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Original Work

Metabolic effects of Olanzapine versus Iloperidone: A 24 weeks randomized, prospective, interventional study

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ABSTRACT: Atypical antipsychotics have become the mainstay of therapy for psychosis. Though extrapyramidal side effects have been reduced with atypical antipsychotics, yet there are increased concerns over metabolic effects. The present study is aimed to comparatively evaluate the metabolic profile of olanzapine and iloperidone in cases of psychosis. A prospective, randomized, open label, observational study of 6 months duration was conducted in the Department of Pharmacology and Department of Psychiatry, Rohilkhand Medical College and Hospital, Bareilly. A total of 62 patients of both sexes newly diagnosed with psychosis (ICD-10, F20- F29) were included in the study, 31 each in olanzapine and iloperidone groups. Demographic parameters were recorded, following which the patient's body weight, BMI, fasting blood sugar and lipid profile were estimated at baseline. Follow-up of the patients was done periodically after one month, three months and six months. Olanzapine treated patients showed markedly significant rise in body weight up to 7 kg at the endpoint ($p<0.0001$) at each follow-up, with a significant increase in BMI. Rise in fasting blood sugar (FBS), total cholesterol (TC), triglycerides (TG) and low-density lipoprotein (LDL) levels werealso statistically significant. At the same time, significant decrease in HDL levels was also observed. Iloperidone treated patients showed statistically significant less rise in body weight (upto 1kg, $p<0.05$) and BMI. No significant changes in fasting blood sugar, total cholesterol, LDL and HDL levels were noted, while TG levels were significantly reduced. Iloperidone caused numerically less rise in bodyweight and BMI, and fewer metabolic adverse effects as compared to olanzapine, and hence should be preferred.

KEY WORDS: ***Atypical antipsychotics; Weight gain; Blood sugar level; Dyslipidemia***

INTRODUCTION

Psychosis is a symptom of mental illness characterized by distorted or non-existent sense of reality. Psychotic disorders have different etiologies, each of which demands a unique treatment approach.[1]The ICD-10, F20-F29 group of psychiatric disorders includes mental and behavioral disorders characterized by prominent disturbances of thought, perception, affect and behavior. The disorders in this section include schizophrenia, schizotypal disorder, persistent delusional disorders, acute and transient psychotic disorders, induced delusional disorder and schizoaffective disorders.[2]

Psychosis is primarily treated with antipsychotic drugs. Antipsychotic drugs are classified as typical and atypical agents. Atypical antipsychotic agents, in addition to their moderate potencies at dopamine receptors, interact with varying affinities at several other classes of receptors like alpha1 and alpha2 adrenergic, 5-HT1A, 5-HT2A, 5-HT2C, M and H1.[3] The clinically effective doses of atypical antipsychotics compared with typical antipsychotic exhibit markedly reduced extrapyramidal symptoms risk.[3] Atypical antipsychotics possess the advantage of treating negative symptoms. Yet there have been increased concerns over metabolic effects like weight gain, hyperglycemia, diabetes mellitus and lipid abnormalities.[3]

A comparative evaluation between olanzapine versus iloperidone has not been investigated

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thoroughly. A few studies have assessed the adverse effect profile of olanzapine with iloperidone, though not in an Indian population. The aims of the present study were to comparatively evaluate olanzapine (OLZ) which is a more commonly used antipsychotic for the treatment of psychosis with iloperidone (ILO) with regard to metabolic profile and assess whether there exists any major advantage of one drug over the other for the Indian population.

METHODOLOGY

A prospective, randomized, observational study of 6months duration (October 2013 to March 2014) was conducted to comparatively evaluate the metabolic safety profile of iloperidone versus olanzapine in the departments of pharmacology and psychiatry of Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh. Approval for the study protocol was obtained from the institutional ethics committee. The CTRI registration number of the study is CTRI/2014/10/005144. Each subject signed an informed consent form and could withdraw without prejudice at any time. Patients 18–65 years and of both genders attending the psychiatry outpatient department during the study period diagnosed with psychosis falling under the group (F20-F29) as per ICD-10 criteria and prescribed monotherapy with olanzapine or iloperidone were eligible to participate in the study.
The exclusion criteria included history of diabetes mellitus, severe cardiovascular disease, hepatic, renal or untreated thyroid disease, current medication such as antiepileptics (valproate or carbamazepine), antiparkinsonian agents (levodopa), birth control pills, steroids, propranolol and thiazide diuretics and agents that induce weight loss, pregnancy or breast-feeding and irregular compliance. A total of 62 patients (OLZ=31 and ILO=31) comprised the sample; of these two patients dropped out of the olanzapine group (n= 29) due to extrapyramidal side effects. All patients were allotted a reference number; the odd numbers were assigned to the olanzapine and even numbers to the iloperidone group. A predesigned, structured and pretested questionnaire was used to collect demographic information.
A complete clinical examination was conducted on all study subjects to rule out any chronic ailments referred to in the exclusion criteria. Data regarding age, sex, socio-economic status, family history, and other demographic parameters were recorded. For calculating BMI, the patient's height and weight were recorded. Blood pressure was measured using a standard protocol. Other relevant investigations were also performed. The patient's bodyweight (BW), body mass index BMI, fasting blood sugar (FBS) and lipid profile (TC, LDL, TG, HDL) was estimated at baseline and on each subsequent follow-up.
Flexible doses of both iloperidone (8-12 mg/day) and olanzapine (10-20mg/day) were administered. No other anti-psychiatric drug therapy was given during the study period though rescue medications like tablets/injections of lorazepam, tablet trihexyphenidyl, tablet clonazepam were administered for managing emergency and side effects, if any.
Patients were subsequently monitored and reassessed after one, three and six months with respect to alterations in biochemical parameters and adverse effects. Blood pressure was recorded to evaluate orthostatic hypotension. The consultant psychiatrist performed psychiatric evaluation of the patients during each visit.
Statistical analysis was performed using the software SPSS, Windows version 20. Mean values of change in BW, BMI, FBS and lipid profile at baseline and after one, three and six months were compared between two groups by using unpaired t-test and, in the groups, by paired t-test.

RESULT

Table 1 shows demographic characteristics. Out of 62 cases of psychosis (31 patients in each group), 45 (72.58%) were males and 17 (27.42%) females. M: F ratio is 2.65:1. The mean age in the olanzapine group was 29.4 ± 9.55 years and the mean age in iloperidone group was 30.81± 11.62.
Fifty (80.64%) patients out of 62 cases belonged to rural areas whereas 12 (19.35%) were from urban areas (rural:urban ratio 4.17:1). Thirty-four patients (54.83%)were illiterate while 28 (45.16%) were literate. Thirty-two (51.61%) patients had low socioeconomic status while 30 (48.38%) belonged to the middle class.
Table 2 shows BW, BMI, FBS, TC, TG, LDL, and HDL levels after one, three and six months with olanzapine. All the parameters were significantly altered. There was statistically significant increase ($p<0.0001$) in BW (upto7kg), BMI (2.49 kg/m^2), FBS (8.18 mg/dl), TC (9.86 mg/dl), TG (8.89 mg/dl) and LDL (5.48 mg/dl) after six months of therapy. HDL values were significantly decreased ($p<0.05$) after three and six months from baseline.
Table 3 depicts a statistically significant rise in body weight (upto 1 kg) and BMI (0.43 kg/m^2) overtime with iloperidone treatment ($p<0.05$ after 6 months). However, there were no significant alterations ($p>0.05$) between the baseline values and follow-up values of FBS, TC, LDL and HDL. Only TG showed a statistically significant decrease ($p<0.05$) after one, three and six months.
Table 4 shows the comparative values of BW and BMI between olanzapine and iloperidone in follow-ups. The two groups were well matched at baseline ($p>0.05$). After one month, treatment bodyweight

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showed no significant change (p=0.1179). After three months, the olanzapine group showed a statistically significant increase in bodyweight (p=0.0109) and bodyweight recorded a further more significant rise (p=0.0006) after six months. In short, olanzapine showed an increase of approximately 7kg over six months compared to 1kg with iloperidone.

Regarding BMI, there was comparatively no significant changes after one month and three months of therapy (p=0.9581 and p=0.1115, respectively). However, after 6 months there was markedly significant increase in BMI with olanzapine as compared to iloperidone (p=0.0025).

Table 5 compares the alterations in FBS between olanzapine and iloperidone treated groups from baseline to one, three and six months. Both groups were comparable at baseline (p>0.05) and after 1 month (p>0.05). However after 3 months statistically marked significant increase in FBS (p = 0.0048, 88.72±7.41 mg/dl in olanzapine group versus 83.77±5.60 mg/dl in iloperidone) was noted, FBS after 6 months became statistically highly significant (p<0.0001, 92.90±1.72 mg/dl in the olanzapine group versus 83.90±5.34 mg/dl in the iloperidone group).

Table 6 shows comparative changes in lipid profile between olanzapine versus iloperidone. Statistically no significant difference in LDL and HDL levels (p>0.05) was noted. Though, TC and TG levels were comparable at baseline after one month and three months (p>0.05), yet the olanzapine group showed statistically significant increase in TC (150± 24.68 mg/dl, p<0.05) and TG (134.41± 16.66 mg/dl, P<0.05) after six months.

Table 1:Distribution of demographic parameters

S.N.	PARAMETERS	OLZ	ILO	TOTAL NO. (%)	Test Value	P-Value
1	Male	24	21	45 (72.58%)	X^2 = 0.7294	0.3930
2	Female	7	10	17 (27.41%)		
3	Mean age ± SD	29.42 ± 9.55	30.81 ± 11.62	30.11 ± 10.57	t = 0.5145	0.6088
4	Rural	25	25	50 (80.64%)	X^2 = 0	1
5	Urban	6	6	12 (19.35%)		
6	Literate	13	15	28 (45.16%)	X^2 = 0.2605	0.6097
7	Illiterate	18	16	32 (51.61%)		
8	Low Socio-economic status	15	17	32 (51.61%)	X^2 = 0.2583	0.6112
9	Middle Class	16	14	30 (48.38%)		

OLZ – Olanzapine; ILO – Iloperidone; p> 0.05 = not significant

Table 2:Effect of olanzapine on BW, BMI, FBS and lipid profile

Parameters	Baseline Mean±S.D.	1 month Mean ± S.D.	t value	p value	3 months Mean ± S.D.	t value	p value	6 months Mean±S.D.	t value	p value
Bodyweight (kg)	55.17 ± 6.12	57.03 ±7.09	6.0293	< 0.0001	59.10 ±7.60	9.3392	< 0.0001	62.10 ±6.12	9.7084	< 0.0001
BMI (kg/m^2)	20.80 ± 1.20	21.4 ± 1.57	4.5556	< 0.0001	22.17 ±1.76	8.7066	<0.0001	23.29 ± 2.37	9.0664	< 0.0001
FBS (mg/dl)	84.72 ±6.11	85.83±5.84	3.016	= 0.0054	88.72 ±7.41	4.7742	< 0.0001	92.90 ± 9.24	6.296	< 0.0001
TC (mg/dl)	140.9 ± 22.53	142.03± 23.24	2.491	= 0.0169	146.17 ± 23.93	6.1592	< 0.0001	150.76± 24.68	6.9195	< 0.0001
TG (mg/dl)	125.52 ±14.10	126.07± 14.74	1.978	= 0.0576	130.93 ± 15.68	6.2718	< 0.0001	134.41± 16.66	7.8434	< 0.0001
LDL (mg/dl)	95.69 ± 16.88	96.97 ± 17.44	2.3593	= 0.0162	99.07 ± 17.94	5.7463	< 0.0001	101.17 ± 18.02	6.8829	< 0.0001
HDL (mg/dl)	45.86 ±4.94	45.62 ± 5.32	0.8262	= 0.4157	44.83 ±5.16	3.198	= 0.0034	43.76±5.49	4.9155	< 0.0001

p< 0.05 = significant; p> 0.05 = not significant

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Table 3:Effect of iloperidone on BW, BMI, FBS and lipid profile

Parameters	Baseline Mean ± S.D.	1 month Mean ±S.D.	t value	p value	3 months Mean ± S.D.	t value	p value	6 months Mean ±S.D.	t value	p value
Bodyweight (kg)	54.13 ± 5.08	54.58 ± 5.27	2.4762	= 0.0019 1	54.58 ±5.61	1.7259	= 0.0947	55.00 ± 5.08	2.6366	= 0.0131
BMI (kg/m^2)	21.19 ± 1.29	21.42 ±1.44	1.9757	= 0.0575	21.48 ± 1.58	1.7585	= 0.0089	21.62 ± 1.67	2.398	= 0.0229
FBS (mg/dl)	83.74 ± 5.74	83.87 ±5.41	0.7247	= 0.4743	83.77 ±5.60	0.1576	= 0.8758	83.90 ± 5.34	0.6139	= 0.5439
TC (mg/dl)	138.35± 22.45	138.13±2 2.47	0.8787	= 0.3866	138.23± 21.37	0.4027	= 0.6900	138.16 ±21.98	0.733	= 0.4692
TG (mg/dl)	125.52 ±13.81	124.72 ± 13.68	2.7864	= 0.0092	124.32 ±13.76	3.6612	= 0.0010	124.84 ±13.52	2.2437	= 0.0324
LDL (mg/dl)	92.23 ±16.65	95.16 ±16.45	0.2732	= 0.7866	95.32±1 6.07	0.4414	= 0.6621	95.19 ±15.68	0.1121	= 0.9115
HDL (mg/dl)	43.74 ±4.26	43.61± 4.06	0.8915	= 0.3798	43.87±3. 95	0.5967	= 0.5552	43.81 ± 3.81	0.2632	= 0.3794

p< 0.05 = significant; p> 0.05 = not significant

Table 4:Comparative evaluation of olanzapine and iloperidone on body weight and BMI

WEIGHT (kg)				BODY MASS INDEX (kg/m^2)			
OLZ (Mean ±S.D.)	ILO(Mean ± S.D.)	t value	p value	OLZ (Mean ± S.D.)	ILO(Mean ± S.D.)	t value	p value
Baseline 55.17± 6.12	**Baseline** 54.12± 5.08	0.7199	= 0.4745	**Baseline** 20.80 ±1.20	**Baseline** 21.19 ± 1.29	1.1966	= 0.2363
1 month 57.03 ±7.09	**1 month** 54.48 ±5.27	1.587	= 0.1179	**1 month** 21.40 ±1.57	**1 month** 21.42 ±1.44	0.0527	= 0.9581
3 months 59.10 ±7.60	**3 months** 54.58 ± 5.61	2.6319	= 0.0109	**3 months** 22.17 ± 1.76	**3 months** 21.48 ± 1.58	1.6163	= 0.1115
6 months 62.10 ±9.07	**6 months** 55.00 ±5.92	3.6133	= 0.0006	**6 month** 23.29 ± 2.37	**6 months** 21.62 ±1.67	3.1646	= 0.0025

p< 0.05 = significant; p> 0.05 = not significant

Table 5:Comparative effects of olanzapine and iloperidone on fasting blood sugar

FASTING BLOOD SUGAR (mg/dl)			
OLZ (Mean ± S.D.)	ILO (Mean ± S.D.)	t - Value	p value
Baseline 84.72± 6.11	**Baseline** 83.74± 5.74	0.6424	= 0.5232
1 month 85.83 ± 5.84	**1 month** 83.87 ± 5.41	1.3463	= 0.1835
3 months 88.72 ±7.41	**3 months** 83.77 ± 5.60	2.9318	= 0.0048
6 months 92.90 ±1.72	**6 months** 83.90 ±5.34	4.6438	< 0.0001

p< 0.05 = significant; p> 0.05 = not significant

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Table 6:Comparative evaluation of lipid profile with olanzapine and iloperidone

TOTAL CHOLESTEROL (mg/dl)				LOW DENSITY LIPOPROTEIN (mg/dl)			
OLZ (Mean ± S.D.)	**ILO (Mean ± S.D.)**	**t value**	**p value**	**OLZ (Mean ±S.D.)**	**ILO (Mean ± S.D.)**	**t Value**	**p value**
Baseline 140.9±22.53	**Baseline** 138.35±22.45	0.4369	= 0.6638	**Baseline** 95.69 ± 16.88	**Baseline** 92.23 ± 16.65	0.1071	= 0.9151
1 month 142.03 ± 23.24	**1 month** 138.13 ±22.47	0.6617	= 0.5108	**1 month** 96.97 ± 17.44	**1 month** 95.16 ±16.45	0.4049	= 0.6870
3 months 146.17 ± 23.93	**3 months** 138.23 ± 21.37	1.3585	= 0.1796	**3 months** 99.07 ± 17.94	**3 months** 95.32 ± 16.07	0.8531	= 0.3971
6 months 150.76 ± 24.68	**6 months** 138.16 ± 21.98	2.0908	= 0.0409	**6 months** 101.17 ± 18.02	**6 months** 95.19 ± 15.68	1.3737	= 0.1748
TRIGLYCERIDES (mg/dl)				**HIGH DENSITY LIPOPROTEIN (mg/dl)**			
Baseline 125.52± 14.10	**Baseline** 125.52± 13.81	0.0003	= 0.9998	**Baseline** 45.86 ±4.94	**Baseline** 43.74 ± 4.26	1.7840	= 0.0797
1 month 126.07 ± 14.74	**1 month** 124.72 ± 13.68	0.353	= 0.7254	**1 month** 45.62 ± 5.32	**1 month** 43.61 ± 4.06	1.6491	= 0.1045
3 months 130.93 ± 15.68	**3 months** 124.32 ± 13.76	1.7381	= 0.0875	**3 months** 44.83 ± 5.16	**3 month** 43.87 ± 3.95	0.8102	= 0.4212
6 months 134.41 ±16.66	**6 months** 124.84 ± 13.52	2.4515	= 0.0173	**6 months** 43.76 ± 5.49	**6 months** 43.81 ± 4.37	0.0394	= 0.9687

p< 0.05 = significant; p> 0.05 = not significant

DISCUSSION

Workers in the field have documented that most atypical antipsychotic agents, except a few, cause significant rapid increase in bodyweight ranging from 2–14 kg which occurs within 12 weeks of treatment and is one of the important adverse effects leading to drop out from the study.[4-7] In the present study, a rapid markedly significant increase in bodyweight was noted with olanzapine, after one (p<0.0001) three (p<0.0001), and six months (p<0.0001) whereas iloperidone caused comparatively less increase in weight during similar periods. The mean change in weight from baseline to endpoint was 7kg with olanzapine compared to 1 kg with iloperidone.

Allison *et al*[8] and Conley *et al*[4] observed that olanzapine caused weight gain of 4.15 kg at 10 weeks from baseline and 3.26 kg at 8 weeks respectively. Similarly, in the CATIE trial,[5] patients taking olanzapine gained an average of 0.9kg /month and a greater proportion of these patients gained 7% or more of their body weight at 18 months. Besides, Ganguli *et al*[9], Garyfallos *et al*[10], Volavka *et al*[6], Bobes *et al*[7], Brier *et al*[11] also observed significant weight gain and BMI increase after treatment with olanzapine and risperidone. Atmaca *et al*[12] have also noted that olanzapine and clozapine caused marked increase in weight. In a meta-analysis of 48 studies, Rummel-Kluge *et al*[13] have noted that olanzapine produced more weight gain than all other second generation antipsychotic agents. The results of the present study with respect to olanzapine are in line with previous findings.

De Hert *et al*[14] in a meta-analysis observed statistically significant weight gain with iloperidone (p<0.001) greater than placebo. Cutler *et al*[15] in a 25-week clinical trial with iloperidone (12 mg BD) noted weight gain (9.2%). Weiden *et al*[16] observed that iloperidone caused a mild weight increase (1.5-2.1 kg) similar to risperidone (1.5kg). Hochfeld *et al*[17] in a meta-analysis of 3200 patients who were administered iloperidone noted an average weight gain of about 2kg following treatment for greater than one year and most weight gain occurred within first six weeks of the studies. Thus, the results of the present study are comparable with these studies for iloperidone and that weight gain has been noticed after 1month of therapy (p=0.0019).

The precise mechanism of weight gain due to atypical antipsychotics is not clearly understood

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and appears to be a multifactorial phenomenon involving basically effects on receptors and neuroendocrine pathways (hypothalamic neurotransmitters and neuropeptides). Serotonin enhances satiety by stimulating Pro-opiomelanocortin (POMC) secretion by an effect mediated by 5-HT2c receptors; antagonists of 5-HT2c receptors prevent or delay the onset of satiety, thereby increasing the size of the meal. Histamine H1 receptor blockade activates hypothalamic AMP-activated protein kinase (AMPK), increasing appetite. Additionally, D2 receptor antagonism has also been implicated in antipsychotic associated weight gain. Further cells in the arcuate nucleus of the hypothalamus express neuropeptide Y (NPY) and Agouti-related protein (AgRP), two highlyorexigenic (appetite enhancing) peptides whose expression is increased by ghrelin and inhibited by leptin.[18]

In the present study we observed a highly significant increase in body mass index (BMI) after one, three and six months ($p<0.0001$) with olanzapine. In contrast iloperidone caused statistically significant increase in BMI only after three ($p=0.0089$) and six months ($p=0.0229$). Thus, comparatively iloperidone has shown a lower and delayed increase in BMI than olanzapine.

Allison *et al*[8] have noted that olanzapine also increased mean BMI by 1.1 kg/m^2. Robinson *et* al[19] have noted that the estimate of adjusted mean of BMI increased from 24.3 (95%, CI= 22.8–22.7) at baseline to 28.2 (95%, CI= 26.7–29.7) at 4 months with olanzapine. Ingole *et al*[20] in a short term trial have similarly observed that bodyweight and BMI show significant increase from baseline with both olanzapine and risperidone. Besides, other workers in the field[6-12] also have observed that an increase in BMI occurred after treatment with olanzapine. Thus the findings in our study on BMI in respect to olanzapine are consistent with that of the above noted workers. Data pertaining to iloperidone are not available.

In our study mean FBS values with olanzapine have shown statistically significant rise in each follow-up and ($p< 0.0001$) after six months. While iloperidone showed no significant alterations in FBS even after 6 months, Lindenmayer *et al*[21] and Atmaca *et al*[12] noted that olanzapine produced more increase in glucose levels than risperidone, ziprasidone and aripiprazole. Ingole *et al*[21] observed that mean blood sugar significantly increased in a short term trial with olanzapine ($p<0.0001$). The results of the present study are in line with the above studies. Fuller *et al*[22] and Farewell *et al*[23] also demonstrated that after one year of therapy, olanzapine use was a significant predictor of developing new onset diabetes and that development of diabetes mellitus takes more than 15 months.

In Phase I of the CATIE trial[5], olanzapine was associated with a significant increase in mean HbA1c. Similar to weight gain, olanzapine and clozapine appear to have the greatest risk for diabetes. A significant association between olanzapine and diabetes mellitus and insulin resistance in olanzapine subjects has also been observed.[24-26]

De Hert *et al*[14] in a meta-analysis haveobserved significant changes in glucose levels during short-term treatment with iloperidone (+ 6.90 mg/dl; 95% CI 2.4,11.8, $p< 0.01$). Hochfeld *et al*[17] observed fasting mean (SD) glucose changes with iloperidone 6.6 (24.0) from baseline to end of study, while Cutler *et al*[15] in a 25-week clinical trial with iloperidone noted that levels of serum glucose, lipids and prolactin were essentially unchanged or decreased during the treatment. Our observations in respect to FBS are in conformity with these authors.

Atypical antipsychotics have been shown to cause dyslipidemia[27-28]. These changes are largely related to concomitant weight gain; therefore, agents associated with the greatest weight gain may have the greatest propensity to cause dyslipidemia[28]. In our study, changes in lipid metabolism were observed in both olanzapine and iloperidone groups. Olanzapine significantly altered lipid parameters (TC, TG, LDL and HDL). TC levels significantly increased from baseline to endpoint ($p<0.0001$). Initially TG levels did not change till one month but rose significantly after three months ($p<0.0001$) and six months ($p<0.0001$). LDL values also increased significantly after each follow up. Cardioprotective HDL levels significantly decreased after three months ($p<0.05$) and six months ($p<0.0001$): these findings are similar to those of other workers who have also documented similar change in lipid metabolism with olanzapine. Lindenmayer *et al*[21] observed significant increase in mean TC at 14 weeks of 20.1mg/dl ($p<0.002$) in patients taking olanzapine. Atmaca *et al*[12] observed that olanzapine produced more changes in TC than risperidone, aripiprazole and ziprasidone besides there beinga marked increase in serum TG and leptin levels. Previous studies have documented a relation between atypical antipsychotics clozapine and olanzapine and serum leptin levels. Leptin has been associated with atypical antipsychotic induced weight gain. Besides, atypical antipsychotics especially clozapine and olanzapine are associated with higher risk of metabolic syndrome.[28]

Iloperidone however, showed no significant changes in TC, LDL, HDL levels from baseline to endpoint of therapy. An interesting result observed in this study was that TG levels were significantly decreased with iloperidone after one ($P<0.05$), three ($P=0.001$) and six months ($P<0.05$). Hochfeld *et al*[17] observed that non-fasting cholesterol showed decrease from baseline to time points after 4 weeks

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and neither short term nor long term treatment with iloperidone led to development of high or borderline high cholesterol in the overall study population. Fasting mean (SD) triglycerides changes were -0.83(82.3) mg/dl. Thus, iloperidone showed small changes in lipids that are unlikely to be of clinical concern. A decrease in TG levels is in line with our observations.

Limitations of the present study include the following: First, as the duration of the present study was relatively short, it was not possible to elicit further changes in bodyweight, BMI, glucose levels and lipid profile. Second, the number of patients included was small.

CONCLUSION

Comparative data are still too sparse to evaluate the metabolic safety profile of the two drugs used. Thus, there is a clear need for further controlled studies to comparatively evaluate which of the two agents is less problematic for short term safety and tolerability for treatment, with respect to weight gain and metabolic disturbances. Our study supports the safety and tolerability of iloperidone over olanzapine for the treatment of psychosis.

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