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Research Article

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Metformin -For the Management and Prevention of Antipsychotics Induced Weight Gain

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Abstract

Background: *Psychiatric disorders, marked by significant psychological or behavioral symptoms, can lead to distress, disability, and limited autonomy. Antipsychotic medications are commonly used for management, but a frequent side effect is antipsychotic-associated weight gain (AAWG), which increases health risks. Antipsychotics are a primary factor in this weight gain. Recent studies suggest metformin, a drug used for diabetes, may effectively reduce AAWG with high efficacy and minimal serious side effects, offering a promising approach to manage this challenging complication.*

Aim: *This study aimed to evaluate the effectiveness of metformin in managing AAWG in patients receiving antipsychotic treatment.*

Methods: *Conducted at the Owaisi Hospital and Research Centre in Hyderabad, this study involved 100 patients in the Psychiatry Department, divided into a test group (n=50) receiving metformin alongside antipsychotic treatment and a control group (n=50) with antipsychotics only. Data was collected from medical records, including both inpatient and outpatient case sheets and treatment charts.*

Results: *The study found that younger adults (18-29 years) comprised the majority of the sample (39%), with females representing 64% of cases. Olanzapine was the most prescribed antipsychotic (34%), with schizophrenia (43%) being the most frequent diagnosis. The test group exhibited significant reductions in both mean weight and BMI, with weight decreasing from 60.45 to 57.98 kg, while the control group showed an increase from 58.24 to 60.94 kg.*

Conclusion: *The results suggest that metformin is effective in managing AAWG, with higher compliance observed among female patients.*

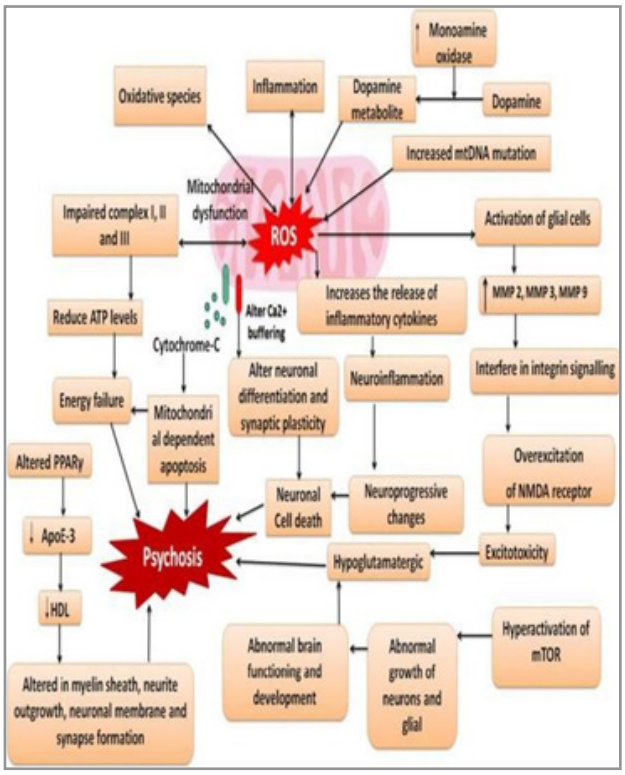
Keywords: AAWG (Antipsychotics Associated Weight Gain), FGA (First Generation Antipsychotics), SGA (Second Generation Antipsychotics).

Introduction

A psychiatric disorder or mental disorder is as a clinically significant psychological or behavioral syndrome that causes significant distress, disability, or loss of freedom. Many factors contribute to weight gain in patients with psychosis antipsychotic treatment are considered the main contributors Factors associated with rapid weight gain Metformin has shown good efficacy with extremely rare serious adverse events in the management of AAWG [1-3].

The pathophysiology of psychosis Has been traditionally linked to the neurotransmitter dopamine. In particular, the dopamine hypothesis of psychosis has been influential and states that psychosis results from an over-activity of dopamine function in the brain, particularly in the mesolimbic pathway. The two major sources of evidence given to support this theory are that dopamine-blocking drugs (i.e. anti psychotics) tend to reduce the intensity of psychotic symptoms, and that drugs which boost dopamine activity (such as amphetamine and cocaine) can trigger psychosis in some people (see amphetamine psychosis).

A Possible dysfunction of the excitatory neurotransmitter glutamate, in particular, with the activity of the NMDA receptor. This theory is reinforced by the fact that dissociative NMDA receptor antagonists such as ketamine, PCP and dextromethorphan/ dextrorphan (at large overdoses) induce a psychotic state more readily than dopaminergic stimulants, even at "normal" recreational doses. The symptoms of dissociative intoxication are also considered to mirror the symptoms of schizophrenia more closely, including negative psychotic symptoms than amphetamine psychosis. Dissociative induced psychosis happens on a more reliable and predictable basis than amphetamine psychosis, which usually only occurs in cases of overdose, prolonged use or with sleep deprivation, which can independently produce psychosis. New antipsychotic drugs which act on glutamate The connection between dopamine and psychosis is generally believed to be complex. While antipsychotic drugs immediately block dopamine receptors, they usually take a week or two to reduce the symptoms of psychosis. Moreover, newer and equally effective antipsychotic drugs actually block slightly less dopamine in the brain than older drugs whilst also affecting serotonin function, suggesting the 'dopamine hypothesis' may be oversimplified [4].



Diagnosis as Continuous symptoms that persist for at least 6 months with at least 1 month of active phase symptoms (Criterion A) and may include prodromal or residual Symptoms.

Criterion A: For at least 1 month, there must be at least two of the following Present for a significant portion of time: delusions, hallucinations, disorganized Speech, grossly disorganized or catatonic behaviour, and negative symptoms. At Least one symptom must be delusions, hallucinations, or disorganized speech.

Criterion B: Significantly impaired functioning.

In first-episode schizophrenia, initiate antipsychotic dosing at the lower end of the Dosing range. Use of SGAs during the first acute episode results in greater treatment Retention and relapse prevention compared to FGAs. Aripiprazole, risperidone, or Ziprasidone may be preferred first line. Risperidone injection is more effective than oral risperidone in preventing relapse Over a 1-year period for first episode schizophrenia. A long-acting antipsychotic Should be considered during stages 1A, 1B, and 2.
In Stage 3, clozapine monotherapy is recommended. For Stage 4, minimal evidence exists for any treatment option for patients who do not Have adequate symptom improvement with clozapine. Use of antipsychotic combinations is controversial, as limited evidence supports increased efficacy, despite this Practice being somewhat common [5].

The incidence of a first-time episode of psychosis is approxi-

mately 50 in 100000 people, while the incidence of schizophrenia is about 15 in 100000 people. The peak age of onset for males is teens to mid-20s, while for females, the onset tends to be teens to late-20's. Earlier onset correlates with poorer outcomes, although early intervention correlates with better results. Psychosis is extremely uncommon in children [6].

Methods

This study was designed as prospective observational study conducted over a period of 6 months. The aim was to prove the use of metformin in management and prevention of antipsychotic induced weight gain. The study took place in Owaisi hospital and research center in Hyderabad specifically within the Department of Psychiatry which provided medical care to both outpatient and inpatient. To gather data for the study, information was collected from patient's case sheet, treatment chart. The drug administered in the study was metformin at dosage of 500mg,850mg,1gram the inclusion criteria for participants included are of 18 years of age and above of both genders. These individuals must be on antipsychotics the patients are divided into 2 groups control and test. Test patients are on metformin along with lifestyle modifications, control patients following lifestyle modifications.

Results

The survey data collected for this study underwent statistical analysis using the SPSS 25 software. To begin with, descriptive analysis was conducted to provide a summary of the variables. The hypotheses formulated for the study were then tested using appropriate statistical tools, focusing on the dependent and independent variables. The results obtained were presented and discussed within the theoretical framework of the study.

Model fitting is a measure of goodness of fit in logistic regression analysis. It is a modification of the Cox and Snell R square, which is derived from the likelihood ratio test statistics, which was found to be >1 i.e. [p=.000]. Nagelkerke R square ranges from 0 to 1, with values closer to 1 indicating a better fit of the model, i.e. [p=.958].

In terms of age distribution, we found that highest 39% of patients were in age group of 18- 29 years and the lowest 2% of patients were in age group of above 60 years. As frequency of age increases the effect decreasing gradually.

In terms of gender distribution, we found that we have observed that females are more prone to disease than males. i.e. with the percentage of 64. In terms of drug, we found Olanzapine i.e. 34% was highly used followed by risperidone 24%, amisulpride 16% & clonazepam 12% compared to least cariprazine 6%, quetiapine 4%, aripripazole4% respectively.

In terms of disease schizophrenia 43% is highly frequent disease followed by bipolar17%, anxiety 14%, compared to least MDD 13%, psychosis 4%, OCD 3%, post trauma 3%, ABS seizures 2%, alcohol D 1%. respectively.

Statistical Analysis

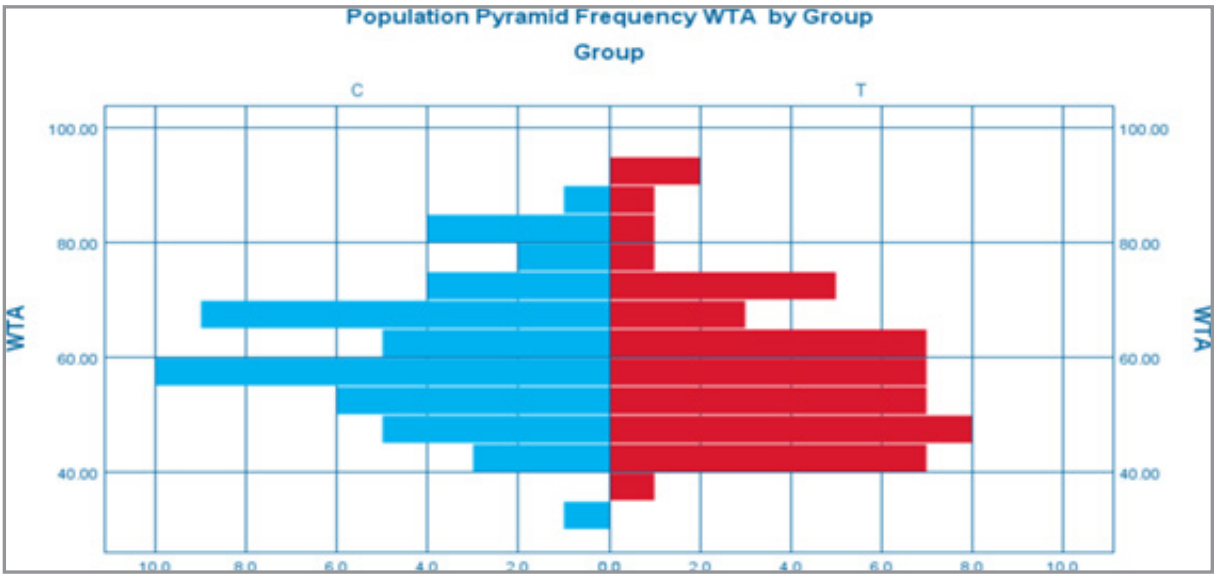
The statistical analysis revealed that patients with ongoing treatment were found to have approximately -6kg lesser weight gain compared to the naive treatment where the weight was found to be maintained and that is statistically significant i.e. [P=.47] 95% CI -2.3 to1.09. Group 1 i.e. test had a weight change of -4kg less when compared to Group 2 i.e. control and that is statistically significance [P = .000] 95% CI -7.5 to -2.4. The difference between ADR was found to be .263 higher weight when compared to no ADR therefore it was found to be statistically insignificant i.e. [P=.833] 95% CI -2.1 to 2.7.

The difference between males and females is 1.69 weight and it was found to be statistically not significant
i.e. [P=.387] 95% CI .880 to 2.27.

Comparison	Estimate	Std Error	Sig.	95% Confidence Interval	
				Lower Bound	Upper Bound
Treatment(O)=1.00 Treatment(N)=2.00	-.623 0a	.876	.447	-2.340	1.094
Group(Test)	-4.998	1.290	.000	-7.526	-2.470
(M+L)=1.00					
Group(Control)	0a				
(L)=2.00					
ADR=1.00	.263	1.247	.833	-2.181	2.707
ADR=2.00	0a				
Gender= 1.00 Gender=2.00	.696 0a	.804	.387	-.880	2.272

Comparison of weight

In Group 1 the mean weight before was found to be 60.45 and weight after was found to be 57.98, i.e. reduction in weight, whereas in Group 2 we found the mean weight before was found to be 58.24 and weight after was found to be 60.94 i.e. increase in weight.



Weight	Group 1 Test (M+L)	Group 2 Control (L)
	(Mean)	(Mean)
WTB (weight before)	60.45	58.24
WTA (weight after)	57.98	60.94

Discussion

A Total 100 patients were collected and randomized into two groups i.e. Ongoing patients of both groups (Antipsychotics + metformin + lifestyle modifications) consisted of 50 patients while naïve patients of both the groups (Antipsychotics +life style modification) consisted of 50 patients. The Prospective interventional study included 100 adults aged 18 years of age and above with associated psychiatric diagnosis such as schizophrenia, bipolar disorder, anxiety followed by MDD, OCD, alcoholic dependence, psychosis, post trauma & absence seizures undergoing treatment with Anti-psychotic drugs such as olanzapine, risperidone, amisulpride followed by clonazepam, cariprazine, risperidone, quetiapine. This study seeks to assess the impact of antipsychotics, with and without concurrent metformin use, on body weight. It has been demonstrated that metformin increases the release of the anorectic hormone peptide YY (PYY) and the weight-loss- promoting incretin glucagon like peptide 1 (GLP-1) which results in weight loss.

The statistical analysis reported that metformin concomitant use caused a significant reduction in the AIWG with a change of -6kg less compared to the naïve group, with the difference being statistically significant [P=0.47] 95% CI -2.3 to 1.09. In group 1 i.e. test had a weight change of -4kg lesser when compared to Group 2 i.e. control and that is statistically significance [P = .000] 95% CI -7.5 to -2.4. These quantitative results are in line with the existing evidence that metformin is effective in controlling AIWG. There were direct clinical benefits to our study population. Participants in the metformin & Lifestyle were able to control their weight better than the participants in the Lifestyle alone throughout the 12 weeks of study. We observed statistically significant reductions in mean weight and BMI among patients in Test group. In test group, the mean weight decreased from 60.45 to 57.98, whereas in Control group we noted an increase in weight from a mean of 58.24 to 60.94 after the study period. Importantly, the study outcomes exhibited that female patient's compliance to take metformin with antipsychotics more than males.

Conclusion

We observed statistically significant reductions in mean weight and BMI among patients in Test group. In test group, the mean weight decreased from 60.45 to 57.98, whereas in Control group we noted an increase in weight from a mean of 58.24 to 60.94 after the study period. Importantly, the study outcomes exhibited that female patient's compliance to take metformin with antipsychotics more than males.

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