%) | 1 (2.5%) | |
| Weight gain while on olanzapine LAI | - | 5 (12.5%) | |
| Discontinuation of olanzapine LAI: No/Yes | | 31 (77.5%)/9 (22.5%) | |
| Reason for discontinuation of LAI | | | |
| Affordability | | 1 (2.5%) | |
| Patient reluctance | | 5 (12.5%) | |
| Loss of response | | 3 (7.5%) | |

SD – Standard deviation, IQR – Interquartile rage; PDSS – Post injection delirium/sedation syndrome; LAI – Long Acting Injectable

Accordingly, there is a need to utilize various approaches to minimize these barriers to the use of LAIs.^[34]

In terms of usefulness, the present study suggests that there is a significant reduction in symptom severity with the use of olanzapine LAI in patients with schizophrenia.

Olanzapine LAI is associated with a significant reduction in CGI severity in patients with and without TRS. This finding supports the available efficacy data of olanzapine LAI in patients with schizophrenia^[27,28] and occasional case reports which have reported a beneficial effect of olanzapine LAI in patients with TRS.^[35,36]

Present study results also show that the majority of the patients continued to receive olanzapine LAI with a mean duration of 17 months. Only about one-fourth of the patients discontinued olanzapine LAI, of whom half were reluctant to receive the injection. Accordingly, it can be said that olanzapine depot is well accepted among patients with schizophrenia. Taken together, these findings re-emphasize that olanzapine LAI must be considered as a treatment option in patients with a history of treatment non-adherence.

In the present study, the incidence of PDSS was found to be low. Existing literature suggests that the incidence of PDSS with olanzapine LAI is 0.07-0.08% per injection and 1.4% per patient.^[37-39] The incidence of 2.5% per patient in the present study is higher than that reported in the existing literature. However, this could be due to the small sample size in the present study.

At the same time, the present study has certain limitations. These include retrospective study design, small sample size, and lack of comparison group. The study followed up patients to a mean period of 37 months on olanzapine LAI, which can be considered as a relatively short period. The usefulness was assessed by using CGI only, and other psychosocial outcomes were not evaluated. Psychopathology was not rated on a standardized scale. The CGI data was retrospectively generated. The side effects of olanzapine LAI were not evaluated by using any standard rating scale. Future studies must attempt to overcome these limitations. Attempts must be made to carry out prospective studies in which efficacy/effectiveness is evaluated by using more standard scales to evaluate the psychopathology and side effects. Additionally, other psychosocial outcomes, such as disability and quality of life, must also be evaluated. Olanzapine LAI is relatively costlier when compared to the LAIs of typical antipsychotics. We did not evaluate the cost-effectiveness of olanzapine LAIs in the present study.

To conclude, the present study suggests that olanzapine depot is useful in the management of schizophrenia in patients who have a history of non-compliance, and it is associated with a low incidence of PDSS. Olanzapine depot is equally useful in patients with and without TRS.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Jablensky A, Sartorius N, Ernberg G, Anker M, Korten A, Cooper JE, *et al.* Schizophrenia: Manifestations, incidence and course in different cultures: A World Health Organization ten-country study. Psychological Medicine Monograph Supplement 20, Cambridge, Cambridge University Press; 1992.
- Janca A, Kastrup M, Katschnig H, Lopez Iborjr JJ, Mezzich JE, Sartorius N. The world health organization short disability assessment schedule (WHO DAS-S): A tool for the assessment of difficulties in selected areas of functioning of patients with mental disorders. Soc Psychiatry Psychiatr Epidemiol 1996;31:349-54.
- Leff J, Sartorius N, Jablensky A, Korten A, Ernberg G. The international pilot study of schizophrenia: Five-year follow-up findings. Psychol Med 1992;22:131-45.
- Leete E. Overcoming the stigma of mental illness. In: Shetler H, Straw P, editors. A New Day: Voices from Across the Land. Arlington, National Alliance for the Mentally Ill; 1982.
- Westermeyer J. Economic losses associated with chronic mental disorder in a developing country. Br J Psychiatry 1984;144:475-81.
- Davies LL, Drummond MF. Economics and schizophrenia: The real cost. Br J Psychiatry 1994;165(Suppl 25):18-21.
- Lacro JP, Dunn LB, Dolder CR, Leckband SG, Jeste DV. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: A comprehensive review of recent literature. J Clin Psychiatry 2002;63:892-909.
- Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, *et al.* Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. NEJM 2005;353:1209-23.
- Wyatt RJ. Neuroleptics and the natural course of schizophrenia. Schizophr Bull 1991;17:325-51.
- Lieberman JA, Sheitman B, Chakos M, Robinson D, Schooler N, Keith S. The development of treatment resistance in patients with schizophrenia: A clinical and pathophysiologic perspective. J Clin Psychopharmacol 1998;18(2 Suppl 1):20S-4S.
- Tacchi MJ, Scott J. Improving Adherence in Schizophrenia and Bipolar Disorders. Chichester, UK: John Wiley & Sons; 2005.
- Olfson M, Mechanic D, Hansell S, Boyer CA, Walkup J, Weiden PJ. Predicting medication noncompliance after hospital discharge among patients with schizophrenia. Psychiatr Serv 2000;51:216-22.
- Sun SX, Liu GG, Christensen DB, Fu AZ. Review and analysis of hospitalization costs associated with antipsychotic nonadherence in the treatment of schizophrenia in the United States. Curr Med Res Opin 2007;23:2305-12.
- Hawton K, Sutton L, Haw C, Sinclair J, Deeks JJ. Schizophrenia and suicide: Systematic review of risk factors. Br J Psychiatry 2005;187:9-20.
- Fleischhacker WW, Miyamoto S. Pharmacological treatment of schizophrenia: Current issues and future perspectives. Clin Neuropharmacol Ther 2016;7:1-8.
- Lehman, AF, Lieberman, JA, Dixon, LB, McGlashan, TH, Miller, AL, Perkins, DO, *et al.* Practice guideline for the treatment of patients with schizophrenia, second edition. Am J Psychiatry 2004;161(2 Suppl):1-56.
- American Psychiatric Association. Practice guideline for the treatment of patients with schizophrenia, second edition. Am J Psychiatry 2004;161(Suppl):1-56.
- Miller, AL, Hall, CS, Buchanan, RW, Buckley, PF, Chiles, JA,

- Conley, RR, *et al.* The Texas medication algorithm project antipsychotic algorithm for schizophrenia: 2003 update. *J Clin Psychiatry* 2004;65:500-8.
19. Kane JM, Leucht S, Carpenter D, Docherty JP. Expert consensus guideline series.Optimizing pharmacologic treatment of psychotic disorders. Introduction: Methods, commentary, and summary. *J Clin Psychiatry* 2003;64(Suppl 12):5-19.
 20. Buchanan RW, Kreyenbuhl J, Kelly DL, Noel JM, Boggs DL, Fischer BA, *et al.* The 2009 schizophrenia PORT psychopharmacological treatment recommendations and summary statements. *Schizophr Bull* 2010;36:71-93.
 21. Leucht C, Heres S, Kane JM, Kissling W, Davis JM, Leucht S. Oral versus depot antipsychotic drugs for schizophrenia – A critical systematic review and meta-analysis of randomised long-term trials. *Schizophr Res* 2011;127:83-92.
 22. Kishimoto T, Nitta M, Borenstein M, Jane JM, Correll CU. Long acting injectable vs. oral antipsychotics in schizophrenia: A systematic review and meta-analysis of mirror image studies. *Neuropsychopharmacology* 2012;38(Suppl.):S417-8.
 23. Kishimoto T, Hagi K, Nitta M, Leucht S, Olfson M, Kane JM, *et al.* Effectiveness of long-acting injectable vs oral antipsychotics in patients with schizophrenia: A meta-analysis of prospective and retrospective cohort studies. *Schizophr Bull* 2017;44:603-19.
 24. Tiihonen J, Haukka J, Taylor M, Haddad PM, Patel MX, Korhonen P. A nationwide cohort study of oral and depot antipsychotics after first hospitalization for schizophrenia. *Am J Psychiatry* 2011;168:603-9.
 25. Fleischhacker WW. Second-generation antipsychotic long-acting injections: Systematic review. *Br J Psychiatry Suppl* 2009;52:S29-36.
 26. Rauch AS, Fleischhacker WW. Long-acting injectable formulations of new-generation antipsychotics: A review from a clinical perspective. *CNS Drugs* 2013;27:637-52.
 27. Lauriello J, Lambert T, Andersen S, Lin D, Taylor CC, McDonnell D. An 8-week, double-blind, randomized, placebo-controlled study of olanzapine long-acting injection in acutely ill patients with schizophrenia. *J Clin Psychiatry* 2008;69:790-9.
 28. Kane JM, Detke HC, Naber D, Sethuraman G, Lin DY, Bergstrom RF, *et al.* Olanzapine long-acting injection: A 24-week, randomized, double-blind trial of maintenance treatment in patients with schizophrenia. *Am J Psychiatry* 2010;167:181-9.
 29. Anand E, Berggren L, Deix C, Tóth Á, McDonnell DP. A 6-year open-label study of the efficacy and safety of olanzapine long-acting injection in patients with schizophrenia: A post hoc analysis based on the European label recommendation. *Neuropsychiatr Dis Treat* 2015;11:1349-57.
 30. Sarangula SM, Mythri SV, Sanjay Y, Reddy MS. Postinjection delirium/sedation syndrome with olanzapine depot injection. *Indian J Psychol Med* 2016;38:366-9.
 31. Upadhyay A, Bhandari SS, Sharma V, Das S. Postinjection delirium/sedation syndrome with long acting olanzapine pamoate in a middle-aged female. *Indian J Psychiatry* 2017;59:517-9.
 32. Venkatesan V, Khanra S, Mandal K, Deepak MB. Postinjection delirium/sedation syndrome after 31st long-acting olanzapine depot injection. *Clin Neuropharmacol* 2019;42:64-5.
 33. Kirschner M, Theodoridou A, Fusar-Poli P, Kaiser S, Jäger M. Patients' and clinicians' attitude towards long-acting depot antipsychotics in subjects with a first episode of psychosis. *Ther Adv Psychopharmacol* 2013;3:89-99.
 34. Parellada E, Bioque M. Barriers to the use of long-acting injectable antipsychotics in the management of schizophrenia. *CNS Drugs* 2016;30:689-701.
 35. Baruch N, Das M, Sharda A, Basu A, Bajorek T, Ross C, *et al.* An evaluation of the use of olanzapine pamoate depot injection in seriously violent men with schizophrenia in a UK high-security hospital. *Ther Adv Psychopharmacol* 2014;4:186-92.
 36. Kasinathan J, Sharp G, Barker A. Evaluation of olanzapine pamoate depot in seriously violent males with schizophrenia in the community. *Ther Adv Psychopharmacol* 2016;6:301-7.
 37. Detke HC, McDonnell DP, Brunner E, Zhao F, Sorsaburu S, Stefaniak VJ, *et al.* Post-injection delirium/sedation syndrome in patients with schizophrenia treated with olanzapine long-acting injection, I: Analysis of cases. *BMC Psychiatry* 2010;10:43.
 38. McDonnell DP, Detke HC, Bergstrom RF, Kothare P, Johnson J, Stickelmeyer M, *et al.* Post-injection delirium/sedation syndrome in patients with schizophrenia treated with olanzapine long-acting injection, II: Investigations of mechanism. *BMC Psychiatry* 2010;10:45.
 39. McDonnell DP, Landry J, Detke HC. Long-term safety and efficacy of olanzapine long-acting injection in patients with schizophrenia or schizoaffective disorder: A 6-year, multinational, single-arm, open-label study. *Int Clin Psychopharmacol* 2014;29:322-31.