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ORIGINAL ARTICLE

Long-term Effectiveness and Tolerability Profile of Iloperidone in Patients of Psychosis

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ABSTRACT

Aim: To evaluate the long-term efficacy, tolerability, and safety profile of iloperidone.

Materials and methods: A 12 month, prospective, interventional, open label, flexible dose study was conducted on 50 drug naïve, first-episode patients aged 18 to 65 years, fulfilling the International Classification of Diseases-10 criteria for psychosis, for assessing long-term efficacy and adverse events, including biochemical parameters of iloperidone. Detailed clinical examination was carried out. Sociodemographic data and baseline parameters were recorded.

Results: Two patients dropped out during the course of therapy. M/F ratio was 1.77:1. Mean age of patients was 28.76 ± 10.28 [mean ± standard deviation (SD)] years. Rural/urban ratio was 2.84:1.25. Patients were illiterate, 18 belonged to low socioeconomic class. It was observed that iloperidone was fairly efficacious not only in preventing relapse or aggravation of symptoms but also well restored the patient to almost near-normal till the end point. After 3 months, 20/48 (41.66%) patients showed significant weight gain that was evident. Mean total weight gain from baseline to end point was 2.89 kg and was statistically significant. There was significant rise in body mass index (BMI) but no patient crossed the upper normal limit. Iloperidone did not cause significant rise ($p < 0.6955$) in fasting blood sugar (FBS), and no significant alterations in total cholesterol (TC), triglyceride, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) cholesterol were recorded. Dizziness was one of the earliest adverse events appearing within 2 to 3 days; others were insomnia, weight gain, increased appetite, anxiety, headache, sedation, etc.

Conclusion: On long-term basis, iloperidone is fairly efficacious and has favorable tolerability profile with modest weight gain and practically no alteration in FBS, and lipid profile as well as absence of extrapyramidal side effects.

Keywords: Atypical antipsychotic, Efficacy, Metabolic profile, Tolerability.

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INTRODUCTION

International Classification of Diseases-10 (ICD-10), F20-F29 group of psychiatric disorders include schizophrenia, schizotypal disorder, persistent delusional disorders, acute and transient psychotic disorders, induced delusional disorder, and schizoaffective disorders. They are characterized by prominent disturbances of thought, perception, affect, and behavior.[1] Atypical antipsychotics have been established as first-line antipsychotic agents and are the pharmacologic treatment of choice because of their effectiveness and safety. A large number of atypical antipsychotic agents are currently available. Hence, choosing antipsychotic agents should primarily be based, first, on the long-term efficacy of the agent as the treatment of psychosis usually requires long-term therapy; second, a favorable tolerability profile with minimal incidence of adverse effects, though some agents have trivial benefits over others in causing minimal extrapyramidal side effects at therapeutic doses.

Different measures of effectiveness for assessing atypical antipsychotics as well as differences in efficacy among individual atypical antipsychotics, especially on long-term use, have given us an impetus to investigate the long-term efficacy of iloperidone. Efficacy is defined here as the magnitude of the effect or effectiveness produced by a given amount of drug, i.e., effectiveness per unit dose; it is the inverse of potency, which is the amount of drug required to produce a given effect. To assess the efficacy of an agent, treatment guidelines categorize well-controlled patients of psychosis as those who are free from recurrence of psychotic attacks or episodes of violent behaviors during the course of therapy (minimal rates of relapse); restoration of the patient to as near-normal as possible to the society and making them well oriented in thought, perception, and behavior; and finally improving quality of life.[2,3] The level of effectiveness required to treat the specific patient or patient groups must also be considered for choosing an atypical antipsychotic agent.

Although it has been argued that atypical antipsychotics are clinically interchangeable, their differences in efficacy as well as their tolerability profile have important consequences in determination of their long-term effectiveness as well as safety profile and compliance.

It is worth mentioning that atypical antipsychotics have gained much notoriety for causing metabolic derangements, including weight gain, dyslipidemia, and hyperglycemia, new-onset type II diabetes mellitus, and risk of developing metabolic syndrome. Moreover, these adverse effects are all risk factors for cardiovascular diseases and along with lifestyle changes and genetic components contribute to the decreased lifespan of patients with schizophrenia.[4] Hence, the aim of the present study was to investigate long-term efficacy as well as the tolerability profile inclusive of metabolic adverse events of iloperidone.

MATERIALS AND METHODS

A 12-month (January to December 2014), prospective, interventional, open label, flexible dose clinical study with iloperidone was conducted in the Department of Psychiatry and Pharmacology, Rohilkhand Medical College & Hospital, Bareilly, Uttar Pradesh, India. Approval for the study protocol was obtained from the Institutional Ethical Committee. Informed consent was taken from each patient or their legal caretakers before initiation of the study and one could withdraw without prejudice at any time. Registration from Clinical Trial Registry India (CTRI) was obtained and the registration number is CTRI/2014/10/005144.

Fifty consecutive patients aged 18 to 65 years who were diagnosed as having first-episode psychosis or its subtypes according to the ICD-10 group (F20-29) criteria and who met inclusion criteria were enrolled for the study. It was ensured that they did not receive any antipsychotic agent earlier since the study was carried out in drug-naïve patients of psychosis. Clinically, nonresponders to typical or other atypical antipsychotics were excluded from the study. Besides, patients with comorbid medical illnesses related to the heart, liver, kidney, thyroid, brain, pancreas, pregnant patients, and smokers were also excluded from the study.

The sociodemographic features were recorded. A detailed clinical examination was carried out and complete baseline investigations were also done. The patients were administered iloperidone monotherapy in doses of 6 to 12 mg/day; only benzodiazepines (lorazepam or clonazepam tablets or injections) were used as concomitant medication if at all required. Initially, lower doses of iloperidone were used and in 90% patients 6 mg/day controlled the symptoms. Further, as per clinical evaluation and response as assessed by consultant psychiatrist, upward titration of the dose was done. Blood pressure (BP) was measured using standard protocol. For calculating (BMI = kg/m^2), patients' height and weight were recorded using measuring tape and weighing machine respectively. Besides, patients' FBS and lipid profile were estimated at baseline. Patients under study were subsequently followed up and reassessed after 1, 3, 6, 9, and 12 months. During each follow-up visit, BP and weight of the patient were taken to calculate BMI; FBS and lipid profile were estimated; and the results were compared with baseline and last follow-up visit details. Additionally, psychiatric evaluation of patients was also done by consultant psychiatrist during each visit to assess efficacy of the drug clinically and to note adverse events or associated side effects during the study period in case report form. The treatment compliance was evaluated at each monthly visits using tablet counts and questioning the parents/relatives.

RESULTS

Of the 50 patients enrolled, only 48 patients completed the study. Two patients dropped out during the course of therapy due to noncompliance. Among them, 32 were males and 18 females; M/F ratio was 1.77:1; and the mean age of patients was 28.76 ± 10.28 [mean ± SD] years. Regarding rural/urban distribution, there was a preponderance of rural patients of 37, urban 13; R/U ratio was 2.84:1. About educational status, 25 patients were illiterate, 11 patients were below high school, and only 4 were graduates. Eighteen patients belonged to low socioeconomic class, 25 to lower middle class, and rest 7 to upper middle class. Iloperidone was evaluated for long-term efficacy. It was observed that it not only prevented relapse or aggravation of symptoms and signs but also well restored the patients to almost near-normal for the society during 12 long months of the study period.

Table 1 shows that FBS at baseline was 83.56 ± 5.39 mg/dL (mean ± SD), and at end point FBS was 83.44 ± 4.72 mg/dL (mean ± SD). Thus, iloperidone did not cause any statistically significant rise in FBS ($p < 0.6955$). Lipid profile with iloperidone did not show any statistically significant alteration in TC levels ($p = 0.8934$) at the end of study, from 143.73 ± 20.52 mg/dL (mean ± SD) at baseline to 143.6 ± 19.78 mg/dL (mean ± SD).

Triglyceride (TG) levels also did not show statistically significant increase ($p = 0.0928$), from 124.69 ± 12.91 mg/dL (mean ± SD) at baseline to 123.48 ± 11.20 mg/dL (mean ± SD) at the end point. Low-density lipoprotein levels too did not show statistically significant increase ($p = 0.7868$) at the end point, from 86.52 ± 6.64 mg/dL at baseline to 86.44 ± 5.90 mg/dL at the end point, and HDL levels also did not show statistically significant alterations ($p = 1.000$)

Table 1: Effect of long-term iloperidone therapy on biochemical parameters

Biochemical parameters	*Follow-up*					
	Baseline	*I (1 month)*	*II (3 months)*	*III (6 months)*	*IV (9 months)*	*V (12 months)*
FBS, mg/dL	83.56 ± 5.39	83.39 ± 5.19	83.33 ± 5.36	83.27 ± 5.22	83.38 ± 4.88	83.44 ± 4.72
p-value		p = 0.5045	p < 0.4413	p < 0.3697	p < 0.5843	p < 0.6955
TC, mg/dL	143.73 ± 20.52	143.98 ± 20.93	143.92 ± 20.15	143.67 ± 20.30	143.56 ± 20.22	143.6 ± 19.78
p-value		p = 0.7691	p = 0.8331	p = 0.9471	p = 0.8575	p = 0.8934
TG, mg/dL	124.69 ± 12.91	124.67 ± 12.48	124.44 ± 12.47	124.58 ± 12.29	123.88 ± 11.54	123.48 ± 11.20
p-value		p = 0.9672	p = 0.6428	p = 0.8535	p = 0.2260	p = 0.0929
LDL, mg/dL	86.52 ± 6.64	86.42 ± 6.26	86.63 ± 6.306	86.54 ± 6.301	86.54 ± 6.091	86.44 ± 5.900
p-value		p = 0.6131	p = 0.6569	p = 0.5069	p = 0.9438	p = 0.7868
HDL, mg/dL	44.68 ± 2.95	44.52 ±2.828	44.58 ± 2.879	44.52 ± 2.89	44.6 ± 2.68	44.63 ± 2.49
p-value		p = 0.7828	p = 0.8963	p = 0.7540	p = 0.9462	p = 1.000

Table 2: Effect of long-term iloperidone therapy on body weight and BMI

Body weight (kg)				*Body mass index (kg/m^2)*			
Baseline (mean ± SD)	*Follow-up (mean ± SD)*	*t-value*	*p-value*	*Baseline (mean ± SD)*	*Follow-up (mean ± SD)*	*t-value*	*p-value*
55.13 ± 5.34	(1 month) 53.42 ± 5.55	2.8327	0.0068	21.7 ± 1.67	(1 month) 21.92 ± 1.68	2.4735	0.0170
	(3 months) 56.04 ± 5.87	4.3181	<0.0001		(3 months) 22.08 ± 1.75	3.2543	=0.0021
	(6 months) 56.42 ± 6.12	5.1866	<0.0001		(6 months) 22.22 ± 1.85	4.0629	=0.0002
	(9 months) 56.75 ± 6.44	5.4956	<0.0001		(9 months) 22.34 ± 1.91	4.4440	<0.0001
	(12 months) 57.17 ± 6.86	5.7151	<0.0001		(12 months) 22.51 ± 2.06	5.0062	<0.0001
	(15 months) 58.02 ± 7.29	4.757	<0.05		(15 months) 23.01 ± 2.34	6.875	<0.05

at the end point, from 44.68 ± 2.95 mg/dL at baseline to 44.63 ± 2.49 mg/dL at the end of study.

Table 2 shows that out of 48 patients who completed the study, 20 (41.66%) patients experienced weight gain. Significant gain in weight was noted after 3 months. Mean body weight with iloperidone at baseline was 55.13 ± 5.34 kg (mean ± SD); it increased to 57.17 ± 6.86 kg (mean ± SD) at the end of 12 months therapy. Thus, there was statistically significant increase in body weight (up to 2.04 kg, $p < 0.0001$) after 12 months, and total increment in body weight at the end of study was 2.89 kg ($p < 0.05$). Body mass index at baseline was 21.7 ± 1.67 kg/m^2 (mean ± SD); it increased to 23.01 ± 2.34 kg/m^2 at the end of study. Statistically significant rise in BMI ($p < 0.05$) was recorded with iloperidone (though within normal range).

Table 3 shows dizziness was one of the earliest adverse events, appearing within 2 to 3 days and was observed in 12 patients owing to orthostatic hypotension. More frequent adverse events were insomnia in 23 patients, weight gain and increased BMI in 20 patients each, an increase in appetite in 15 patients, sedation, and headache.

Table 3: Adverse effects with iloperidone

Adverse effects	*Iloperidone No. (%)*
Insomnia	23 (46)
Weight gain	20 (40)
Increased BMI	20 (40)
Increased appetite	15 (30)
Orthostatic hypotension	12 (24)
Dizziness	12 (24)
Sedation	5 (10)
Headache	4 (8)
Anxiety	4 (8)
Somnolence	2(4)
Tremors	1 (2)
Constipation	1 (2)
Dry mouth	1 (2)
Extrapyramidal side effects	0 (0)
Impaired FBS	0 (0)
Dyslipidemia	0 (0)

DISCUSSION

Psychosis is a mental disorder in which the thoughts, affective response, ability to communicate and relate to others are sufficiently impaired to interfere grossly with the capacity to deal with reality; the classic characteristics of psychosis are impaired reality testing, hallucinations, delusion, and illusion.[5] Currently, atypical antipsychotics (second-generation drugs) are the sheet anchors for the therapy of psychosis owing to improvement in negative symptoms and lack of extrapyramidal symptoms.[6,7] However, there have been increased concern over metabolic effects of antipsychotic treatment.[8] Atypical antipsychotics enhance patient's quality of life with fewer relapses and reduced hospital stay, number of physician visits, and overall care

costs.[8,9] Thus, while considering the use of iloperidone as antipsychotic agent, one has to ask if this approach is sufficiently effective to halt the progression of disease and eventually reversing the condition and safety. But to develop effective, safe antipsychotic agent is quite challenging. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study also underlines the need for the development of new antipsychotic agents that provide more effective symptom control and improve outcomes while addressing the tolerability concerns seen with the current available agents.[10]

Chemically, iloperidone is a piperidinyl-benzisoxazole derivative structurally related to risperidone.[11] The second-generation or atypical antipsychotics are efficacious in treating positive symptoms as older agents coupled with better tackling of negative symptoms.[6] They act by dual serotonin and dopamine antagonism.[11,12] Atypical antipsychotic agents, in addition to their moderate potencies at dopamine receptors, interact with varying affinities at several other classes of receptors like alpha-1 and alpha-2 adrenergic, 5-hydroxytryptamine (HT)1A, 5-HT2A, 5-HT2C, M, and H1.[11,13]

A total of 50 patients were enrolled who had first-episode psychosis and were drug naïve to study the efficacy and to investigate various metabolic and other treatment emergent adverse events. Two patients in iloperidone group dropped out owing to irregular compliance because of cost of medicine or poor awareness that despite adequate control one has to take medicine for fairly long periods to prevent recurrences. The CATIE study also reported that antipsychotic treatment was marked by poor compliance, drug discontinuation with both conventional and atypical antipsychotics.[10]

Regarding sociodemographic features, there was preponderance of male patients (M/F ratio 1.77:1) and mean age of patients was 28.76 ± 10.28 (mean ± SD) years. Majority of patients belonged to rural area (R/U ratio 2.84:1), and mostly from low socioeconomic class and lower middle class. Concurring our observations, Robinson et al[14] also observed a higher prevalence (70%) of psychosis in males, usually from low to lower middle-class socioeconomic background. In the present study, most patients were from rural area since our catchment area was predominantly rural. Shah et al[15] in contrast reported that incidence of schizophrenia was higher in urban than in rural settings.

Iloperidone was assessed for long-term evaluation as it has proven efficacy, causes minimal adverse effects as well as exhibits better compliance and tolerability. The present study was conducted to verify the above noted observations in this region of Indian population. For assessing the long-term efficacy, the primary efficacy variable was time to relapse or aggravation of symptoms and signs and to restore the patients to as near-normal as possible to the society.[2] A decrease in symptoms was noted after 1 month and marked improvement after 2 months. None of the patient showed relapse during the course of therapy. Potkin et al[16] evaluated the efficacy of iloperidone *vs* placebo, using risperidone as the active control. A significantly better improvement in the Positive and Negative Syndrome Scale (PANSS) and Brief Psychiatric Rating Scale (BPRS) scores was found with patients treated with iloperidone 4 to 8 mg/day and 10 to 16 mg/day compared with placebo. Cutler et al[17] in a 4-week trial observed that iloperidone was found to have similar improvements *vs* ziprasidone in the PANSS total score (–12.01 *vs* –12.27 respectively) and BPRS score (–7.4 *vs* –7.2 respectively). In another study, iloperidone was shown to be as effective as risperidone treatment, after 6 weeks of treatment.[18]

Kane et al[19] described long-term efficacy result of three pooled, 52 weeks, prospective, randomized, multicenter, double-blind studies. Iloperidone and haloperidol groups were found to have only slight different rates of relapse. Further, when compared with haloperidol, iloperidone was not inferior in preventing relapse (iloperidone 43.5%, haloperidol 41.2%). The mean time to relapse in the iloperidone group and haloperidol group was 89.8 and 101.8 days respectively, and this difference was not statistically significant. We did not encounter any relapse during our long-term maintenance therapy since the patients were of first episode and drug naïve. Further, there were also generally no significant differences in long-term efficacy between iloperidone and haloperidol groups according to secondary end points. We cannot comment over secondary end points.

It was obvious from our observations that iloperidone remained effective throughout and that tolerance to iloperidone did not develop even on long-term basis since upward titration of doses at intervals was not required and majority of patients were well controlled on maintenance dose. Shah et al[15] observed that between 25 and 50% of schizophrenic patients attempt suicide, and 10% eventually succeed, contributing to a mortality rate eight times greater than that of the general population. In our study, none of the patients attempted suicide, indicating iloperidone not only prevented suicidal attempts but was also fully efficacious in controlling signs and symptoms of the disease.

Regarding biochemical parameters, tolerability, and adverse effects, it was observed that oral iloperidone was generally well tolerated in adult patients both in short- and long-term clinical study, and none of the patients stopped treatment because of adverse effects. Other short- and long-term clinical trials also observed similar findings including those of ours.[16,17,19-21] It was observed

that iloperidone caused no significant alternations in FBS in all the follow-ups compared with baseline values. Studies with respect to long-term effect of iloperidone on blood glucose level are very limited. De Hert et al[22] in a meta-analysis, which included data from 56 trials, majority being < 12 weeks duration, reported significant changes in blood glucose levels with iloperidone [±6.90 mg/dL; 95% confidence interval (CI) 2.4, 11.8, $p < 0.01$]. Similarly, Weiden et al[23] in short-term studies with three dose ranges of iloperidone observed mild elevation in serum glucose. Hochfeld et al[24] conducted a meta-analysis and data were analyzed from 3,210 patients who received iloperidone for up to 2 years. Three-dose ranges of iloperidone 4 to 8, 10 to 16, and 20 to 24 mg/day were used. Mean glucose level increased 5.4 mg/dL from baseline to week 4, and between 1.98 and 5.4 mg/dL from baseline to time point after week 6. Mean glucose levels for iloperidone 20 to 24 mg/day increased 9.0 mg/dL from baseline to time point after week 6. Mean glycosylated hemoglobin (HbA1C) levels did not change from baseline to the end of study. These authors observed that changes in glucose levels were unlikely to be of clinical concern. These findings are in contrast to our observations. Cutler et al[20] in a 25-week clinical trial of iloperidone observed that levels of serum glucose were essentially unchanged or decreased during treatment. These findings are in line with our observations.

Similarly no alterations in TC, TG, LDL, and HDL values were noted in all the follow-ups till end point. There is scanty literature in respect to effects of iloperidone on lipid profile and none of the studies have reported dyslipidemia following short- or long-term treatment with iloperidone. Supporting our observations, Cutler et al[20] reported that levels of serum lipids were essentially unchanged or decreased during treatment with iloperidone. De Hert et al[22] analyzed data from 56 trials mostly of short-term duration regarding asenapine, iloperidone, lurasidone, and paliperidone. Although statistically significant in general, no clinically meaningful differences were observed between four atypical antipsychotics and placebo regarding the mean change from baseline to end point in cholesterol levels.

In a short-term study, Weiden et al[23] reported that iloperidone (three-dose ranges) was not associated with any change from baseline in TC, but a slight decrease in TG levels were observed. Hochfeld et al[24] in a meta-analysis analyzed data from 3,210 patients who received three-dose ranges of iloperidone, where mean TG levels decreased from baseline to all points following iloperidone administration (–0.83 mg/dL). Fasting mean cholesterol change from baseline to the end of study was 8.2 mg/dL. This is in contrast to our findings. Hochfeld et al[24] observed that neither short-term nor long-term treatment with iloperidone led to development of high or borderline high cholesterol for the overall study period. Baseline fasting LDL and HDL cholesterol levels were within the normal limits and mean levels changed by 5 to 10 mg/dL following 4 weeks of treatment. With long-term treatment, these levels continued to improve or remain the same.

In the present study, the most frequent short-term adverse effects were dizziness, orthostatic hypotension (noted on 2nd or 3rd day of therapy owing to high affinity for alpha-1 receptors), insomnia, increased body weight, increased appetite, anxiety, headache, etc. Thus, monitoring of orthostatic vital signs should be considered in patients who are vulnerable to hypotension. Whereas on long-term therapy more frequent adverse effects increased, i.e., body weight, increased appetite, increased BMI, insomnia, sedation, headache, anxiety, etc. Both short- and long-term adverse effects noted were in line with other workers.[16,17,21,23]

Adverse effects did not cause any discontinuation of therapy in our study. Other authors observed that iloperidone discontinuation due to adverse events was similar to placebo (i.e., 4.8%).[16,23] Further, neither extrapyramidal signs and akathisia, nor hypersensitivity to iloperidone was observed. This was in contrast to CATIE study, which reported 4 to 8% extrapyramidal symptoms even with newer agents.[10] Additionally, we observed iloperidone did not affect metabolic syndrome incidence owing to minimal effects on FBS, lipid profile, and BP, despite significant weight gain. Metabolic syndrome has been recognized as a risk factor in patients with severe mental illnesses like schizophrenia.[25] However, De Hert et al[26] reported prevalence of metabolic syndrome to be three times more in second-generation antipsychotic treated group than in the first-generation treated patients contrary to our findings.

Majority of atypical antipsychotics have been associated with weight gain. We observed that a significant increase in weight became evident after third month in 20/48 (41.66%) patients. Statistically significant weight gain mean of 2.04 kg was noted at the end of 12 months and later the pace of increase in weight was slowed down during 13th to 15th months, and total mean increase in weight from baseline to end point was 2.89 kg ($p < 0.05$). Since there was preponderance of male patients, process to gain weight was noted more in males over 40 years compared with females. Further, because of lesser sample size and less number of women patients, we cannot comment over weight gain on gender basis. Weiden et al[23] in short-term study on iloperidone with three-dose ranges observed a mild weight gain (1.5–2.1 kg) similar to that of risperidone (1.5 kg). De Hert et al[22] in a meta-analysis of 56 trials mostly <12 weeks duration also noted a statistically significantly weight gain ($p < 0.001$) with iloperidone

(1 trial, n = 300, ±2.50 kg, 95% CI 1.92, 3.08). Findings of these authors supported our observations. Kane et al[19] in three long-term 52 weeks multicenter studies with 4 to 16 mg/day of iloperidone noted an increase in weight of 2.6 kg (SD ±3.7, n = 1,239) after <6 weeks of treatment. Hochfeld et al[24] in a meta-analysis reported that iloperidone administered to 3,210 patients for 2 years led to an average weight gain of 2.1 ± 6.8 kg following treatment for greater than 1 year and most weight gain occurred within first 6 weeks of the studies. These observations in respect to weight gain corroborated our findings though in variance, we observed significant weight gain after 3 months. Cutler et al[20] in a 25-week open label extension of a 4-week placebo and ziprasidone-controlled clinical trial of iloperidone also observed weight gain in 9.2% of patients of iloperidone (12 mg/BD). In contrast, we observed weight gain in greater percentage (41.66%) of patients with 8 to 12 mg/day of iloperidone.

There were no studies reporting long-term iloperidone-induced increase in BMI, an indicator of general obesity. We observed a statistically significant ($p < 0.05$) increase in BMI in each follow-up visit, and BMI at end point was 23.01 kg/m^2 and that none of the patients crossed upper normal range (24.99 kg/m^2). Long-term data in respect to BMI with iloperidone are quite sparse, hence, they cannot be compared. Thus, among atypical antipsychotics, iloperidone is fairly efficacious and has superb tolerability profile in terms of modest weight gain, practically no alterations in lipid and glucose parameters, and absence of extrapyramidal side effects including akathisia. Similar observations have been reported by Arif and Mitchell[27] that iloperidone is usually well tolerated and associated with low risk of causing extrapyramidal symptoms, hyperprolactinemia, and adverse metabolic effects.

LIMITATIONS

The main limitation of our study is the absence of a control group comprising subjects matched for age and sex and treated with placebo, or other prototypical antipsychotic agents were not used, and neither was a periodic hormonal assay done to establish the reasons for weight gain with iloperidone. Moreover, waist hip ratio, an indicator of abdominal obesity, and HbA1C level were also not measured.

CONCLUSION

The results of the study revealed that there is a significant gain in weight with iloperidone on prolonged treatment, which is related to age > 40 years and an increase in appetite. The association of weight gain and their potential to cause long-term complications will need further study to prevent and diagnose these complications early so that adequate precautions can be initiated. Iloperidone should be preferred in patients who are sensitive to akathisia, and cannot tolerate sedation or weight gain which are more common with other antipsychotics. Clearly, more robust prospective data from multicentric studies including control group could provide stronger evidence for efficacy and tolerability of iloperidone in the treatment of patients with psychosis.

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