Schizophrenia is a heterogeneous, chronic, severe, and disabling brain disorder that has affected people throughout history. Schizophrenia is a severely debilitating psychiatric disorder observed worldwide, with a median lifetime prevalence of 0.7%–1.0%. Iloperidone possesses stronger affinity for serotonin (5-HT2A) than dopamine (D2) receptors, and its efficacy is roughly comparable to that of other (nonclozapine) antipsychotics. In May 2009, the Food and Drug Administration approved iloperidone for the acute treatment of schizophrenia in adults. Iloperidone may be a useful and safe option for the treatment of schizophrenia. Several confirmatory trials of iloperidone reported to reduced the symptoms of schizophrenia at oral doses from 12 to 24 mg, which was more effective than placebo in reducing positive and negative syndrome total score and Brief Psychiatric Rating scale scores. Iloperidone was found to be as effective as haloperidol and risperidone in post-hoc analysis. In several clinical studies, most common adverse events reported were dizziness, dry mouth, dyspepsia and somnolence, with few extra pyramidal symptoms and metabolic changes in short and long-term studies in adults. As per adverse effect concern, akathisia was rare in case of iloperidone but prolongation of the corrected QT (QTc) interval was comparable to haloperidol and ziprasidone. Further comparative studies are needed to assess the benefit/risk profile of iloperidone and its role in the treatment of schizophrenia.

Key words: Antipsychotics, Dopamine (D2) receptors, Schizophrenia, Serotonin (5-HT2A).

INTRODUCTION

Schizophrenia is a heterogeneous syndrome characterized by fundamental distortions of language, perception, thinking, social activity, affect, and volition.1 The syndrome commonly begins in late adolescence, has an insidious onset but sometimes, acute onset, and, often, a poor outcome, progressing from social withdrawal and perceptual distortions to recurrent delusions and hallucinations. Patients may present with positive symptoms (such as delusions, hallucinations, distortions or exaggerations in language and communication, disorganized speech, disorganized behavior or catatonic behavior) or negative symptoms (blunted affect, emotional withdrawal, poor rapport, passivity, apathetic social withdrawal, difficulty in abstract thinking, alogia i.e., restrictions in fluency and productivity of thought and speech, abolation i.e., restrictions in initiation of goal-directed behaviour, anhedonia i.e., lack of pleasure, attentional impairment, etc) and must have at least two of these for a 1-month period and continuous signs for at least 6 months to meet formal diagnostic criteria. "Negative" symptoms predominate in one-third of the schizophrenic population and are associated with a poor long-term outcome and a poor response to drug treatment. However, marked variability in the course and individual character of symptoms is typical.2 The four main subtypes of schizophrenia are catatonic, paranoid, disorganized, and residual. Many individuals have symptoms of more than one type. Catatonic-type describes patients whose clinical presentation is dominated by profound changes in motor activity, negativism, and echolalia or echopraxia. Paranoid-type describes patients who have a prominent preoccupation with a specific delusional system and who otherwise do not qualify as having disorganized-type disease, in which disorganized speech and behaviour are accompanied by a superficial or silly affect. In residual-type disease, negative symptomatology exists in the absence of delusions, hallucinations, or motor disturbance. The term schizoaffective disorder describes patients who meet the symptom requirements but not the duration requirements for schizophrenia, and schizoaffective disorder is used for those who manifest symptoms of schizophrenia and independent periods of mood disturbance. Prognosis depends not on symptom severity but on the response to antipsychotic medications.1

Epidemiology and Pathophysiology

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1.0%. Countries from the developing world have a lower prevalence of schizophrenia (Figure 1). Overall, the prevalence of schizophrenia does not vary between the sexes. While the incidence of schizophrenia is higher in urban than rural settings, this is not reflected in the overall prevalence data. The prevalence of schizophrenia is higher in migrants than native-born individuals.

Epidemiologic surveys identify several risk factors for schizophrenia including genetic susceptibility, fetal second-trimester viral and nutritional insults, birth complications, early developmental insults, winter birth, increasing parental age and substance abuse in the late teen or early adult years.

Genetic factors are involved in at least a subset of individuals who develop schizophrenia. Schizophrenia is observed in ~6.6% of all first-degree relatives of an affected person. If both parents are affected, the risk for offspring is 40%. The concordance rate for monozygotic twins is 48%, compared to 9% for dizygotic twins.\(^1,2\)

Schizophrenia is also associated with gestational and perinatal complications, including Rh factor incompatibility, fetal hyoxia, prenatal exposure to influenza during the second trimester, and prenatal nutritional deficiency.\(^1,2\)

A number of structural and functional abnormalities have been identified in schizophrenia, like cortical atrophy and ventricular enlargement; specific volume losses in the amygdala, hippocampus, right prefrontal cortex, fusiform gyrus, and thalamus; and progressive reduction in cortical volume over time.\(^1,2\)

The dopamine hypothesis of schizophrenia is based on the discovery that agents that diminish dopaminergic activity also reduce the acute symptoms and signs of psychosis, specifically agitation, anxiety, and hallucinations. Amelioration of delusions and social withdrawal is less dramatic.

While the DA hypothesis is an advance over earlier conceptualizations of psychosis, it does not account for the cognitive deficits and negative symptoms in schizophrenia. The DA hypothesis also does not explain the psychotomimetic effects of agonists of other pathways (e.g., d-lysergic acid, a potent serotonin 5-HT\(_2\) receptor agonist), or the effects of phencyclidine and ketamine, antagonists of the N-methyl-D-aspartate (NMDA) glutamate receptor. These findings point towards possible involvement of serotonin and excitatory amino acids in pathophysiology of schizophrenia.\(^1,2\)

**Burden of Schizophrenia**

- Schizophrenia affects about 24 million people worldwide.
- Schizophrenia is a treatable disorder, treatment being more effective in its initial stages.
- More than 50% of persons with schizophrenia are not receiving appropriate care.
- 90% of people with untreated schizophrenia are in developing countries.
- Care of persons with schizophrenia can be provided at community level, with active family and community involvement.

Wide variation occurs in the course of schizophrenia (Figure 2). Some people have psychotic episodes of illness lasting weeks or months with full remission of their symptoms between each episode; others have a fluctuating course in which symptoms are continuous but rise and fall in intensity; others have relatively little variation in the symptoms of their illness over time. At one end of the spectrum, the person has a single psychotic episode of schizophrenia followed by complete recovery; at the other end of the spectrum is a course in which the illness never abates and debilitating effects increase.\(^5\)

Between 25 and 50 percent of schizophrenia patients attempt suicide, and 10 percent eventually succeed, contributing to a mortality rate eight times greater than that of the general population. The life expectancy of a schizophrenic patient may be 20 to 30 years shorter than that of the general population, not only due to suicide but in particular due to premature cardiovascular disease. Accelerated mortality from premature cardiovascular disease in schizophrenic patients is caused not only by genetic factors and lifestyle factors such as smoking, unhealthy diet, and lack of exercise leading to obesity and diabetes but also, by treatment with some antipsychotic drugs, which cause an increased incidence of obesity and diabetes and thus increased cardiac risk.\(^2\)
This disorder is not only associated with an increased risk of mortality but also imposes a huge financial burden on society. Optimal treatment of the disease could lessen this burden but it is still challenging to develop effective, safe antipsychotic drugs.\(^6\,7\)

**Need for novel antipsychotics**

Conventional antipsychotics such the well-known phenothiazines (e.g., chlorpromazine), butyrophenones (e.g., haloperidol) and diphenylbutylpiperidine derivatives (e.g., pimozide) are used as first-line therapy for schizophrenia although this trend is changing and second-generation drugs, are now preferred as mainstay of treatment in several countries. As general rule first-generation agents are antagonists at the dopamine type 2 (D\(_2\)) receptors and their clinical efficacy is strongly correlated with their binding affinities for the receptor subtype.\(^6\)

The dopaminergic theory postulates that possibly the disease is due to alterations in central dopaminergic transmission, with increased dopamine transmission in the mesolimbic pathway which lead to positive symptoms, and reduced dopamine transmission in the mesocortical pathway explaining negative symptoms. Accordingly, the blockade of dopamine receptors in the mesolimbic pathway by these antipsychotics controls positive symptoms in a substantial proportion of patients.\(^9\)

However, these drugs offer little benefit in controlling negative symptoms or cognitive deficits, and can result in extrapyramidal symptoms (EPS) and a progressively increasing risk of tardive dyskinesia. Prolactin elevation, which can lead to sexual side effects, is also a frequent adverse reaction to these drugs, and occurs with some second-generation antipsychotics too. Besides being dopamine receptor antagonists, second-generation antipsychotics have

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**Figure 1:** The average risks for developing schizophrenia for different groups of people

(Source: Gottesman, 1991)

**Figure 2:** Different courses of Schizophrenia\(^5\)

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PTB Reports, Vol 1, Issue 2, May-Aug, 2015
an additional range of binding activity at various other receptor sites. While each drug has its own receptor profile, most of them show higher affinity for serotonin type 2A (5-HT$_2A$) than D$_2$ receptors; this ratio of affinities has been suggested to account for their enhanced efficacy and lower rates of EPS.$^{10}$

The blockade of 5-HT$_{2A}$ receptors may partly reduce the blockade of dopamine transmission. Fewer EPS and lower risk of tardive dyskinesia would result from the reversed D$_2$ blockade in the striatum, although the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study found that there is still 4%–8% EPS even with these newer agents. Antagonism at 5-HT$_{2A}$ receptors in the mesocortical pathway and the consequent increase in dopamine transmission in the prefrontal cortex has also been suggested to account for the efficacy against negative symptoms. However, like first-generation antipsychotics, these newer agents are not free of side effects such as weight gain, hyperglycemia and dyslipidemia; drug-related cardiac changes (QTc prolongation) have also been reported.$^{10,11}$

The CATIE study$^{11}$ showed that antipsychotic treatment was marked by poor compliance, drug discontinuation and frequent switching attributable to lack of efficacy and intolerance in patients with chronic schizophrenia; this was true for the older, conventional antipsychotics (commonly defined as "first-generation" antipsychotics) as well as the second-generation drugs (referred as "atypical antipsychotics"). This overall high rate of all-cause discontinuation (overall 74% with 23.7% for lack of efficacy and 11% for intolerability) underlines the need for the development of new antipsychotic agents that provide more effective symptom control while addressing the tolerability concerns seen with the currently available agents.$^{11}$

These limitations have prompted a continuing effort to develop more effective and safer antipsychotics to improve outcomes for schizophrenic patients. These resulted in development of many newer drugs, one of them is the mixed D$_2$/5-HT$_2$ antagonist iloperidone whose efficacy in the treatment of schizophrenia, reassuring metabolic and safety profiles have been established in double-blind placebo-controlled clinical trials.$^{11}$ In May 2009, the Food and Drug Administration (USA) approved iloperidone for the acute treatment of adult patients with schizophrenia.$^{14}$

**ILOPERIDONE REVIEW**

**Pharmaceutical data**

Table 1: Describes Physico-chemical properties of iloperidone$^{15}$

**Clinical Pharmacology**

- Chemically, iloperidone is a piperidinyl-benzisoxazole derivative structurally related to risperidone.
- Iloperidone adheres to the 5-HT$_2$ and D$_2$ receptor hypothesis in that it has higher affinity for the 5-HT$_2$ receptor than for the D$_2$.$^{16,17}$
- Theoretically it should have greater efficacy and fewer EPS than first-generation antipsychotic drugs.$^{12}$
- Iloperidone binds to other serotonin receptors also. It has moderate affinity for 5-HT$_{3A}$, 5-HT$_{3C}$, and 5-HT$_{5}$ behaving as an antagonist at 5HT2C and 5HT6 receptors, and as a partial agonist at SHT$_{3A}$.
- With other dopamine receptor subtypes, it showed high affinity for the dopamine type 3 receptor and moderate affinity for the dopamine type 4 receptor.
- In addition to its affinities for serotonin and dopamine receptors, iloperidone has high affinity for alpha1 receptors and moderate affinity for alpha 2C receptors. Blockade of these receptors may contribute to the drug’s efficacy, particularly on mood and cognition, although it may also cause postural dizziness or orthostatic hypotension.

<table>
<thead>
<tr>
<th>Receptor binding</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>High affinity to Serotonin 5-HT$_{2A}$ and Dopamine D$_2$ and D$<em>3$ receptors; moderate affinity to 5-HT$</em>{3C}$</td>
<td>Antipsychotic action against both positive and negative symptoms</td>
</tr>
<tr>
<td>Higher affinity to 5-HT$_{2A}$ receptors compared with dopamine D$_2$ receptors</td>
<td>Antipsychotic effect without causing extra pyramidal symptoms</td>
</tr>
<tr>
<td>300-fold greater activity in dopamine receptors of limbic tract than in the nigrostriatal tract</td>
<td>Little / No risk of extra pyramidal symptoms</td>
</tr>
<tr>
<td>Blockade of $\alpha_1$, $\alpha_2C$</td>
<td>Drug’s efficacy, on mood &amp; cognitive symptoms, antidepressant and anxiolytic activity S/E: dizziness, orthostatic hypotension</td>
</tr>
<tr>
<td>Low affinity for the histamine H$_1$</td>
<td>Less sedation, Little weight gain</td>
</tr>
<tr>
<td>No affinity for cholinergic muscarinic receptors M$_1$–M$_3$</td>
<td>No anticholinergic effects</td>
</tr>
</tbody>
</table>

**Table 2: Summary of mechanism$^{16,17}$**
Iloperidone has demonstrated a set of relative affinities and has been shown to have 300-fold greater activity in the limbic tract than in the nigrostriatal tract. Due to its receptor profile, it is anticipated that iloperidone will have efficacy in the treatment of psychosis and little to no risk of extrapyramidal symptoms. Iloperidone has a low affinity for histaminergic receptors and therefore is expected to have a low risk of sedation or weight gain.

Summary of mechanism
Mechanism of iloperidone is summarized in Table 2.

Pharmacokinetic Properties

- Iloperidone is metabolized mainly in the liver by three pathways: carbonyl reduction, hydroxylation (mediated via CYP2D6) and O-demethylation (mediated via CYP3A4). The two major metabolites of iloperidone are P88 (the active metabolite) and P95 (the inactive metabolite).
- The pharmacokinetic profile of iloperidone is dependent on whether patients are poor or extensive metabolizers as determined by their CYP2D6 genotype, 7-10% of Caucasians and 3-8% of African Americans are poor metabolizers.
- The mean elimination half-lives of iloperidone, P88 and P95 in extensive metabolizers are 18, 26 and 23 hours, respectively, whereas those in poor metabolizers are 33, 37 and 31 hours.
- Steady-state levels of iloperidone are attained within 3-4 days.
- There were no clinically relevant effects on the pharmacokinetic profile of iloperidone and its metabolites (P88 and P95) in adult patients with chronic severe renal impairment (creatinine clearance <30 mL/min).
- However, since CYP2D6 and CYP3A4 isoenzymes are involved in the metabolism of iloperidone, inhibitors of CYP3A4 (e.g., ketoconazole) or CYP2D6 (e.g., fluoxetine, paroxetine) can inhibit iloperidone elimination and cause increased blood levels.
- The dosage of iloperidone should be halved during concomitant administration with these agents.

Indications
Acute treatment of schizophrenia in adults; it is generally recommended that treatment it should be continued beyond the acute response. 

Dosage and administration
Iloperidone must be titrated slowly from a low starting dose to avoid orthostatic hypotension due to its alpha-adrenergic blocking properties. The recommended starting dose for iloperidone tablets is 1 mg twice daily. It should be increased to attain the desired therapeutic response or up to the dose range of 6-12 mg twice daily. After initiating therapy with 1 mg twice daily, titration may be made with daily dosage adjustments to 2 mg twice daily, 4 mg twice daily, 6 mg twice daily, 8 mg twice daily, 10 mg twice daily, and 12 mg twice daily on days 2, 3, 4, 5, 6 and 7, respectively. Efficacy was demonstrated with iloperidone in a dose range of 6 to 12 mg twice daily. The maximum recommended dose is 12 mg twice daily (24 mg/day). Iloperidone can be administered without regard to meals.

Maintenance Treatment
It is generally recommended that responding patients be continued beyond the acute response. Patients should be periodically reassessed to determine the need for maintenance treatment.

Contraindications
Iloperidone is contraindicated in individuals with a known hypersensitivity reaction to the product. Reactions have included pruritus and urticaria.

Drug interactions
Both CYP3A4 and CYP2D6 are responsible for iloperidone metabolism. Inhibitors of CYP3A4 (e.g., Ketoconazole, Itroconazole) or CYP2D6 (e.g., Fluoxetine, Paroxetine) can inhibit iloperidone elimination and cause increased blood levels.

Orthostatic hypotension and syncope
Iloperidone should be used with caution in patients with known cardiovascular disease (e.g., heart failure, history of myocardial infarction, ischemia, or conduction abnormalities), cerebrovascular disease, or conditions that predispose the patient to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications). Monitoring of orthostatic vital signs should be considered in patients who are vulnerable to hypotension.

Increased mortality and cerebrovascular adverse events, including stroke
Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death and higher incidence of cerebrovascular adverse events (cerebrovascular accidents and transient ischemic attacks compared to placebo). Therefore, iloperidone is not approved for the treatment of patients with dementia-related psychosis.

Iloperidone is usually well-tolerated and associated with a low risk of causing extrapyramidal symptoms, hyperprolactinemia and adverse metabolic effects, even though like other antipsychotic drugs, it is recommended for clinicians to exercise precaution for following conditions while treating patients with iloperidone.

The short-term (4 to 6 weeks' duration) efficacy of iloperidone was active comparator-controlled, multicentre trials in adult patients with schizophrenia with an active comparator (risperidone). A total of 616 patients were randomized to receive iloperidone 4–8 mg daily (n=153), iloperidone 10–16 mg daily (n=154), risperidone 4–8 mg daily (n=153), or placebo (n=156). A significantly better improvement in the PANSS and BPRS scores was found with patients treated with iloperidone 4–8 mg daily and 10–16 mg daily compared to placebo.

In another study given in same report23 706 patients were randomized to receive iloperidone 12–16 mg daily (n=244), iloperidone 20–24 mg daily (n=145), risperidone 6–8 mg daily (n=157), or placebo (n=160). A significant improvement in the PANSS and BPRS score was found in both iloperidone 12–16 and 20–24 mg/day compared to placebo.

Another placebo-controlled study was not designed to evaluate the relative efficacy of iloperidone versus the active comparators; but this was evaluated in subsequent post hoc analysis.13 in which, iloperidone was shown to be as effective as risperidone treatment, as determined using a simplified pattern mixture model in which results were adjusted for the 4-day difference in titration schedule and the impact this potentially had on the length of stay in the study. There were no statistically significant differences in changes from baseline for BPRS (−8.1, −9.2 and −9.6, respectively) and PANSS−T (−12.6, −15.4 and −15.6) scores between the iloperidone 12–16 mg/day, iloperidone 20–24 mg/day and risperidone 6–8 mg/day group after 6 weeks’ treatment.

Above mentioned both studies used dosage-escalation schemes in their protocols, allowing for risperidone to reach steady-state levels faster than did iloperidone. The use of such a method may have led to greater overall improvements in PANSS total and BPRS scores in the active-comparator group (risperidone) versus the iloperidone-treated group.

In order to overcome a mismatched dosage-escalation scheme, Cutler and colleagues24 conducted a four-week, double-blind, multicenter Phase III trial in which 593 patients were randomized to receive iloperidone, ziprasidone, or placebo on a similar schedule. Patients had a one-week dosage-escalation period, receiving iloperidone 1, 2, 4, 6, 8, 10, and 12 mg twice daily on days 1–7, respectively, or twice daily dosing of ziprasidone 20 mg on days 1 and 2, 40 mg on days 3 and 4, 60 mg on days 5 and 6, and 80 mg on day 7. Patients in the placebo group received placebo twice daily. After this adjustment period, patients entered a three-week maintenance phase of fixed-dose iloperidone 24 mg daily, ziprasidone 160 mg daily, or placebo. Iloperidone was found to be superior to placebo in improvement in PANSS total score (−12.01 versus −7.08, respectively; p=0.006), BPRS score (−7.4 versus −4.6, respectively; p < 0.05), PANSS positive symptoms subscale score (−4.21 versus −2.22, respectively; p<0.001), and PANSS negative symptoms subscale score (−2.96 versus −1.91, respectively; p < 0.05) at four weeks. Iloperidone was found to have similar improvements versus ziprasidone in the PANSS total score (−12.01 versus −12.27, respectively) and BPRS score (−7.4 versus −7.2, respectively).

Long-term Efficacy

Though a decrease in symptoms of schizophrenia can be seen within 2–3 weeks of treatment, full improvement (reduction in PANSS or BPRS scores) can take 6–8 weeks. Kane and colleagues25 described long-term efficacy results of three pooled, 52-week, prospective, randomized, multicenter, double-blind studies. Iloperidone and haloperidol groups were found to have only slightly different rates for relapse. After a 6-week stabilization phase, patients were eligible to continue a 46-week maintenance phase if they had a decrease of 20% or more in their PANSS total score and a CGI-C score scale of <4. During the maintenance phase, the primary efficacy variable was time to relapse. The mean iloperidone dose was 11.8 mg daily at the end of the initial 6-week stabilization phase and 12.5 mg daily at the end of the 46-week
maintenance phase, both of which are lower than the approved target dosage of 24 mg daily. A non-inferiority analysis found that when compared with haloperidol, iloperidone was non-inferior in preventing relapse (iloperidone, 43.5%; haloperidol, 41.2%). The mean time to relapse in the iloperidone and haloperidol groups was 89.8 and 101.8 days and this difference was not statistically significant.

There were also generally no significant differences in long-term efficacy between the iloperidone and haloperidol group according to secondary endpoints, including adjusted mean changes from baseline in PANSS-T (−16.1 vs −17.4), PANSS-N (−4.7 in both groups), PANSS-P (−4.2 vs 5.3; p = 0.006), PANSS-GP (−7.1 vs −7.4) and BPRS (−9.0 vs −9.6) scores. By study end, approximately two-thirds of patients in each group achieved an improvement in CGI-C scores (65% vs 66% in the haloperidol group).

**ADVERSE EFFECTS AND TOLERABILITY**

Oral iloperidone was generally well tolerated in adult patients in short- and long-term clinical trials.23,24,26

**Acute Treatment**

Iloperidone’s safety profile was evaluated in double-blind phase III short-term trials.

The most frequent adverse events (AEs) with iloperidone were dizziness, dry mouth, dyspepsia, somnolence, increased bodyweight and tachycardia (Figure 3).23,27

With iloperidone, discontinuation due to adverse events was similar to placebo (i.e., 4.8%) whereas it was 7.6% for haloperidol and 6.2% for risperidone.23,27

In the short-term studies EPS was assessed using the Extrapyramidal Symptom Rating subscale (ESRS). In the pooled analysis of four short-term trials 27, iloperidone treatment was associated with a low incidence of EPS. Overall rating of EPS in the three six-week, placebo and haloperidol/risperidone-controlled trials indicated improvement from baseline to end-point with all iloperidone doses (4–8, 10–16 and 20–24 mg/day). This was in sharp contrast to haloperidol (15 mg/day), which showed worsening in most of the ESRS subscales.

In a short-term 6-week trial, recipients of iloperidone 12–16 or 20–24 mg/day appeared to show a trend to a lower risk for akathisia than placebo recipients.28

There were no clinically relevant changes in laboratory parameters (routine haematology, urinalysis and biochemical) or in total cholesterol and triglyceride levels, according to pooled analyses.18,27,29

In a pooled analysis of nine phase II and III double-blind or open-label trials evaluating iloperidone treatment in 4838 patients with schizophrenia, there were no clinically relevant changes in metabolic parameters like blood glucose, total cholesterol, triglyceride and prolactin levels (abstract report).29

**Maintenance Treatment**

Iloperidone treatment for 1 year was generally well tolerated in patients with schizophrenia, based on a pooled analysis of three 52-week trials.30

The most common adverse events occurring in the iloperidone group were insomnia, anxiety and aggravation of schizophrenia. In this long-term pooled safety analysis, iloperidone recipients also experienced a favourable long-term tolerability profile with respect to EPS (akathisia), weight gain and changes in metabolic parameters. The ESRS score improved in iloperidone recipients, whereas it worsened in haloperidol recipients (no quantitative data reported). Both groups showed minimal changes in bodyweight and QTc values.20,21

**CONCLUSION**

- Iloperidone is a second-generation antipsychotic agent indicated for the acute treatment of schizophrenia in adults.
- It works for both positive and negative symptoms of schizophrenia.
- Favorable safety profile
  - Well tolerated: Discontinuation rate due to adverse events is similar to placebo.
  - No or minimal extra-pyramidal side effects.
  - No Akathisia.
  - Minimal metabolic side effects: No clinically relevant changes in metabolic parameters like blood glucose, total cholesterol, triglyceride and prolactin levels.
  - Minimal Sedation
  - No anticholinergic side effects
  - ILOPRIDE can be considered suitable for switch-over therapy in patients who experience EPS with other medications.
  - It has similar efficacy to risperidone & ziprasidone for control of acute symptoms of schizophrenia in a short term studies.
  - It has similar efficacy to haloperidol for maintenance & for prevention of relapses in long-term studies.
• The tolerability profile of iloperidone is noteworthy in terms of modest weight gain, no medically important changes in lipid and glucose levels, little in the way of prolactin elevation, and absence of extrapyramidal side effects, including akathisia.

• Iloperidone may be best suited for patients who are sensitive to akathisia or who are unable to tolerate the sedation and weight gain that can occur more frequently with other antipsychotics.

Highlights of Paper

• Schizophrenia is a heterogeneous syndrome characterized by fundamental distortions of language, perception, thinking, social activity, affect, and volition.
• Schizophrenia affects about 24 million people worldwide.
• Schizophrenia is a treatable disorder, treatment being more effective in its initial stages.
• Conventional antipsychotics such the well-known phenothiazines (e.g., chlorpromazine), butyrophenones (e.g., haloperidol) and diphenylbutylpiperidine derivatives (e.g., pimozide) are used as first-line therapy for schizophrenia although this trend is changing and second-generation drugs, are now preferred as mainstay of treatment in several countries.
• Iloperidone has demonstrated a set of relative affinities and has been shown to have 300-fold greater activity in the limbic tract than in the nigrostriatal tract. Due to its receptor profile, it is anticipated that iloperidone will have efficacy in the treatment of psychosis and little to no risk of extrapyramidal symptoms.
• In May 2009, the Food and Drug Administration (USA) approved ‘Iloperidone’ for the acute treatment of adult patients with schizophrenia.
• Iloperidone may be best suited for patients who are sensitive to akathisia or who are unable to tolerate the sedation and weight gain that can occur more frequently with other antipsychotics.
• ILOPRIDE can be considered suitable for switch-over therapy in patients who experience EPS with other medications.
• The tolerability profile of iloperidone is noteworthy in terms of modest weight gain, no medically important changes in lipid and glucose levels, little in the way of prolactin elevation, and absence of extrapyramidal side effects, including akathisia.

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CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article

ACKNOWLEDGEMENT

Authors convey thanks to Dr. Hanmant Barkate, Dr. Rajendra Rane for their special guidance and moral support.


