

Effects of antidepressant drugs on renal function and HbA1c level in male population of Khyber Pakhtunkhawa, Pakistan

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Objective: To study the effects of various antidepressant drugs on the HbA1c level and renal functions in male population of our province of Khyber Pakhtunkhawa.

Methodology: This hospital based cross sectional study was conducted to assess the effects of medium term use of (03- 36 months) anti-depressant drugs on the HbA1c level and renal functions in male population of Northern Pakistan in the province of Khyber Pakhtunkhawa. It comprised of 117 males in the age group of 18-60 years. The blood sample was analyzed for serum creatinine, urea and HbA1c.

Results: The mean serum urea of for SSRI group (25.76 ± 7.31 mg/dl) was higher than control (24.50 ± 5.14 mg/dl) and TCA group (24.88 ± 2.66 mg/dl) ($p = 0.02$). The mean serum creatinine of

control group was 1.10 ± 0.23 mg/dl, for SSRI group was 1.76 ± 0.14 mg/dl and for TCA was 1.63 ± 0.45 mg/dl. The mean HbA1c of control group was 5.91 ± 0.58 , for SSRI was 5.70 ± 0.51 and for TCA it was $5.66 \pm 0.55\%$. HbA1c was negatively correlated with age, BMI and duration in month for TCA. The correlation with duration in month was highly significant ($p = 0.34$). No significant correlation was found with dosage in mg per day in both the patient group.

Conclusions: Medium term use of antidepressant may cause obesity in male population and may impair renal function. The effect on the HbA1c level is still not clear and needs further studies. (Rawal Med J 201;42:13-17)

Key words: Anti-depressant, urea, creatinine, HbA1c.

INTRODUCTION

Pakistan is at the forefront on the global war against terrorism and affecting the local populations of Khyber Pakhtunkhawa more than the other provinces of Pakistan.¹ Psychological problems are on the rise, affecting all aspects of the lives of the local inhabitants.² Mental health problems in Pakistan are linked to both the current violence in the country³ and also disruption in the social fabric of the society.⁴ WHO projects that Mental disorder will be one of the leading causes of disability worldwide by 2020.⁵

About one-third of the people suffering from mental disorders are using anti-depressant drugs, including Selective Serotonin Reuptake Inhibitors (SSRIs), Tricyclic Anti-depressants (TCAs), and Monoamine Oxidase Inhibitors (MAOIs).⁶ Most of the anti-depressants drugs increase Noradrenergic and/or Serotonergic Neurotransmission following acute administration.⁷ It results from Reuptake Inhibition of Norepinephrine or Serotonin in the

neuronal synapse.⁸

Recent publications show that long-term use antidepressant drugs enhance the risk of diabetes.⁹ A study based on the UK General Practice Research Database reported that those individuals who had used antidepressants for more than 24 months had increased risk of diabetes.¹⁰ Ryan et al reported that more than 50% of otherwise non-diabetic patients in the Bipolar Cohort had increased HbA1c levels (>7.0) and they postulated that the higher prevalence of abnormal HbA1c in patients with Bipolar Disorder could predate the use of psychotropic agents.¹¹ Turpeinen et al reported that bupropion may lead to increase level of serum creatinine without increasing other signs of renal injury.¹² A study hypothesized in that chronic kidney disease would be independently related with some or all of the factors of lithium variables like (duration, dose, long acting formulation, increase age and medical comorbidity).¹³ The present study was carried out to study the effects of various

antidepressant drugs on the HbA1c level and renal functions in male population of Northern Pakistan in the province of Khyber Pakhtunkhawa.

METHODOLOGY

The study was carried out at Khyber Teaching Hospital (KTH) and Shafique psychiatric clinic, Peshawar, Pakistan from February 19, 2016 to May 15, 2016. The study was approved by the ethical committee of KTH and Informed consent was sought from each patient. Male patients from 18-60 years of age were included in the study. Patients with hypertension, diabetes, renal disorders and use of antidepressant drugs for less than two months and more than thirty six months were excluded from the study.

Data from both the group regarding their age, weight, height and medical history was recorded. 5 ml of fresh venous blood (fasting sample) was taken from each patient and was analyzed in the central Pathology laboratory of KTH for the required biochemical parameters using standard kits and protocols. Serum urea and creatinine levels were determined on autoanalyser (Erbamannheim chemistry autoanalyser, Germany) using standard Erba kits. The normal ranges were 05-45 mg/dl for Urea and 0.5-1.5 mg/dl for Creatinine. HbA1c was determined by standard procedure.¹⁴

Statistical analysis was performed on SPSS version 21.0. Pearson's correlation was applied to look for association between required variables. A two-tailed $p < 0.05$ was considered statistically significant.

RESULTS

The present cross sectional study was conducted on 117 men, 18-60 years of age hailing from different parts of Khyber Pakhtunkhawa province of Northern Pakistan. These were further grouped in to two classes, the Control group (CG) and Patient group (PG). CG comprises of normal individual while the PG were taking various types of antidepressant drugs. The PG was further subdivided into SSRI group and TCA group. The results are discussed below.

The mean age of control group (CG) was 29.10 ± 7.52 years, for SSRI group was 37.71 ± 14.65

years and for TCA group was 37.80 ± 13.93 years. The mean BMI of control group was 24.54 ± 2.01 , for SSRI was 28.72 ± 4.51 and for TCA was 29.86 ± 3.31 . The mean BMI of patients in TCA group was higher than the CG & SSRI group. The patient in the SSRI group has used a mean dosage of 36mg/day for a mean period of 12 months while the TCA group has used a mean dosage of 75mg/day for a mean period of 16 months.

Figure 1. Comparison of urea and creatinine.

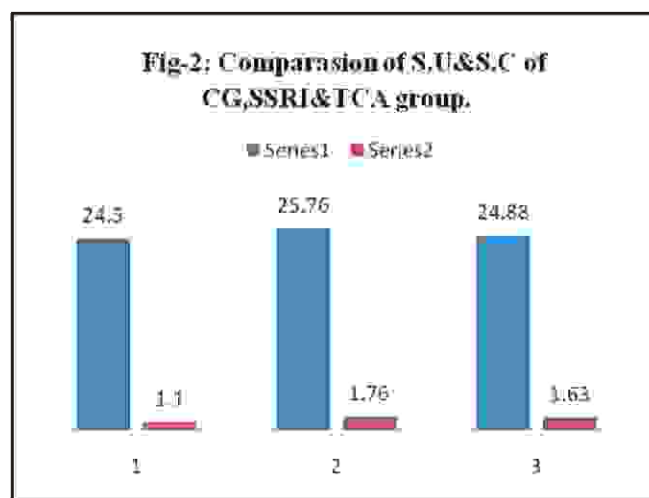
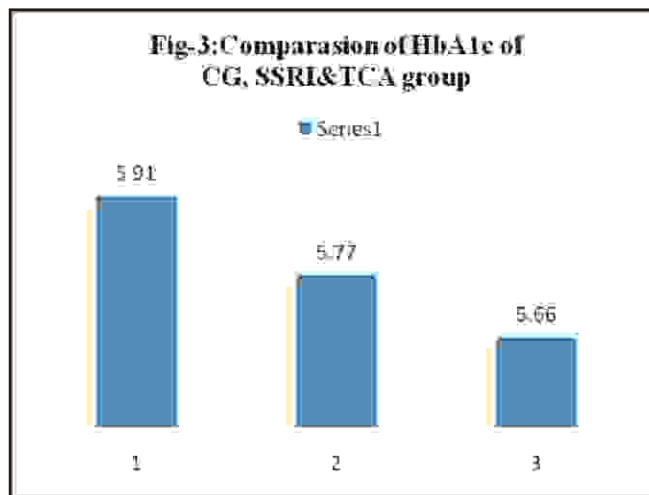


Figure 2. Comparison of HbA1c.



The mean serum urea of CG was 24.50 ± 5.14 mg/dl, for SSRI group was 25.76 ± 7.31 mg/dl and for TCA was 24.88 ± 2.66 mg/dl. The mean serum creatinine of control group was 1.10 ± 0.23 mg/dl, for SSRI group was 1.76 ± 0.14 mg/dl and for TCA was

1.63±0.45 mg/dl. The serum creatinine of SSRI and TCA group was higher than the control group (Figure 1). The mean HbA1c of control group (CG) was 5.91± 0.58, for SSRI (PG) was 5.70 ±0.51 and for TCA it was 5.66±0.55%. The HbA1c of SSRI was higher than TCA while lower than the CG (Figure 2).

Table 1. Correlation analysis of renal markers and diabetic markers.

Group ID n=57	Parameters	Renal Markers		Diabetic marker
		Urea (mg/dl) r (p)	Creatinine (mg/dl) r (p)	HbA1c (%) r (p)
SSRI group	Age (Years)	0.06 (0.82)	0.21 (0.46)	.28(.33)
	BMI (Kg/m ²)	-0.13 (0.65)	-0.27 (0.35)	.06(.85)
	Duration in months	-0.59* (0.02)	-0.20 (0.49)	-.17(.56)
	Dosage in mg/day	0.27 (0.35)	-0.01 (0.99)	-.07(.93)
TCA group	Age	0.65 (0.23)	0.73 (0.16)	-.16(.75)
	BMI	0.43 (0.68)	0.70 (0.18)	-.58(.23)
	Duration in months	-0.25 (0.68)	0.04 (0.95)	-.85*(0.34)
	Dosage in mg/day	-0.73 (0.16)	-0.51 (0.38)	-

TCA= Tricyclic Antidepressant

SSRI= Selective Serotonin Reuptake Inhibitor

Serum urea was highly significantly correlated with duration in months in SSRI group (p=0.02). No significant correlation was found between serum creatinine and other parameters in any of the patient group. The HbA1c was positively correlated with age and BMI while negatively correlated with duration in month and dosage in mg per day for SSRI. HbA1c was negatively correlated with age, BMI and duration in month for TCA. The correlation with duration in month was highly significant (p=0.34). No significant correlation was found with dosage in mg per day in both the patient group (Table 1).

DISCUSSION

Controversy continues among researchers around the various side effects of antidepressant drugs, one of the most prescribed groups of drugs worldwide. Both kidney diseases and depression are enormous health problems. Several chronic illnesses are co-morbid with depression, and diabetes is not an exception. Scientists and epidemiologists have long been conducting research on the relationship between diabetes and depression. Several epidemiological studies confirm this relationship.

In our study, out of 117 men, 57 were patients and 60 were controls. The patient group was found to be more obese (BMI>25m/Kg²) than the control group. It may be due to the use of drugs as treatment may have increased BMI in the patients.¹⁵ The level of HbA1c was found to be lower in the patient group as compared to the control group. This result is in agreement with Lustman et al, who found that level of HbA1c is reduced during the open treatment stage and remains reduced during depression-free maintenance, regardless of the type of antidepressant used for the treatment of the patient.¹⁶ Pyykkonen et al reported an association between antidepressants use and increased insulin resistance as evaluated by Homeostasis Model Assessment of Insulin Resistance (HOMAIR).¹⁷

Our data showed that the patients group who were taking SSRIs and TCAs had higher level of urea and creatinine as compared to control. Similar results have been reported by other studies.¹⁸ These results suggest that antidepressants may have a risk of kidney diseases among men.

The duration of medication with the anti-depressant drug has a profound effect on the HbA1c level and consequently on the renal impairment. Outcomes of our study revealed that serum urea was highly significantly correlated with duration in months in SSRI group (p= 0.02). No significant correlation was found between serum creatinine and other parameters in any of the group (SSRI, TCA).

The HbA1c was positively correlated with age and BMI while negatively correlated with duration in month and dosage in mg per day for SSRI. HbA1c was negatively correlated with age, BMI and duration in month for TCA (PG).The correlation was highly significant with duration in month

($p=0.34$). No correlation was found with dosage in mg per day. The results of Diabetes Prevention Program suggest that those individuals who had used the antidepressants regularly for a long time had an increase of more than two times in the risk of diabetes.¹⁹ Some studies found a less important and weak connection in between the antidepressants medication use and risk of diabetes.²⁰ Lustman et al considered that hormonal changes caused by depression can stimulate the cortisol level in the body to enhance and weakens the insulin tolerance.²¹

The strong point of our study is that there is no such report from this area of Northern Pakistan. The study limitation include small sample size, data collection from two centers only and lack of finance and time limitations. Further studies involving larger population are required for better results.

CONCLUSION

The antidepressant drugs may induce obesity in human beings although this may not be true for every individual. The long term use of these drugs may impair renal function but as far as regarding the HbA1C level no significant differences were found between controls and patients.

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 Critical revision of the article for important intellectual content: Mohammad Yousaf
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