Short Term Comparative Evaluation of Metabolic Adverse Effects Profile of Mirtazapine Versus Paroxetine

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ABSTRACT

Introduction: Depression is the common psychological disorder worldwide and is a leading cause of disability. Second generation antidepressants (mirtazapine and paroxetine) are now acknowledged to be the first line treatment for depression. Aim of the study was to comparatively evaluate mirtazapine and paroxetine with regards to metabolic adverse effects (body weight, BMI, FBS, lipid profile) in cases of depression.

Material and methods: It is a short term prospective, randomized, open label, interventional clinical study of 6 months duration was conducted in the Department of Pharmacology and Psychiatry, Rohilkhand medical college and Hospital, Bareilly. A total of 60 newly diagnosed patients of depression (ICD-10, F32.0- F32.8) of age group 18-65 years of both the sexes were enrolled. Patients were randomly divided in two groups and were administered flexible dose of mirtazapine 7.5mg – 30mg daily and paroxetine 12.5mg – 37.5mg daily. A complete clinical examination and investigations were conducted on all subjects to rule out any chronic ailments referred to in exclusion criteria. Demographic parameters were recorded, following which patient's weight, BMI, fasting blood sugar and lipid profile was estimated at baseline. Follow up of the patients was done at 1, 3 and 6 months.

Results: Mirtazapinegroup shows statistically significant increase in Body weight from baseline 54.11 $\pm$ 5.07 kg (mean $\pm$ SD) to 59.61 $\pm$ 4.87 kg after 6 months of therapy. Thus there was a marked increase in body weight (upto 5 kgs, $p<0.0001$), Similarly BMI also increased from baseline 21.14 $\pm$ 1.44 kg/m^2 (mean $\pm$ SD) to 23.30 $\pm$ 1.86 kg/m^2 after 6 months. However, none of the patients crossed the normal range. Statistically significant increase in B.W. and BMI was observed at each follow-up visits at 1,3 and 6 months. Data shows no statistically significant changes in FBS, TC, TG, HDL, LDL values.

Conclusion: In this short term study, Paroxetine was found to be associated with less increase in weight and BMI to Mirtazapine when used for the treatment of depression. However, definitely long term study with both the drugs is required to comparatively evaluate metabolic adverse effect profile in terms of weight gain, BMI, FBS and lipid profile.

Keywords: depression, mirtazapine, paroxetine, metabolic adverse effects.

INTRODUCTION

Depression is one of the common psychological disorder which affects about 121 million people worldwide. World health organization (WHO) had already stated that depression is one of the major cause of disability and the fourth mojor contributors to the global burden of disease.[1]

Pharmacological treatment dominates the management of depressive disorders. Trends in pharmacotherapy in depression have changed over the past few years. Selective serotonin reuptake Inhibitors (SSRIs) and newer antidepressants namely mirtazapine, duloxetine etc. has replaced tricyclic antidepressants (TCA) and monoamine oxidase inhibitors (MAOIs).[2]

Antidepressant drugs increase the risk of weight gain, Type 2 DM, dyslipidemia and other metabolic adverse effects leading to discomfort and discontinuation of treatment.[3]

There is evidence that antidepressant drugs may induce a variable amount of weight gain but results are sparse and contradictory. SSRIs induced weight gain is most likely caused due to alteration in serotonin 2C receptor activity, increase in apetite, craving for carbohydrate, or recovery from clinical depression.[4]

Mirtazapine is a new antidepressant with unique pharmacological profile that differs from currently available antidepressants. It is a specific antagonist of alpha-2 receptors, which has only a marginal effect on alpha-1 receptors. Blockade of presynaptic alpha-2 auto receptors causes increased norepinephrine release, and direct blockade of inhibitory alpha-2 heteroreceptors, located on serotonin (5-HT) terminals, leads to increased serotonin release. As the 5-HT$_2$ and 5-HT$_3$ receptors are blocked by mirtazapine, however, serotonin release is produced exclusively by stimulation of the 5-HT1 receptors. This dual action, via both neurotransmitter systems, is the reason that mirtazapine has been termed a noradrenergic and specific serotonergic antidepressant (NaSSA).[5]

Paroxetine is a selective serotonin reuptake inhibitor (SSRI) which is indicated for the treatment of depression and also for obsessive-compulsive disorder, panic disorder, social phobia, generalized anxiety disorder, post traumatic stress disorder, premenstrual dysphoric disorder and chronic headache. Paroxetine is the most potent inhibitor of 5-HT reuptake of all currently available antidepressants. It is a very weak inhibitor of norepinephrine uptake but it is still more potentate this site than the other SSRIs and this may contribute to its efficacy at higher doses. The selectivity of paroxetine, i.e. the ratio of inhibition of uptake of NE to 5-HT is amongst the highest of the SSRIs.[6]

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Indians are more susceptible to the metabolic effect of psychotropic drug and there are very less studies conducted in this regard.[3] Because of less data available on Indian Studies[2], we conduct this short term study to compare the metabolic adverse effects profile of Mirtazapine versus Paroxetine.

Aim and objective of the research was to comparatively evaluate mirtazapine and paroxetine with regards to metabolic adverse effects (body weight, BMI, FBS, lipid profile) in cases of depression.

MATERIAL AND METHODS

A six months (short term) prospective, randomized, interventional, open label flexible dose clinical study to compare the metabolic adverse effects in patients of depression receiving treatment with either mirtazapine or paroxetine was conducted in the department of Pharmacology and department of Psychiatry, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh. Approval for the study protocol was obtained from the Institutional Ethical Committee. Each subject signed an informed consent statement prior to participation and could withdraw without prejudice at any time.

Patients of 18-65 years age group and of both genders attending to Psychiatry outpatient department during the study period diagnosed with depression falling under the group (F32.0-F32.8) as per criteria of the 10th edition of the International Classification of Diseases (ICD-10) receiving either mirtazapine or paroxetine were included in the study. It is ensured that they have not received any antidepressant agent earlier as the study was carried out in drug naïve individuals of depression.

A total of 60 patients (MIR=30 and PAR=30) comprised of sample size and all patients were allotted a reference number. Simple randomization was done and the odd numbers were assigned to mirtazapine and even numbers to paroxetine group.

Flexible dose schedule of both drugs were used, mirtazapine 7.5-30mg/day and paroxetine 12.5-40mg/day depending on evaluation of clinical condition and clinical response by the consultant psychiatrist, though initially lower doses were administered. No other antidepressant drug therapy was given to patients except test drugs during the study period. All the patients who were enrolled and participating in the clinical study were emphatically told that they have to take the prescribed medicine for at least 6months despite adequate control to prevent reoccurrence of depression.

Newly diagnosed, first episode cases of depression (ICD-10, F32.0- F32.8, drug naïve patients) of age group 18-65 years, of both sexes were included in the study.

Following patients were excluded from the study: Patient of age group less than 18 and more than 65 years. Pregnant and lactating females. Patients with history of taking antidepressant before the study. Patients with history of Diabetes mellitus. Dyslipidemic and obese patients. History of significant and untreated medical illnesses including severe cardiovascular disease, hepatic, renal, or untreated thyroid disease, hepatitis and HIV. Patients currently taking the following medication, antiepileptic, antipsychotic, antiparkinsonian drugs, birth control pills, steroids, propranolol, thiazide diuretics and agents that induce weight loss.

Following investigations to be done for screening of patients: Fasting Blood sugar; Lipid profile: LDL, HDL, TG, TC; ECG; Renal function test; Liver function test; T3, T4, TSH; Pregnancy test (females); Urine routine and microscopy. While fasting blood sugar and lipid profile done in each follow up.

A complete preliminary clinical examination was conducted on all the subjects included in the study to rule out any chronic ailments referred to in the exclusion criteria. After initial screening, the socio demographic data regarding age, sex, socio-economic status, family history and other demographic parameters were recorded in the case report form. Patients were then evaluated by senior consultant psychiatrist.

For calculating body mass index (BMI= kg/m^2) patient's height and weight were taken using measuring tape and weighing machine respectively. Blood pressure was measured with using standard protocol. Thereafter, relevant

Characteristic	Group A(Mir)	Group B (parx)	table-Value	P-Value	Significance
Age	39.13 ± 5.77	40.2 ± 6.70	0.6628	0.5101	NS
Sex					
Male	13	14	0.067	0.795	NS
Female	17	16			
Locality					
Ruler	19	14	1.684	0.1943	NS
Urban	11	16			
Education					
Illiterate	14	11	0.617	0.4321	NS
Literate	16	19			
Socio-economic Status					
Lower	9	2	8.455	0.0762	NS
Lower middle	8	12			
Upper	0	1			
Upper Lower	11	9			
Upper middle	2	6			

Table-1: Demographic characteristic

Parameters	Baseline	1 Month	t-value	p-value	3 Months	t-value	p-value	6 Months	t-value	p-value
Body Weight	54.11 ± 5.07	55.00 ± 4.97	5.3986	0.0001	56.18 ± 4.78	5.3853	0.0001	59.61 ± 4.87	6.7562	0.0001
BMI	21.14 ± 1.44	21.48 ± 1.46	4.7868	0.0001	21.42 ± 1.40	5.3202	0.0001	23.30 ± 1.86	6.5979	0.0001
FBS	84.46 ± 5.19	84.61 ± 5.73	0.1779	0.8601	84.11 ± 4.86	0.3287	0.7449	84.29 ± 6.23	0.1125	0.9113
TC	138.82 ± 16.33	138.29 ± 12.23	0.2007	0.8424	138.75 ± 16.18	0.0202	0.9841	138.50 ± 23.14	0.603	0.9502
TG	124.25 ± 13.75	124.96 ± 8.10	0.3989	0.6931	124.21 ± 6.11	0.0159	0.9874	124.32 ± 6.55	0.0239	0.9811
LDL	85.32 ± 5.36	85.04 ± 3.55	0.2546	0.8009	85.96 ± 6.81	0.4121	0.6835	85.57 ± 4.24	0.1738	0.8633
HDL	44.75 ± 3.01	44.89 ± 3.44	0.1768	0.861	44.00 ± 2.39	0.133	2.2672	44.93 ± 2.91	0.2461	0.8075

Table-2: Shows the effect of mirtazapine on mean body weight BMI, FBS and lipid profile

Parameters	Baseline	1 Month	T-value	P-value	3 Months	T-value	P-value	6 Months	T-value	P-value
Body Weight	55.45 ± 6.16	55.55 ± 6.03	1.7974	0.0831	55.71 ± 5.92	2.5564	0.0163	56.48 ± 5.55	3.9761	0.0004
BMI	20.85 ± 1.22	20.90 ± 1.17	1.8431	0.075	20.95 ± 1.15	2.5033	0.0184	21.27 ± 1.11	3.9223	0.0005
FBS	83.97 ± 3.98	83.93 ± 4.92	0.0333	0.973	83.69 ± 5.02	0.2294	0.8202	83.66 ± 5.41	0.2780	0.7831
TC	136.59 ± 14.20	136.17 ± 11.54	0.3662	0.7170	136.76 ± 8.14	0.1045	0.9152	136.24 ± 5.94	0.1631	0.8716
TG	125.14 ± 8.36	125.17 ± 10.18	0.0214	0.9831	125.0 ± 13.49	0.0583	0.954	125.06 ± 11.33	0.0317	0.9750
LDL	83.66 ± 4.30	83.38 ± 4.00	0.2514	0.8030	83.72 ± 3.32	0.0759	0.9400	83.76 ± 3.79	0.1080	0.9147
HDL	45.66 ± 3.66	45.65 ± 2.53	0.0000	1.000	45.17 ± 2.70	0.6834	0.5000	45.69 ± 2.42	0.0429	0.9661

Table-3: Shows the effect of paroxetine on mean body weight BMI, FBS and lipid profile.

investigations were done. Patient's fasting blood sugar and lipid profile was estimated at baseline. After baseline investigations, patients were randomly divided in two groups one group was administered flexible dose of mirtazapine 7.5-30 mg daily and the other group received flexible dose of paroxetine 12.5-40 mg daily as per the clinical response.

Patients under study were subsequently monitored and reassessed at 1month, 3 month and 6 month. During each follow up visit weight of the patient was recorded to calculate body mass index, blood glucose level and lipid profile were also estimated and the result of investigations was compared from baseline and last follow up visit details. Psychiatric evaluation of the patients was also done by the consultant psychiatrist during each visit. All adverse events or associated side effects during treatment were recorded in case report form. The treatment compliance was evaluated at each monthly visits using tablet counts and questioning the parents/relatives.

STATISTICAL ANALYSIS

Statistical analysis was performed with (SPSS) windows version 20. Change in meam values of body weight, body mass index (BMI), blood sugar level and lipid profile (at baseline,1 month, 3 month, 6 month) were compared between two groups by using unpaired 't' test and in the groups by paired 't' test.

RESULTS

Table–1 shows the demographic parameters and socioeconomic status of the patients enrolled in the study. There were no statistically significant difference between both the groups with respect to age (p=0.5101), Sex (p= 0.795), locality (p = 0.194), education (p= 0.432) and socioeconomic status (p= 0.0762).

Table-2 shows statistically significant increase in body weight from baseline 54.11 ±5.07 kg (mean ± SD) to 59.61 ± 4.87 kg after 6 months of therapy. Thus there was a marked increase in body weight (upto 5 kg, p<0.0001), weight gain was evident after 1 month of therapy with mirtazapine.

Similarly mirtazapine also increased mean BMI from baseline 21.14 ± 1.44 kg/m^2 (mean ± SD) to 23.30 ± 1.86 kg/m^2 after 6 months. However, none of the patients crossed the normal range. Statistically significant increase in B.W. and BMI was observed at each follow-up visits at 1,3 and 6 months.

Regarding effect of Mirtazapine on FBS, mean FBS at baseline was 84.46 ± 5.19 mg/dl and at the end point was 84.29 ± 6.23 mg/dl, thus reflecting no significant changes in FBS (p= 0.9113). No statistically significant alteration at end point in TC (p=.9505) and TG (p=.9811) levels were recorded LDL and HDL levels also showed no statistically significant increased p= 0.8633 and 0.8075 at end point respectively thus indicating that mirtazapine did not significantly altered lipid profile parameters.

Mean body weight at baseline was 55.45 ± 6.16kg and it increased to 56.48 ± 5.55 kg at the end of 6 months. Thus, paroxetine also showed a statistically significant increased in body weight (upto 1.1kg p = 0.0004) and the increase was evident as early as after 2nd follow-up visit at 3 months.

Mean BMI at baseline was 20.85 ± 1.22 mg/m^2 and it was statistically significantly increased to 21.27 ± 1.11kg/m^2 at the end point. The increase in BMI was observed after 3 months of treatment. However, none of the patients crossed the normal range (18.5 – 24.99kg/m^2).

Weight	Group A(Mir)	Group B (parx)	P-Value	Significance
Baseline	54.11 ± 5.07	55.45± 6.16	0.3743	NS
1 month	55.00± 4.97	55.55± 6.03	0.7111	NS
3month	56.18± 4.78	55.71± 5.92	0.7431	NS
6month	59.61± 4.87	56.48± 5.55	0.0283	Significant
BMI				
Baseline	21.14± 1.44	20.85± 1.22	0.4277	NS
1 month	21.48± 1.46	20. 90± 1.17	0.0960	NS
3month	21.92± 1.40	20.95± 1.15	0.0057	Very significant
6month	23.30± 1.86	21.27± 1.11	<0.0001	Highly significant

Table-4: Comparison of Meanweight and BMI in Group A and Group B in Follow-up visit

FBS	Group A(Mir)	Group B (parx)	t-Value	P-Value	Significance
Baseline	84.46± 5.19	83.97± 3.98	0.4008	0.6901	NS
1 month	84.61± 5.73	83.93± 4.92	0.4813	0.6322	NS
3month	84.11± 4.86	83.69 ± 5.02	0.3208	0.7496	NS
6month	84.29± 6.23	83.66± 5.41	0.4081	0.6848	NS

Table-5: Comparison of Mean FBS in Group A and Group B in Follow-up visit.

TC	Group A(Mir)	Group B (parx)	t-Value	P-Value	Significance
Baseline	138.82± 16.33	136.59± 14.20	0.5507	0.5840	NS
1 month	138.29± 12.23	136.17± 11.54	0.6733	0.5036	NS
3 month	138.75± 16.18	136.76± 8.14	0.5897	0.5578	NS
6 month	138.50± 23.14	136.24± 5.94	0.5090	0.6128	NS
TG	Group A(Mir)	Group B(parx)	t-Value	P-Value	Significance
Baseline	124.25± 13.75	125.14± 8.36	0.2965	0.7680	NS
1 month	124.96± 8.10	125.17± 10.18	0.0860	0.9318	NS
3 month	124.21± 6.11	125.0± 13.49	0.2830	0.7782	NS
6 month	124.32± 6.55	125.06± 11.33	0.3005	0.7650	NS

Table-6: Comparison of Mean TC and TG in Group A and Group B in Follow-up visit.

Adverse Effects	Mirtazapine (n=30)	Paroxetine (n=30)
Somnolence	20 (66.66%)	0(0.00%)
Dizziness	8 (26.66%)	0(0.00%)
Headache	4 (13.33%)	2 (6.66%)
Insomnia	0 (0.00%)	13 (43.33%)
Nausea	7 (23.33%)	20 (66.66%)
Anxiety	2 (6.66%)	5 (16.66%)
Tremors	1 (3.33%)	5 (16.66%)
Dry Mouth	2 (6.66%)	0 (0.00%)
Sexual Dysfunction	0 (0.00%)	4 (13.33%)

Table-7: shows main adverse effects associated with mirtazapine versus paroxetine

Paroxetine does not significantly alter the mean FBS as FBS at the baseline was 83.97 ± 3.98mg/dl (mean ± SD) and after 6 months 83.66 ± 5.41.

No statistically significant rise in mean TC (p= .9502) and mean TG (p= 0.9811)level from baseline till the end point. Also mean LDL (p=0.9147) and mean HDL (p= .9661) were not significantly raised, which indicated that on lipid profile parameters paroxetine had no significant effect.

Table-4 Shows comparative evaluation of mirtazapine and paroxetine on body weight and BMI, both agents caused increase in body weight but mirtazapine comparatively cause more increased in body weight at 6 month. Significant difference in body weight between two agents were noted only after 6 months, a markedly significant p value (p=0.0283) was obtained.

Similarly mirtazapine caused more marked significant rise in BMI compared to paroxetine and statistically significant difference was noted after 3 months onwards.

Table-5 shows comparative evaluation of FBS between mirtazapine and paroxetine treated groups. No statistically significant difference in mean FBS was observed in both the groups.

Table-6, shows comparative evaluation of mirtazapine and paroxetine on TC, TG, LDL and HDL levels. No statistically significant difference was recorded between two groups in lipid profile.

The present study also compared various other adverse effectsover 6 monthstreatment who received mirtazapine and paroxetine. The most common adverse experiences occurring during 6 months treatment with mirtazapine were somnolence (66.66%), Dizziness (26.66%), headache (13.33%), Nausea (23.33%), anxiety (6.66%), dry mouth (6.66%). With paroxetine the common adverse effects noted were insomnia (43.33%), Nausea (66.66%) anxiety (16.66%), tremors (16.66%) and sexual dysfunction in males (13.33%).

DISCUSSION

Depression is one of the leading causes of global disease, burden and disability.[7] The Pharmacological tretament of

depression include TCAs, Monoamine oxidase Inhibitors (MAOIs) and SSRIs. Because of serious adverse effect and dangerous food interactions TCAs and MAOIs are not preferred these days and are being largely replaced by SSRIs and novel antidepressants like mirtazapine, duloxetine etc.

Mirtazapine is a new antidepressant that is noradrenergic and specific serotonergic antidepressant. Paroxetine is specific serotonergic receptor Inhibitor. There is a limited data available among Indian population regarding the associated between these drugs and metabolic adverse effect profile.

The primary objective of our study was short term comparison of the metabolic adverse effect of Mirtazapine versus Paroxetine. In the present study, patients of young age group predominated with insignificant difference in number of males and females.

In this study, Mirtazapine caused significant increase in weight as early as after 1 month onward and marked increase up to approximately 5.5 kg at the end point (6th month) whereas Paroxetine caused lesser increase in weight approx. 1.04kg. Our findings are in the accordance with the studies of Chen-Jee Hong et al,[7] who observed greater weight increase for the mirtazapine treated patients. In a retrospective study done by Lahon et al.[2] treatment with Mirtazapine for depression was associated with weight gain. The association of Mirtazapine with weight gain is also supported by previous studies.[8] Weight gain was with the highest incidence in the Mirtazapine groups (p=0.04) when compared with fluoxetine (SSRIs).[9]

In our study Mirtazapine showed statistically significant increase in weight in the all follow-ups within the group (5.5.kg at end point). Paroxetine also showed increase in weight (1.04 at end point) but the pattern of increase in weight differed in both with higher gain with Mirtazapine group.

Although some SSRIs are typically associated with weight loss during initial therapy.[10,11] Weight is often regained after 6 months and can be followed by additional weight gain with long term use. Uncontrolled studies have reported weight gain of 10.80 kg for paroxetine after 6-12 months of therapy.[10] Nihalani Net al[12] in their study reported that Mirtazapine had shown greater weight gain when compared to SSRIs (Paroxetine, Fluoxetine and Citalopram). In a double-blind design study,[13] Mirtazapine showed statistically significant increase of 2.5% body weight over the course of the study that appeared to reach a plateau as early as 3 weeks of the study. In an 8 weeks open-level pilot study[14] of Mirtazapine in children (age 8-12 years) with social phobia showed significant weight gain was observed with Mirtazapine. Lamer M et al[15] in their 6 weeks period controlled clinical study trial observed mean $\pm$ SD body weight increase from 63.6 $\pm$ 13.1 kg to 66.6 $\pm$ 11.9kg during Mirtazapine treatment (p= 0.27) and fat mass increase in study subjects from 20.9 $\pm$ 9.6kg to 22.1 $\pm$ 9.3kg (p= 0.018). In these studies weight gain with mirtazapine occurred in early weeks of treatments. Our findings consistent with these authors.

Short-term antidepressant therapy studies have suggested that the chances of weight gain is less likely to occur when SSRI are used in the short term (3 to 6 months).[8] In contrast to this a 24 weeks double blind study of paroxetine and sertraline showed significantly gain in weight.[16] Four US studies in their meta analysis report found that there was gain in weight with mirtazapine during the first four weeks of treatment.[17] This is in line with our observations. Though blockade of histamine H_1, and Serotonin 2C receptors mirtazapine is likely to be related to weight gain in both the short-term and long term.[18]

Paroxetine may be more likely than other SSRIs to cause weight gain during short-term or long-term treatment.[13] Weight change induced by Paroxetine is probably related to alliteration in serotonin 2C receptor activity, appetite increase, carbohydrate craving or recovery from clinical depression.[16] Moreover, there were no patients who had significant weight gain (increase of $\geq$ 7% to baseline body weight) among 60 patients at the end point in both the group. Weight gain as a side effect of antidepressant therapy[19] in the short-term (3 to 6 months) and the long term (1 year or longer) contribute to the reluctance of patients to continue or start treatment.[16]

In our study, highly significant increase ($p<0.0001$) in BMI was observed with mirtazapine after each 1,3 and 6 months follow-up. 17 cases (56.66%) showed increase BMI with mirtazapine. Paroxetine also caused significant increase in BMI after 3 months of therapy and observed in only 8 patients (26.66%).

Few studies have reported increase on BMI with SSRI.[20,21] Kim EJ et al[22] in their study observed that after 3 months of paroxetine treatment BMI was unchanged which is not in line with our observations.

In our study, regarding FBS, it was observed that both mirtazapine and paroxetine treated groups did not significantly after FBS values. Hyperglycemia was associated with mirtazapine in retrospective study done by Lahon et al.[2] Derijks H J et al[23] also observed that mirtazapine was associated with hyperglycemia. Hyperglycemia was reported by star Khoza et al[24] following treatment with mirtazapine and paroxetine. The time to onset of glucose dysregulation ranged from 4 days to 5 months after initiation of antidepressant therapy. More than two thirds (68%) of the cases (n=1) reported glucose control disturbances with 1 month of therapy. All these observation do not support our study regarding glucose disturbances.

Reader et al[25] reported an association between the use of SSRI and abdominal obesity, hypercholesterolemia and a trend toward diabetes. Mirtazapine did not influence the glucose homeostatic in 6 weeks study by Lamer M. etal[15,] which as supporting our study. A number of research workers[2,26,13] observed hypercholesterolemia and abnormal lipid profile when mirtazapine prescribed for depression and commented that mirtazapine was a drug that was known to cause dyslipidemia. Mirtazapine subjects also showed significantly increased TC at week 4 (p=0.16) and a transient rise in TG that normalized by week 4 no significant changes observed in any of the other lipid parameters.

Paroxetine cause increased cholesterol, increased LDL as well as HDL in the 3 months study by Kim et al.[22] Julie L et al[27] in their study found that mirtazapine associated hypertriglyceridemia had contributing to the development of acute pancreatitis and diabetic ketoacidosis.

Dyslipidemia was noted in 2 (6.66%) patients with mirtazapine group which was not significant.

The adverse effect profile is an important consideration while prescribing drug in the treatment of depression. The present study also compared various other adverse effects over 6 months treatment who received mirtazapine and paroxetine. The most common adverse experiences occurring during 6 months treatment with mirtazapine were somnolence (66.66%), Dizziness (26.66%), headache (13.33%), Nausea (23.33%), anxiety (6.66%), dry mouth (6.66%). With paroxetine the common adverse effects noted were insomnia (43.33%), Nausea (66.66%) anxiety (16.66%), tremors (16.66%) and sexual dysfunction in males (13.33%).

Dropouts within the mirtazapine group were 2 subjects because of somnolence and weight gain.1subject receiving paroxetine dropped-out of the study because of insomnia.

There were some differences in the adverse effects profile of the two antidepressants. Many authors[28,29] observed similar type adverse effects with mirtazapine and paroxetine in short term studies. However, Wade et al,[30] in their 24 weeks treatment observed only one adverse effect which state significantly higher incidence of fatigue with paroxetine found increased sweating, headache and nausea**.** Davis R et al[31] short term 5 to 6 weeks randomized double-blind comparative trial observed drowsiness, excessive sedation, dry mouth, increased appetite occurred significantly more frequently with mirtazapine. In another prospective, open randomized comparative 8 weeks study done by Tae Sukkim et al.[32] Reported that the subject (12%) paroxetine treated groups discontinued therapy because somnolence and other common adverse effects were nausea, headache, sweating, dizziness and sexual dysfunction. Metabolic syndrome has been recognized as a risk factor in patients with severe mental illnesses like schizophrenia.[33,34]

In the present study mirtazapine treated group had been largely associated with increase in Bodyweight, BMI as compared to paroxetine treated group while effect on glucose, and lipid levels were unaffected by the both drugs. In our study no serious adverse effect which required hospitalization were found with either drugs.

Limitation

Because short duration of study and relative small sample size any definite conclusion could not be achieved.

CONCLUSION

In this short term study, Paroxetine was found to be associated with less increase in weight and BMI to Mirtazapine when used for the treatment of depression. However, definitely long term study with both the drugs is required to comparatively evaluate metabolic adverse effect profile in terms of weight gain, BMI, FBS and lipid profile.

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