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Pharmacy

IMPACT OF PATIENT COUNSELLING AND PATIENT EDUCATION BY THE CLINICAL PHARMACISTS IN THE MANAGEMENT OF DELUSIONAL DISORDER,ANXIETY,MANIAC PATIENTS WITH PSYCHOSIS BY ADMINISTERING PLACEBO IN REPLACEMENT OF OLANZAPINE: A RANDOMIZED SINGLE BLIND CONTROLLED STUDY.

Mounika Pamukuntla*	Department of Pharmacy Practice, MNR College of Pharmacy, Fasalwadi,Sangareddy, TS, India. *Corresponding Author
Deepika Bojja	Department of Pharmacy Practice, MNR College of Pharmacy, Fasalwadi,Sangareddy, TS, India.
Mounika Burgupally	Department of Pharmacy Practice, MNR College of Pharmacy, Fasalwadi,Sangareddy, TS, India.
Mekala Anusha	Department of Pharmacy Practice, MNR College of Pharmacy, Fasalwadi,Sangareddy, TS, India.
Nikhil Chinka	Department of Pharmacy Practice, MNR College of Pharmacy, Fasalwadi,Sangareddy, TS, India.

ABSTRACT

Back ground of the study Psychosis, anxiety, maniac,delusional disorders are the major central nervous system disorders which are causing major change to the patients of all the ages.

Objectives The objective of this study is to evaluate the role of clinical pharmacist in providing affective patient counselling by replacing olanzapine with placebo in psychosis patients

Study design, Study duration

A Prospective, Single blind , Randomized controlled trial was conducted from Dec 2017-May 2018 at a 350-beded Tertiary care teaching hospital in Sangareddy, Telangana.

Methodology 200 patients were enrolled in this study and divided into two Groups .To Group A (Control group) patients were given with conventional antipsychotics therapy and to group B patients (Case group) where Olanzapine was replaced with placebo. Successive patient counselling sessions were performed for case group by clinical pharmacist while leaving the control group for conventional therapy and not performed any patient counselling. Patient response was analyzed.

Results Males(59%) were more prone to psychosis when compared with female(41%).More side effects were experienced by Group A patients when compared to Group B .T-test have been performed where P- value is 0.0128, $P < 0.05$ so there is statistically significant difference between two groups .Group B (20%) patients gained less weight when compared with Group A(40%). So Group B is more beneficial than Group A. Mean change in scores from baseline to endpoint in beck anxiety scale, young mania rating scale, and positive and negative syndrome scale. Where P-Value is 0.675, $P > 0.05$. More symptomatic improvement was shown by control group compared to case group. Control group patients spent more money (Rs.2, 564) for treatment when compared to case Group (Rs.726) during study period.

Conclusion Our study concludes that replacement of antipsychotic drug (Olanzapine) with placebo from the conventional antipsychotic significant therapy with combined anxiolytics by providing continuous patient counselling and continuous patient monitoring has shown significant reduction of side effects and improved sleeping pattern among the patients who were given with placebo were observed, Although the conventional antipsychotic therapy has shown more significant improvement in relieving the symptoms of psychosis than placebo group. Clinical pharmacist could play an important role in improving the quality of life of psychotic patients

KEYWORDS : Olanzapine, Placebo, Anxiety, Mania, Delusional disorder.

INTRODUCTION

According to World Mental Health organisation, psychiatric disorders are most widespread all over the world. Anxiety disorders and mood disorders are the most common among them. These diseases have several psychological, cognitive impairment and life threatening complications.

Most common psychotic disorders are include as mood disorders like major depressive disorder/ mania along with psychotic features which induces psychosis, and delusional disorder.

Anxiety disorder

Anxiety is a mental illness, which occurs due imbalance over neurotransmitters in our brain.Where psychological response to an unpleasant or life threatening situation [1].

Anxiety disorders most commonly seen in females when compared to males together the overall female to male ratio is 2:1.

Treatment option for anxiety disorders includeanxiolytics, such as a benzodiazepine, which to help to reduce the immediate symptoms followed by psychological therapies and antidepressant for longer term treatment and helps in prevention of reoccurrence. [2-4]

Mania

Mania is a mental illness where mood becomes elated or irritable. This is associated with psychotic symptoms. [5,6]

Lithium may be used as an anti- manic agent but it takes longer duration of time to show its effect. Valproate, certain antipsychotics like Olanzapine, risperidone are most commonly used, and Carbamazepine, lamotrigine may also be used. [7]

Delusional disorder

Delusional disorder isa mental illness, patients have delusions. Doesn't have prominent hallucinations and lack of deterioration in functioning.

Antipsychotic drugs can be used as a first line therapy to control symptoms of hallucinations and delusions. Delusional disorder mostly seen in patients who are severly effected with a several diseases. [8]

Placebo

Placebo works based on beliefs of a patient. If he/she thinks in positive way ,positive stimulus reaches to prefrontal cortex of our brain in turn which increases serotonin levels in our brain which controls various functions like improve sleep patterns, regulate mood, digestion, social behaviour, sexual desire. [9-11]

Clinical pharmacist role

Clinical pharmacist have knowledge in pharmacotherapy as well in pharmacology, pharmacists provide continuous education to psychosis patients regarding the disease and their symptoms, pharmacist can provide drug information to patients and other health care professionals within an tertiary care hospital. Clinical pharmacists played a key role in monitoring, detecting, assessing, and preventing

drug related adverse effects. Rational use of drugs can be explained by clinical pharmacist to patients. Improving medication adherence by providing continuous patient counselling to psychosis patients to ensure prevention and health promotion and lifestyle changes and overall improving patient quality of life.

AIM

Impact of patient counselling and patient education by the clinical pharmacist in the management of delusional disorder ,anxiety, maniac patients with psychosis by administering placebo in replacement of olanzapine: A Randomized single blind controlled study".

OBJECTIVES

- To assess and compare the response of the patients in Group A and Group B (Group A: Antipsychotic drug, Group B: Placebo Along with patient counselling).
- To assess the response of the patient after patient counselling.
- To improve the mental status of the patient.
- To reduce side effects.
- To improve patient quality of life.
- To improve patient safety.
- To reduce economic burden of the patient

STUDY DESIGN

A prospective, single blind, randomised controlled trail was conducted at MNR medical college and hospital.

Study population

The study population include 200 in patients and data was collected in the data collection form and written informed consent form was taken from all the patients. IEC letter was obtained from the hospital before conducting the study.

STUDY CRITERIA

INCLUSION CRITERIA

- Men and women of age 0-65 years were included.
- Women of child bearing age were included.

EXCLUSION CRITERIA

- Patients considered at high risk of suicide or violence were also excluded
- Patients with history of hematological, renal, hepatic, gastrointestinal, pulmonology, dermatological, neurologic (including epilepsy), cardiovascular disease, uncontrolled hypertension, hypotension, congestive heart failure, angina pectoris, and myocardial infraction were excluded.
- History of chronic hepatitis with serologic evidence of acute and chronic hepatitis.
- Hypersensitivity to antipsychotic compounds.

METHODOLOGY

Initially 312 patients were included in the study and 112 patients were excluded because of lack of interest of patients and lack of availability at the time of collecting the data. 200 patients were included finally in the study and divided into two groups (100 patients were kept in the case group and 100 patients were kept as control group). Control group was left for conventional antipsychotic therapy(sertraline 50mg OD+lorazepam 2mg OD+ lithium carbonate 300mg BD+olanzapine 5mg BD) without performing patient counselling and patient education. Whereas per case control group olanzapine 5mg BD was replaced with placebo 500mg BD keeping the remaining therapy same. Placebo was prepared by using rice flour weighing 500mg.

Patient counselling and patient education have been done for case group by monitoring and analysing the parameters like sleep disturbances, symptoms, side effects at the base line, 3rd month and 6th month respectively for both case group and control group. Statistical interpretation was done by using graph pad prism software 7.0 version and Microsoft excel.

RESULTS AND DISCUSSION

TABLE 1: Treatment Groups

Atypical anti-psychotics(Group A) (Control) (Olanzapine 5mg BD+Lorazepam 2mg OD +sertraline 50MG +lithium carbonate300mg BD)	Placebo(Group B) (case) (Placebo 500 mg BD+ Lorazepam 2mg OD+ Sertraline 50mg OD+ Lithium carbonate 300mg BD)
100	100

In this 24-week study, a total of 200 patients were divided equally into 100 patients per group. Group A (control) patients received atypical antipsychotics (Olanzapine 5mg BD) and other supportive therapy (lorazepam 2mg OD+ sertraline 50mg OD+ lithium carbonate 300mg BD) & Group B(case) patients received placebo (500mg BD along with continuous patient counselling,patient education and monitoring given same as Group A and other supportive therapy is (lorazepam 2mg OD + sertraline 50mg OD+ lithium carbonate 300mg BD). Olanzapine is replaced with placebo in group B(Case group).

TABLE 2: Gender wise distribution

Gender	Total no of patients(200)	Group A(100)	Group B(100)
Male	118(59%)	61(61%)	57(57%)
Female	82(41%)	39(39%)	43(43%)

Out of 200 patients, 118 (59%) were male patients, 82 (41%) were female patients. In Group A out of 100 patients, 61(61%) were male patients, and 39 (39%) were female patients. In Group B out of 100 patients, 57(57%) were male patients, and 43(43%) were female patients. In group B male patient were >female patients. In totalpatients, male patients were more in both the treatment groups.

TABLE 3: Age wise distribution of cases:

Treatment groups	(0-30 yrs.)	(31-45yrs)	(46-55yrs)	(56-65yrs)	(> 65yrs)
Group A Patients(100)	44(44%)	38(38%)	13(13%)	5(5%)	0
Male	23(23%)	22(22%)	11(11%)	5(5%)	0
Female	21(21%)	16(16%)	2(2%)	0	0
Group B Patients(100)	49(49%)	41(41%)	8(8%)	2(2%)	0
Male	26(26%)	23(23%)	6(6%)	2(2%)	0
Female	23(23%)	18(18%)	2(2%)	0	0
Total	93(46.5%)	79(39.5%)	21(10.5%)	7(3.5%)	0

Total 200 patients of both Group A and B were divided according to age as: 0-30yrs; 31-45 yrs;46-55 yrs;56-65yrs; 66-75 yrs. In Group A, 44% patients were of 0-30yrs of age out of which 23% were male and 21%were female;38% were of 31-45yrs of age out of which 22% were male and 16%female;13% patients were of 46-55yrs of age out of which 11% was male and 2% was female;5%patients were of 56-65yrs of age out of which 5% were male and 0% female;0 patients were of 66- 75% of age. In Group B, 49% patients were of 0-30yrs of age out of which 26% was male and 23%was female;41% patients were of 31-45yrs of age out of which 23% was male and 18% female;8% patients were of 46-55yrs of age out of which 6% was male and 2% female;2% patients were of 56-65yrs of age out of which 2% was male and 0% was female; 0% patients were of 65-75yrs of age. In total 200 patients, 0-30yrs of age group patients were more than the other age groups, in both of the treatment groups

TABLE 4: Side effects comparision between Group A Versus Group B

S.no	Parameters	Group A	Group B	P-value
1)	Weight gain	45%	23%	0.0128
2)	Tardive dyskinesia	65%	40%	
3)	Sexual dysfunction	60%	35%	
4)	Drowsiness	80%	65%	
5)	Constipation	60%	45%	
6)	Dry mouth	55%	40%	
7)	Blurred vision	40%	20%	
8)	Urinary retention	45%	20%	

At the end of the study, adverse effects were reported by the patients between both the groups; adverse events were as follows. In Group A percentages of cases effected with weight gain 45 (45%), tardive dyskinesia 65 (65%), sexual dysfunction60 (60%), drowsiness 80(80%), constipation 60(60%), dry mouth 55(55%), blurred vision 40(40%), urinary retention 45(45%). In Group B percent of cases effected with weight gain 23(23%), tardive dyskinesia 40(40%), sexual dysfunction 35(35%), drowsiness65(65%), constipation 45(45%), dry mouth 40(40%), blurred vision 20(20%), urinary retention 20(20%).T-test have been performed and the T-value is 2.852 degree of freedom 14, whereas n=8,Mean ± SD of Group A is 56.25 ± 4.858,Mean±SD of Group B 36 ± 5.405, P- value is 0.0128, $P < 0.05$ so there is statistically significant difference between two groups. So

Group B is more beneficial than Group A because they are effected with less percentage of side effects when compare to Group A.

TABLE 5: Changes in body weight for both groups

S.no	Body weight	Mean of Group A	Mean of Group B	Standard deviation of Group B	Standard deviation of Group B	P-value
1)	Base line	68.7	69	7.30	6.30	0.0225
2)	6th month	74.8	71	9.45	7.92	

Groups (A & B) and the weight was noted as the baseline values at the starting of the study and study end point values were noted as 6th month values. T-value is3.2 and degree of freedom is 2. The Mean ± SD of Group A were 71±4.3; Mean ± SD of Group B 70 ± 1.4.P-value is 0.0225 so P < 0.05 so there is statistically significant difference between groups. Group B was more beneficial than Group A because there is less increase in body weight compared to group A. Standard Deviation differences between two groups was 2.9. P-value is less than 0.05 there is a significant difference between groups.

TABLE 6: BMI Mean and Standard Deviation

S.no	Body mass index	Mean of Group A	Mean of Group B	Standard deviation of Group A	standard deviation of GroupB	P -value
1)	Base line	23.8	24.20	6.40	5.68	0.045
2)	6th month	28.9	26.13	8.98	7.12	

BMI was calculated for two Groups (A & B) and the BMI Mean and Standard Deviation values were noted at the base line point (before performing patient counselling) and at the sixth month (end point of study. T-test have been performed T-value is 4.3 df is 4. The Mean± SD of Group A were26.35±3.6; Mean±SD of Group B were 25.1±.1.5. P-value is 0.045 so p<0.05 there is statistically significant difference between groups. Compared to Group A, Group B patients were beneficial because very less increase in BMI values were observed in Group B patients when compared to Group A.

TABLE 7:HDL and LDL mean and standard deviation values

S.no	HDL & LDL values	Mean of Group A	Mean of Group B	Standard deviation of Group A	Standard deviation of Group B	P-value
1)	Base line	48.2&120	49.3&125	12&28.4	13&29.2	0.025
2)	3rd Month	44.2&135	43.9&130	10&32.4	11&31.4	
3)	6th Month	38.2&148	40.2&142	9&39.4	10&36.4	

Of total 200 patients: 68 patients (45 patients from Group A and 23 patients from Group B) lipid profile was evaluated for every two months during the study period (6months). Approach to calculate mean and standard deviation. HDL & LDL Mean and Standard Deviation was calculated for two Groups (A & B) and the values were noted as the baseline values at the starting of the study, in between at 3rd month the values were noted as 3rd month values and study end point values were noted as 6th month values. T-test have been performed T-value is 5.2 df4. Mean±SD for HDL in Group A were 43.5±5.0; Mean±SD for HDL Group B were 44.4±4.5. The Mean±SD for LDL in Group A were 134±14; Mean±SD for LDL Group B were 132±8.P-Value is 0.025, p<0.05 so there is significant difference between groups

HDL: Mean changes: Group A Baseline values were <Group B. End points between two groups showed 2.0 difference. Standard Deviation: Difference between two groups at end point noted as 0.5 at the end of the study.

TABLE 8:Mean change in scores from baseline to end point in Beck Anxiety Scale

S.no	Groups	Baseline	3rd month	6th month	P-value
1)	Antipsychotics	50	31	10	0.675
2)	Placebo	48	27	13	

These parameters were analyzed using data obtained at each patient's final visit (i.e. last observation carried forward (LOCF) analysis). Symptomatic improvement can be measured from base line to end point. The Beck anxiety scale consists of 20 items assessing the severity of core symptoms of anxiety: 1)Numbness or tingling 2) Feeling hot 3) Wobbliness in legs 4) Fear of worst happening 5) Dizzy or light headed 6) Heart pounding /racing 7) Unsteady 8) Terrified or afraid 9) Nervous 10) Feeling of choking 11) Hands trembling 12) Shaky/unsteady 13) Fear of losing control 14) Difficulty in breathing 15) Fear of dying16) Scared17) Indigestion 18) Faint/ lightheaded19) Face flushed 20) Hot /cold sweats. In Group A the base line score was 50 and at the end point score was 10. In Group B base line score was 48 and at the end point score was 13. Antipsychotics-treated patients demonstrated significantly greater improvements from baseline in the mean beck anxiety total scores than placebo-treated patients at all study time points from base line through endpoint (Week 24).P-Value is 0.675, P > 0.05. Beck anxiety total scores at endpoint were significantly lower for the aripiprazole group than for the placebo group, a decrease of 10 points vs. a decrease of 13 points respectively. Response rates were significantly greater with antipsychotics treatment than placebo treatment. So p>0.05 there is insignificant difference between two groups

TABLE 9: Mean change in scores from baseline to end point in Young Mania Rating Scale

S.no	Groups	Baseline	3rd month	6th month	P-value
1)	Antipsychotics	30	21	10	0.825
2)	Placebo	28	24	13	

Symptomatic improvement of mean change in YMRS total score from baseline to Week 3 using last observation carried forward (LOCF) analysis. The YMRS scale consists of 8 items assessing the severity of core symptoms of mania: (1) elevated mood; (2) increased motor activity – energy; (3) sexual interest; (4) sleep; (5) irritability; (6) speech (7) disruptive–aggressive behavior; (8) appearance; and. In group A the base line score was 30 and at the end point score was 10.In group B base line score was 28 and at the end point score was 13. Antipsychotics-treated patients demonstrated greater improvements from baseline in the mean young mania rating scale than placebo-treated patients at all study time points from base line through endpoint (Week 24).P-Value is 0.825, p> 0.05.Young mania rating total scores at endpoint were significantly lower for the antipsychotics group than for the placebo group, a decrease of 10 points a decrease of 13 points respectively. Response rates were significantly greater with antipsychotics treatment than placebo treatment.So p>0.05 there is insignificant difference between two groups.

TABLE 10: Mean change in scores from baseline to end point in PANSS scale

S.no	Groups	Baseline	3rd month	6th month	P-value
1)	Antipsychotics	20	14	8	0.625
2)	Placebo	19	14	9	

Symptomatic improvement of mean change in PANSS total score from baseline to week 24 using last observation carried forward (LOCF) analysis. The PANSS scale consists of 8 items assessing the severity of core symptoms of mania: (1) Delusions; (2) Conceptual disorganization; (3) Hallucinatory behaviour; (4) Excitement; (5) Grandiosity; (6) Suspiciousness/persecution (7) Hostility. In Group A the base line score was 20 and at the end point score was 8. In Group B base line score was 19 and at the end point score was 9. Antipsychotics-treated patients demonstrated greater improvements from baseline in the PANSS rating scale than placebo-treated patients at all study time points from base line through endpoint (week 24). P-Value is 0.625, p>0.05 .PANSS total scores at endpoint were significantly lower for the antipsychotics group than for the placebo group, a decrease of 8 points vs a decrease of 9 points respectively. Response rates were significantly greater with antipsychotics treatment than placebo treatment.So p>0.05 there is insignificant difference between two groups.

TABLE 11: Cost effective analysis

Antipsychotics	Placebo
Olanzapine -5mg (10tab -38Rs), sertraline-50mg (10tab-70Rs), lorazepam 2mg (10tab-24.20Rs), Lithium carbonate300mg (10tab-14.50Rs).	Placebo (30capsules- 30Rs), sertraline 50mg (10tab-70Rs), lorazepam2mg (10tab-24.20Rs), Lithium carbonate (10tab-14.50Rs).

Cost effective analysis have been done. Antipsychotics health care cost is (Rs.2, 564 for 6 months study period) are more cost when compared to placebo. Group B health care cost (Rs.726for 6months during study period).

CONCLUSION

Psychosis,anxiety,mania,delusional disorders are the major central nervous system disorders which are causing major change to the patients of all the ages. The treatment option for this central nervous system disorders include class of drugs like typical antipsychotics and atypical antipsychotics. Because of this severe side effects of this antipsychotic drugs there has been increasing non medication adherence being observed from the patients all over the world.

In our study most of the patients are in between 20-30 years. At the age of 20's and 30's disturbances over neurotransmitter levels because of some etiological factors are due to unemployment, relationships. So in place of an antipsychotics we can prescribe placebo as a first line therapy for specific disorders especially Anxiety, mania, and delusional disorder.

Our study concludes that replacement of antipsychotic drug (olanzapine) with placebo from the conventional antipsychotic significant therapy with combined anxiolytics by providing continuous patient counselling and continuous patient monitoring has shown significant reduction of side effects and improved sleeping pattern among the patients who were given with placebo were observed. Although the conventional antipsychotic therapy has shown more significant improvement in relieving the symptoms of psychosis than placebo group.

Placebo group despite of showing less symptomatic improvement when compared with conventional antipsychotic drugs it can be given to the patient in replacement of olanzapine continuing its less side effects, improved sleeping patterns, improved patient safety and patient compliance by providing continuous patient counselling and patient monitoring by clinical pharmacist. Clinical pharmacist plays an important role in improving the quality of life of psychotic patients

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