

An evaluation of the metabolic effects of antipsychotic medications in patients suffering from psychiatric illness

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ARTICLE INFO

Article history:

Received on: 23/01/2014

Revised on: 17/02/2014

Accepted on: 11/03/2014

Available online: 28/04/2014

Key words: Metabolic effects, psychiatric illnesses, olanzapine, risperidone, haloperidol.

ABSTRACT

Present study evaluates the effects of antipsychotic medications on metabolic parameters in patients suffering from psychiatric illness. The study was carried out at tertiary care teaching hospital, department of psychiatry after obtaining written informed consent from the patients. They were randomized into three groups - Group I (n=31) (haloperidol 10 mg/day, orally), Group II (n=34) (risperidone 4-6 mg/day, orally) and Group III (n=38) (olanzapine 10 mg/day, orally). Metabolic parameters [fasting blood sugar (FBS), post prandial blood sugar (PP₂BS), glycosylated haemoglobin (HbA_{1c}), serum cholesterol, triglyceride, low density lipoprotein (S.LDL) and high density lipoprotein (S.HDL)] were measured at the end of 3 and 6 months. Data was analysed using a suitable statistical tests. In group II significant changes ($p < 0.05$) were observed in FBS, HbA_{1c}, cholesterol, S.LDL and S.HDL while in group III significant changes ($p < 0.05$) were observed in all the metabolic parameters at the end of 6 months. In group III, FBS, PP₂BS, HbA_{1c}, Serum cholesterol, triglyceride and S.LDL levels were increased 9.41%, 7.09%, 8%, 6.25%, 7.68% and 9.92% respectively, at the end of 6 months. Patients treated with haloperidol showed minimum changes in metabolic parameters at the end of 6 months. Olanzapine is associated with more disturbances in metabolic parameters as compared to risperidone and haloperidol.

INTRODUCTION

Worldwide about 450 million people are estimated to be suffering from neuropsychiatric illness with 10 % prevalence in adult population (WHO, 2012). In India the prevalence of psychiatric illnesses are reported to be 58 to 73 per 1000 population as per different studies (Math et al., 2007). Pharmacological treatment is the most effective evidence based treatment in psychiatric illness. Anti anxiety, antidepressants, mood stabilizers and antipsychotic medications are used for the treatment of various psychiatric illnesses. Despite the different conventional medications there may be considerable overlap in the disorders for which they are actually indicated, and there may also be off-label use of these medications (Fielding and Lah, 1978). An antipsychotic agents are tranquilizing medications primarily used for the treatment of psychosis including delusions or hallucinations as well as disordered thought, particularly in schizophrenia and bipolar disorder. In 1990, the first atypical antipsychotic, clozapine was introduced followed by olanzapine, quetiapine, paliperidone, risperidone, zipracidone and aripiprazole.

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They have been approved to overcome extra pyramidal side effects associated with the use of typical antipsychotics at clinically effective doses. Despite these benefits, uses of atypical antipsychotics have been associated with adverse drug reactions like weight gain, diabetes and abnormal lipid profile. Weight gain and abdominal obesity are important risk factors for insulin resistance and dyslipidemia. It was discovered that some atypical antipsychotic agents like olanzapine and clozapine can increase insulin resistance and triglyceride levels without associated weight gain, while some atypical antipsychotic agents may have more direct adverse effects on glucose metabolism independently of any effects on body weight (Mcintyre et al., 2007, Lindenmayer et al., 2003). Recent findings from the CATIE study report a 40% prevalence of metabolic syndrome in patients with schizophrenia (McEvoy et al., 2005). So the metabolic profile monitoring of atypical antipsychotic agent are important when considering treatment options in this patient population. Cardiovascular diseases (CVD) are the most pressing healthcare problem and leading cause of death worldwide (Bonow et al., 2002). The World Health Organization estimates approximately 16.7 million deaths globally due to CVD every year, specially from myocardial infarction and strokes (WHO, 2012). Cardiovascular diseases contribute to 27% of death and its crude mortality is 227/100000 in India.

Because of limited number of studies were carried out in western part of India to evaluate the metabolic effects of antipsychotic medications in patients of psychiatric illness hence the present study was carried out to evaluate the same at civil hospital, a tertiary care teaching hospital, Ahmedabad.

MATERIAL AND METHODS

The current study was carried out at civil hospital, a tertiary care teaching hospital, ahmedabad over a period of 18 months (October 2010 to April 2012) after obtaining an approval of Institutional Ethics Committee (Ref no: EC/A/98/10/25.10.10), permission from Medical Superintendent and Head of the Department of Psychiatry. An observational, continuous, prospective, single centre study was carried out in patients prescribed with antipsychotic medications enrolled at Department of Psychiatry.

Patients ageing ≥ 18 years, with either gender reporting to the psychiatry outpatient department or admitted in psychiatric ward, diagnosed as a new case of psychotic disorder and prescribed same brand of antipsychotic drugs (either haloperidol, risperidone, or olanzapine) were included in the study after obtaining written informed consent from patients guardian. Patients associated with comorbid conditions like diabetes, cardiovascular diseases, already on other medications or concomitant medications which were likely to interact with antipsychotic medications, pregnant and lactating females were excluded from the study.

A total of 116 patients were enrolled and divided randomly in three groups as: a) Group I, haloperidol (10mg/day, orally) (n=36) b) Group II, risperidone (4-6 mg/day, orally) (n=40) and c) Group III, olanzapine (10 mg/day, orally) (n=40) treated group and followed up at the end of 3rd and 6th months. Compliance was assessed by pill count method and directly questioning the patients guardian at each follow-up visit and at the end of the study.

Metabolic parameters [fasting blood sugar (FBS), post prandial blood sugar (PP₂BS), glycosylated haemoglobin (HbA_{1c}), serum cholesterol, serum triglyceride, serum low density lipoprotein (S. LDL) and serum high density lipoprotein (S. HDL)] levels were measured at the baseline level, at the end of 3rd and 6th months.

All patients were advised to stop smoking and consumption of alcohol during the study period. The laboratory parameters were performed in validated fully automated biochemistry analyzer ERBA XL – 640 in biochemistry department by following methods:

- FBS and PP₂BS : Glucose oxidase-peroxidase method.
- HbA_{1c} : Enzyme immunoassay (EIA) method.
- Serum cholesterol: Cholesterol oxidase-phenol amino-phenazone method.
- Serum triglyceride : Glycerol-3-phosphate oxidase-phenol aminophenazone method.

- Serum LDL : Direct enzymatic method.
- Serum HDL : Direct enzymatic method.

The data were recorded and maintained in pretested and validated case record form. After proper compilation they were entered in Microsoft Excel spreadsheet 2007 and analyzed by repeated measures analysis of variance (ANOVA) and students unpaired 't' test for intergroup comparisons. *p* value < 0.05 was considered to be statistically significant.

RESULTS

A total of 116 patients were enrolled during study period, out of these, 103 patients were followed up at the end of 3 and 6 months while 13 patients were lost to follow up and hence, analysis was carried out for 103 patients.

Baseline comparison

It was observed that all the metabolic parameters were comparable and there was no statistical significant difference observed in above mentioned parameters between all three groups at baseline level.

Comparison before treatment, at 3rd and 6th month

There was no statistical significant change observed in all metabolic parameters in haloperidol treated group at the end of 3rd and 6th month as compared to the base line (Table I). In risperidone (4-6 mg/day) treated group statistically significant changes (*p*<0.05) were observed in FBS, HBA_{1c}, cholesterol, LDL and HDL at the end of 3 months and 6 months as compared to baseline.

The statistically significant (*p*<0.05) change was also observed in serum triglyceride levels at the end of 6 months as compared to baseline but it was not significant as compared to 3rd follow up (Table I). In group III (olanzapine 10mg/day), statistically significant changes (*p*<0.05) in all the metabolic parameters was observed the end of 6 months as compared to baseline and 3rd follow up (Table I, Figure IA,B,C).

Comparative analysis in between groups

Comparative analysis of the metabolic parameters at the end of 3 months showed that there was a statistically significant difference (*p*<0.05) observed in HbA_{1c} and serum triglyceride levels (ANOVA) however other metabolic parameters were not showing any statistical significance between all three groups (Table II).

Statistically significant (*p*<0.05) difference was observed in FBS, PP₂BS, serum cholesterol, serum triglyceride and serum LDL at the end of 6 months (ANOVA) (Table II). When it was compared between all three groups, differences HbA_{1c} and serum HDL levels were highly significant (*p*<0.001) however there was significant difference in other parameters at the end of 6 months (Table II).

Table 1: Analysis of metabolic parameters in patients treated with antipsychotic medications (n = 103).

Metabolic parameters	Haloperidol (10 mg/day)			Risperidone (4-6 mg/day)			Olanzapine (10 mg/day)		
	Baseline	3 months	6 Months	Baseline	3 months	6 Months	Baseline	3 months	6 Months
FBS (mg/dl)	93.8 ± 2.12	94.2 ± 1.82	94.5 ± 1.77	90.6 ± 1.58	93.8 ± 1.41*	96 ± 1.17*#	93.5 ± 2.12	97.7 ± 2.62*	102.3 ± 2.61*#
PP ₂ BS(mg/dl)	128 ± 1.96	129.6 ± 1.73	130.1 ± 1.30	124.7 ± 1.90	126.5 ± 1.66	127.9 ± 1.75	126.9 ± 1.58	131 ± 1.85*	135.9 ± 1.75*#
HbA _{1c} (%)	4.9 ± 0.036	4.9 ± 0.034	4.9 ± 0.032	4.9 ± 0.072	5 ± 0.069*	5.1 ± 0.065*#	5 ± 0.072	5.3 ± 0.069*	5.4 ± 0.081*#
S. Cholesterol (mg/dl)	169.4 ± 2.35	170.3 ± 2.40	170.7 ± 2.26	175.9 ± 5.33	178.7 ± 5.06*	181.1 ± 0.94*#	172.8 ± 3.77	178.8 ± 3.93*	183.6 ± 3.63*#
S. Triglyceride (mg/dl)	127.7 ± 2.71	127.8 ± 2.54	129 ± 2.30	126.6 ± 5.50	129.5 ± 4.96	131.5 ± 4.20*	135.4 ± 3.99	140.8 ± 4.19*	145.8 ± 3.96*#
S. LDL (mg/dl)	95.1 ± 1.69	95.8 ± 1.65	96.3 ± 1.57	93 ± 2.98	96.9 ± 2.74*	98.7 ± 2.90*#	94.8 ± 2.17	100.2 ± 2.21*	104.2 ± 2.13*#
S. HDL (mg/dl)	47.3 ± 1.44	46.7 ± 1.39	47.2 ± 1.82	47.5 ± 1.56	45.3 ± 1.25*	44.2 ± 1.20*#	45.2 ± 1.10	41.4 ± 1.00*	39.1 ± 0.94*#

Values are expressed in mean ± SEM; * = $p < 0.05$ as compared to baseline,

= $p < 0.05$ as compared to 3rd follow-up (Students un paired 't' test)

Table 2: Comparative changes in metabolic parameters at the end of 3rd and 6th months (n = 103).

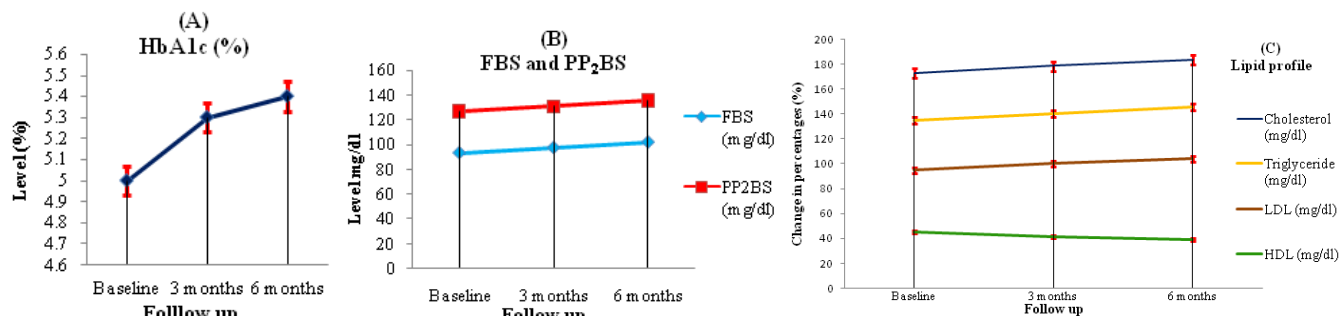
Metabolic parameters	At the end of 3 month			p value	At the end of 6 month			p value
	Group I (Haloperidol 10 mg/day) (n = 31)	Group II (Risperidone 4-6 mg/day) (n = 34)	Group III (Olanzapine 10 mg/day) (n = 38)		Group I (Haloperidol 10 mg/day) (n = 31)	Group II (Risperidone 4-6 mg/day) (n = 34)	Group III (Olanzapine 10 mg/day) (n = 38)	
FBS (mg/dl)	94.2 ± 1.90	93.8 ± 1.41	97.7 ± 2.42	$p > 0.05$	94.5 ± 1.96	96 ± 1.24	102.3 ± 2.61	$p < 0.05$
PP ₂ BS (mg/dl)	129.6 ± 1.82	126.5 ± 1.66	131 ± 1.75	$p > 0.05$	130.1 ± 1.44	127.9 ± 1.85	135.9 ± 1.75	$p < 0.05$
HbA _{1c} (%)	4.9 ± 0.04	5 ± 0.07	5.3 ± 0.07	$p < 0.05$	4.9 ± 0.036	5.1 ± 0.069	5.4 ± 0.081	$P < 0.001$
S. Cholesterol (mg/dl)	170.3 ± 2.51	178.7 ± 5.06	178.8 ± 3.72	$p > 0.05$	170.7 ± 2.5	181.1 ± 0.99	183.6 ± 3.63	$p < 0.05$
S. Triglyceride (mg/dl)	127.8 ± 2.66	129.5 ± 4.96	140.8 ± 3.96	$p < 0.05$	129 ± 2.55	131.5 ± 4.44	145.8 ± 3.96	$p < 0.05$
S. LDL (mg/dl)	95.8 ± 1.72	96.9 ± 2.74	100.2 ± 2.09	$p > 0.05$	96.3 ± 1.74	98.7 ± 3.07	104.2 ± 2.13	$p < 0.05$
S. HDL (mg/dl)	46.7 ± 1.46	45.3 ± 1.25	41.4 ± 0.94	$p < 0.05$	47.2 ± 2.01	44.2 ± 1.27	39.1 ± 0.94	$P < 0.001$

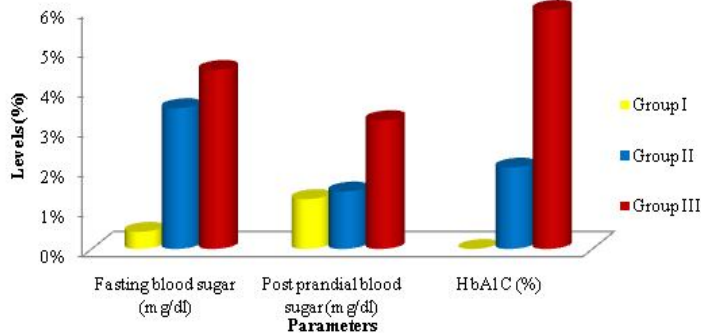
Values are expressed in mean ± SEM; One way ANOVA; $p < 0.05$ significance.

Table 3: Comparative mean differences of changes in metabolic parameters at the end of 3rd and 6th months (n = 103).

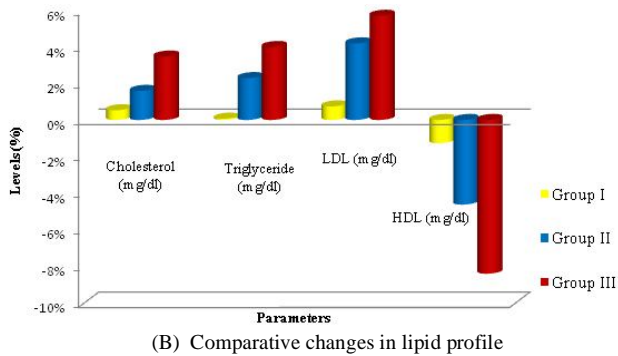
Metabolic parameters	At the end of 3 month			At the end of 6 month		
	Group I (Haloperidol 10 mg/day) (n = 31) (%)	Group II (Risperidone 4-6 mg/day) (n = 34) (%)	Group III (Olanzapine 10 mg/day) (n = 38) (%)	Group I (Haloperidol 10 mg/day) (n = 31) (%)	Group II (Risperidone 4-6 mg/day) (n = 34) (%)	Group III (Olanzapine 10 mg/day) (n = 38) (%)
FBS (mg/dl)	0.4 (0.43%)	3.2 (3.53%)	4.2 (4.49%)	0.7 (1.07%)	5.4 (5.96%)	8.8 (9.41%)
PP ₂ BS (mg/dl)	1.6 (1.25%)	1.8 (1.44%)	4.1 (3.23%)	2.1 (1.64%)	3.2 (2.57%)	8.7 (7.09%)
HbA _{1c} (%)	-	0.1 (2.04%)	0.3 (6%)	-	0.2 (4.08%)	0.4 (8%)
S. Cholesterol (mg/dl)	0.9 (0.53%)	2.8 (1.59%)	6 (3.47%)	1.3 (0.77%)	5.2 (2.96%)	11.6 (6.25%)
S. Triglyceride (mg/dl)	0.1 (0.07%)	2.9 (2.29%)	5.4 (3.99%)	1.3 (1.02%)	4.9 (3.87%)	10.4 (7.68%)
S. LDL (mg/dl)	0.7 (0.74%)	3.9 (4.19%)	5.4 (5.70%)	1.2 (1.26%)	5.7 (6.13%)	9.4 (9.92%)
S. HDL (mg/dl)	-0.6 (-1.27%)	-2.2 (-4.63%)	-3.8 (-8.41%)	-0.1 (-0.21%)	-3.3 (-6.95%)	-6.1 (-13.5%)

Note: Baseline values are taken as 100% in each group.

**Fig. 1:** Analysis of the metabolic parameters in patients treated with olanzapine (10mg/day) (n = 103) (mean ± SEM).



(A) Comparative changes in blood glucose and glycosylated haemoglobin.



(B) Comparative changes in lipid profile

Fig. 2: Difference of mean in metabolic parameters in patients treated with antipsychotic medications at the end of 3rd follow up (n = 103).

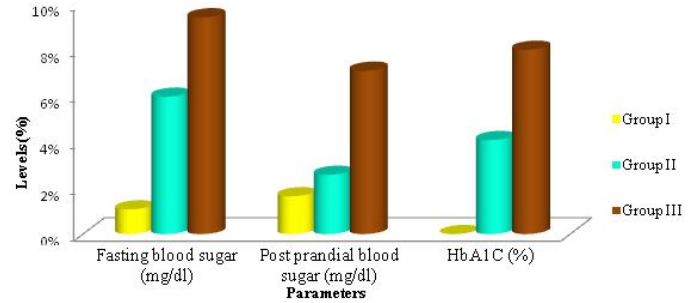
Differences(%) in metabolic parameters at the end of 3rd and 6th month

It was observed that at the end of 3 months, FBS, PP₂BS and HbA₁C levels were increased higher in olanzapine (10 mg/day) treated group which was 4.49%, 3.23% and 6% respectively (Table III, Figure IIa). Lipid profile levels were also changed more in olanzapine (10 mg/day) treated group (figure IIb) where as patients treated with haloperidol showed minimum changes in metabolic parameters at the end of 3 months (Table III and Figure IIa,B). It was observed that at the end of 6 months, FBS, PP₂BS and HbA₁C levels were increased higher in olanzapine (10 mg/day) treated group which was 9.41%, 7.09% and 8% respectively (Table III, Figure III A).

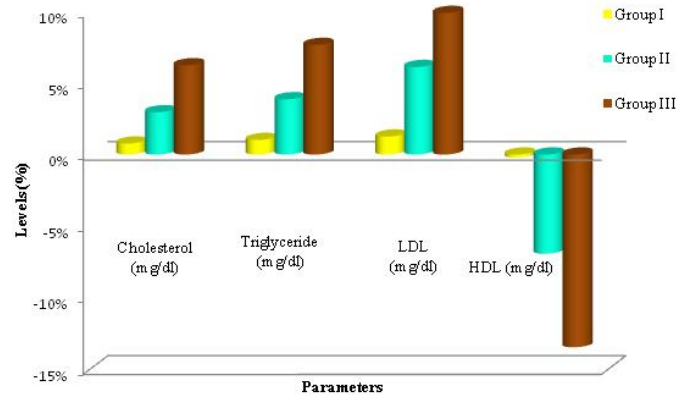
Serum cholesterol, triglyceride and LDL levels were increased 6.25%, 7.68% and 9.92% respectively, while HDL was decreased 13.5% (figure III B). Patients treated with haloperidol showed minimum changes in metabolic parameters at the end of 6 month (Table III and Figure III A,B).

DISCUSSION

There was no statistically significant difference observed in all metabolic parameters after 3 and 6 month of treatment in patients treated with haloperidol. Krakowski M *et al.*, (2009), and Lindenmayer JP *et al.* (2003) revealed that patients on haloperidol showed no significant increase in blood glucose levels and lipid profile after 12 weeks and 14 week of treatment respectively which was similar to present study (Krakowski *et al.*, 2009).



(A) Comparative changes in blood glucose and glycosylated haemoglobin.



(B) Comparative changes in lipid profile.

Fig. 3: Difference of mean in metabolic parameters in patients treated with antipsychotic medications at the end of 6th follow up (n = 103).

Haloperidol associated with less chances of significant increase in visceral obesity which may be an important factor for development of insulin resistance and metabolic syndrome (Lindenmayer *et al.*, 2003). We observed in risperidone (4-6 mg /day) treated group showed statistically significant ($p < 0.05$) change in blood glucose levels (FBS, HbA₁C) and lipid profile (cholesterol, triglyceride, LDL, HDL) at the end of 3 and 6 months of treatment. Similar results have been reported by various studies with significant change in metabolic parameters. Changes in metabolic parameters reported in different studies are different which may be due to cultural and ethnic variation or difference in the follow up periods and sample size between the studies. In our study, olanzapine (10mg/day) treated group showed mean increase of 8.8 mg/dl in FBS after 6 months of treatment which was statistically significant ($p < 0.05$). Similar results were observed in a 14 week trial with olanzapine in patients with schizophrenia where mean change in FBS value was 14.3 mg/dl which was also statistically significant ($p < 0.05$) (Lieberman *et al.*, 2005). We also observed statistically significant ($p < 0.05$) increase in HbA₁C level after 6 month treatment with olanzapine, which was synonymous with other study results (Brown and Michael, 2005). In present study, there was a significant ($p < 0.05$) increase serum cholesterol (11.6 mg/dl), serum LDL (9.4 mg/dl) and serum triglyceride (10.4 mg/dl) after 24 week of olanzapine (10 mg/day) treatment, which was similar to study carried out by Newcomer *et al.* (2009) showing significant ($p < 0.05$) increase in weight (4.6 kg), serum cholesterol (21.1 mg/dl), serum LDL (20.5 mg/dl) and serum

triglyceride (30 mg/dl) after 24 weeks treatment of olanzapine (5 mg/day) (Newcomer *et al.*, 2002). Similar observations in lipid profile were reported by other studies as mentioned in table 10. Though changes in metabolic parameters are different in different studies, may be due to cultural and ethnic variation, difference in the follow up periods and sample size. Comparative analysis of all groups in the present study showed that there was statistically significant changes in weight, BMI, HbA_{1c}, serum triglyceride and serum HDL at the end of 3 months treatment, which was similar to study carried out by Gautam S *et al.*, (2011), reported significant ($p < 0.05$) changes in blood glucose levels and lipid profile at end end of 3 months (Gautam and Meena, 2011). There are various possible mechanisms which may be responsible for disturbances in metabolic parameters with different antipsychotic treatments.

Dysglycemia

Dwyer DS *et al.*, (1999) have shown that certain antipsychotic agents, including clozapine, olanzapine and chlorpromazine can inhibit glucose uptake via interactions with glucose transporter proteins in in-vitro studies whereas other agents such as haloperidol, had a marginal effect on glucose transport (Dwyer and Donohoe, 2003).

Risperidone can also interact with these intracellular proteins, but the limited lipophilic nature of this agent results in reduced tissue to plasma concentration ratio, suggesting that intracellular protein interactions as well as intracellular drug concentrations may be critical to the prediction of drug effects in this area. Differing effects on glucose transport can be hypothesized to underlie the clinical observation of different adiposity-independent antipsychotic drug effects on insulin sensitivity.

Dyslipidemia

The mechanisms underlying the changes in lipid parameters associated with antipsychotic therapy have been little studied although a number of possible mechanisms have been suggested. Epidemiological studies in the general population provide a variety of data showing that weight-gain and obesity increase the risk of dyslipidemia. Obesity and weight gain are associated with increased triglyceride and LDL-cholesterol levels and reduced HDL-cholesterol. Antipsychotic agents differ markedly in their weight gain potential, suggesting that the effects on lipid levels seen with antipsychotic agents may primarily be related to their effect on bodyweight and adiposity (Dwyer and Donohoe, 2003).

Other factors may also play a role in the development of treatment associated dyslipidemia. The development of glucose intolerance would be expected to affect lipid levels, as insulin resistance is a key factor in the pathophysiology of dyslipidemia. A few reports of substantial elevations in triglyceride levels with only modest weight gain raise the possibility of a direct antipsychotic effect on lipid levels by some as yet unknown mechanism (Newcomer *et al.*, 2002).

Increase food intake and weight gain

Decrease in noradrenaline and adrenaline turnover and plasma concentrations during olanzapine treatment may also be relevant to understanding drug effects on glucose metabolism that could occur independent of changes in adiposity. As decrease in noradrenaline concentration leads to lesser stimulation of β_3 receptors in brown adipose tissue, which eventually leads to decrease fat burning and more fatty tissue accumulation and development of metabolic syndrome (Rebecca and Sahakian, 1995). Olanzapine-induced body weight gain may be associated with functional changes in the muscarinic neurotransmission in the dorsal vagal complex and hypoglossal nucleus as olanzapine, but not haloperidol, treatment induces a significant decrease in the binding density of M2 receptors in dorsal vagal complex of rats (Deng *et al.*, 2007).

The mechanism for weight gain and eventually metabolic disturbances with atypical antipsychotics has been correlated to blockade of 5-HT_{2c} receptors, which is supported by the evidence that mutant mice in which 5-HT_{2c} “knockout” been produced are becoming obese. Drugs which block 5-HT_{2c} receptors make the body unable to shut off appetite, and are associated with increased weight gain (Stahl *et al.*, 2009). Olanzapine having more 5-HT_{2c} receptors blocking property than risperidone (Kroeze *et al.*, 2003). Recently H₁ receptor blockade is another reason for the weight gain, which can be produced by clozapine and olanzapine (Eder *et al.*, 2001). The mechanisms by which H₁-histamine antagonism might induce weight gain are currently unknown, although prior studies have demonstrated that H₁-histamine receptor antagonism increases feeding in rodents and depletion of neuronal histamine increases feeding (Matsui-sakata *et al.*, 2005).

Another receptor association been found out for these metabolic changes and these are associated with β_3 - adrenergic receptors (Gebhardt *et al.*, 2010). Blockade of β_3 receptors in brown adipose tissue, which eventually leads to decrease fat burning and more fatty tissue accumulation (Sahakian *et al.*, 1983).

Leptin is an adipocyte derived hormone which acts on leptin receptors present in the hypothalamus of the brain, where it inhibits appetite by counteracting the effects of neuropeptide Y (a potent feeding stimulant secreted by cells in the gut and in the hypothalamus) and promoting the synthesis of melanocyte stimulating hormone (an appetite suppressant). Number of studies reported that adiposity and plasma leptin concentration are associated with metabolic changes (Haupt and Newcomer, 2005). Ghrelin is an orexigenic peptide whose concentration increases with the treatment with atypical antipsychotic agents (Murashita *et al.*, 2005). Ghrelin increases the release of neuropeptides like neuropeptide Y, agouti related peptide, orexin A and B, endorphins which eventually stimulates the appetite centres in lateral hypothalamus. Sporn AL *et al.*, (2005), suggested that olanzapine induced metabolic changes are associated with failure of mitochondrial function and fat oxidation results in ectopic fat storage, insulin resistance and type II diabetes mellitus (Sporn *et al.*, 2005). Recent preclinical study also favours the findings suggesting that olanzapine and clozapine are associated with an

increase in fat intake which increases a level of free fatty acids and eventually metabolic syndrome which is less with haloperidol (Hartfield *et al.*, 2003).

Genetic factors also play an essential role in development of metabolic dysregulations with olanzapine. Muller DJ *et al.* (2005) revealed that polymorphism of SNAP-25 and Mnl I and tai I gene is associated with antipsychotic induced weight gain (Muller *et al.*, 2005). Ellingrod VL *et al.* (2002), reported a positive association between 759 C polymorphism of the 5HT2C receptor gene and olanzapine induced weight gain (Ellingrod *et al.*, 2002).

CONCLUSION

Hence we conclude that typical antipsychotic agents are associated with less metabolic disturbances in comparison with atypical antipsychotic agents. Atypical antipsychotic agents produce significant disturbances in blood glucose and lipid profile levels. Olanzapine treatment is associated with high risk of abnormal metabolic changes. Prescribers should be aware about detailed pharmacological information of antipsychotic medications. Prescribing of atypical antipsychotics should be considered after assessment - history including personal and family, general and laboratory parameter measurement. Atypical antipsychotics should be avoided in high risk patients like, obesity, insulin resistance, hypertension, hyperlipidemia. Thus prescription of antipsychotic agents must be based on patient's metabolic parameters and they should be measured during the course of treatment.

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How to cite this article:

Nimit Nitinkumar Goswami, Anuradha M Gandhi, Prakruti P Patel, Ram Kumar Dikshit. An evaluation of the metabolic effects of antipsychotic medications in patients suffering from psychiatric illness. *J App Pharm Sci*, 2014; 4 (04): 014-019.