Comparing the Effect of Fluoxetine and Escitalopram on Inflammation & Glycemic Control in Patients Having Psychiatric Illness with Type 2 Diabetes Mellitus

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***ABSTRACT*: Diabetes and Psychiatric disorders influence each other in multiple ways. This can inturn result in elevated C - reactive protein, which acts as a biomarker of inflammation, thereby increasing the risk of Cardio-Vascular Diseases. C - reactive protein is a pentameric protein found in blood plasma whose level rise in response to inflammation, which is produced predominantly by the hepatocytes. Several research suggests a bi-directional relationship between Type 2 Diabetes Mellitus (T2DM) and Psychiatric illness& the two disorders may share similar pathophysiological mechanisms.Fluoxetine and Escitalopram belongs to the Selective Serotonin Reuptake inhibitors class of Anti-depressants.The present review is aimed to compare the two anti-depressants, Fluoxetine and Escitalopram on their effect in reducing C-reactive Protein and Fasting Blood Sugar in patients with Psychiatric illness and Type 2 Diabetes Mellitus.The better anti-depressant that can be added along with the oral hypoglycemic agent to improve the glycemic control and also which has the potential to reduce the risk of inflammationcould be analyzed.**

***KEYWORDS*: Psychiatric illness, Type2 Diabetes Mellitus, C - reactive protein, Fasting Blood Sugar.**

INTRODUCTION

Psychiatric disorders have been considered as "mental" rather than as physical illness. This is because they manifest with disorder functioning in the area of emotion, perception, thinking and memory. The types include : Stress related disorders , Anxiety disorders, Affective disorders, Schizophrenia and Delusional disorders, Substance misuse disorder, Organic disorder, Disorders of adult personality and behavior , Eating disorders, Somatoform disorders, Neurasthenia , Puerperal mental disorder. The etiology of psychiatric disorders is multi-factorial with a combination of biological factors (Genetic factors , Brain structure and function); Psychological and behavioural factors (Early environment, Personality and Behavior) and social causes (Social isolation and Stressors).[1]

C-reactive protein, it is a sensitive systemic marker of inflammation and tissue damage and is produced by hepatocytes predominantly under transcriptional control by the pro-inflammatory cytokine interleukin 6. Major depression has been shown to be associated with activation of the inflammatory response. These changes include increased numbers of peripheral leucocytes, both monocytes and neutrophils . Positive acute-phase proteins (including C-reactive protein) are increased.

Stress can result in inflammation in predisposed individuals that can inturn lead totheactivation of indolamine 2,3 dioxygenase pathwayand thus reduces serotonin availability and increased glutamate receptor activation leading to Major Depressive Disorder.

Current research suggests a bi-directional relationship between Type 2 Diabetes Mellitus (T2DM) & depression & the two disorders may share similar pathophysiological mechanisms[14]. Depression was associated with a 60% increase of type 2 diabetes while type 2 diabetes was only associated with a moderate (15%) risk of depression[15]. On one side, depression could facilitate the onset of diabetes through disturbances in eating behaviors, increase in potentially damaging behaviors (smoking and alcohol consumption), drug induced weight gain, decreased self-care activities or activation of stress-related hormonal pathways (stimulation of the hypothalamic–pituitary–adrenal (HPA) axis, resulting in increased cortisol levels and a resulting increase in blood glucose, eventually progressing to diabetes) and pro-inflammatory cytokines which interfere with glucose metabolism[16]. On the other hand, limitations on diet and physical and social activities determined by diabetes, together with some diabetes-related symptoms (e.g., fatigue induced by hyperglycemia), could induce depressed mood[17].The recognition of depression becomes important as cost-effective treatment is available resulting in improvement of diabetic care as well. In addition, few studies have evaluated the impact of specific antidepressant therapies on glycemic control in people with diabetes and fewer still have examined the incidence of new-onset diabetes among those treated for depression. Depression can lead to diabetes via insulin

resistance through the activation of Hypothalamus Pituitary Adrenal Axis and Sympathetic Nervous System.[5]Antidepressants are medicines that treat depression. They may help improve the way the brain uses certain chemicals that control mood or stress.

Fluoxetine belongs to Selective Serotonin Reuptake Inhibitor class and it acts by inhibiting the 5HT(HydroxyTryptamine) receptor, which leads to an increase of serotonin level. It antagonises muscarinic, histaminergic, and α1–adrenergic receptors which leads to various anticholinergic, sedative actions. It is the longest acting SSRI and the plasma half life is 2 days.

Escitalopram is the stereo isomer of Citalopram and is used in Major depressive disorder (MDD) and Generalized anxiety disorder (GAD).It is a potent and selective inhibitor of central neuronal serotonin reuptake with little to no effect on nor epinephrine or dopamine reuptake.[3],[7]

REVIEW OF LITERATURES

[2]**JILL MATHEWS,** *et al.*,(2016); conducted "An Observational Study Of The Effect Of Escitalopram& Etizolam in Type2 DM Patientswith Depression." In this method OP Type 2 Diabetes Mellitus patients taking treatment for atleast three months were considered as per the inclusion and exclusion criteria. Patients of age ≥ 18 years, male or female, those diagnosed as type 2 diabetes mellitus and taking treatment regularly for at least 3 months and those with uncontrolled blood sugar level were included in the study. The patients were divided into 2 groups: Treatment group: Escitalopram 10mg + Etizolam 0.5mg for 30days ; Control group: Patients who were not treated for depression. The results showed that out of 125 patients of type2 diabetes screened, 43 were diagnosed with depression & anxiety; 23 with both and 20 patients with Depression only and the study showed that there were significant improvement in clinical features of depression in 51 patients.Prevalence of depression among type 2 diabetes mellitus was found to be 35% in this study. Fifty one patients treated with escitalopram + etizolam improved clinically as well as biochemically. There was significant improvement in Blood Sugar Level -Fasting, Blood Sugar Level-Post Prandial and HbA1c. Escitalopram may be considered as antidepressant of choice in such cases.

[3]**KARUN KUMAR,***et al.*, (2015); conducted a study on "Comparitive Effect OfAgomelatine V/S Escitalopram on Glycemic Control& Symptoms Of Depression In Patients With Type 2 Diabetes And Depression." This was an open labelled randomised study. Patients diagnosed as T2DM with moderate to severe depression(Hamilton Depression Rating Scale Score ≥ 14) were randomised to receive Escitalopram (10mg daily) or Agomelatine (25mg daily) with anti-diabetic agents. Depression was assessed using HDRS and Montgomery Asberg Depression Rating Scale (MADRS). The results showed thatEscitalopram group showed a significant reduction in FBS as compared to Agomelatine at 1 and 2 months. The discussion was that depression was associated with a 60% increase of T2DM while T2DM was associated with a moderate 15% risk of depression. The proposed mechanism by which Escitalopram lowers the FBS can be attributed to the fact that Escitalopram is the most selected SSRI which increases the level of Serotonin in the synaptic cleft. Serotonin inhibited glucose induced hyperglycemia and enhanced the increase of insulin levels elicited by glucose. It was concluded from the study that Escitalopram seems to be better than Agomelatine for glycemic control and ameliorating symptoms of depression in patients of T2DM and depression.

[4]**HS DHAVALE,***et al.*, (2013);conducted a study on " Depression And Diabetes And impact Of Antidepressant Medications On Glycemic Control." In this study, 100 patients with Depression and Type 2 DM were selected .The socio demographic details of the patients were collected using a specially designed semi structured proforma .Patients detected with depression were started on Tab. Escitalopram 10mg, keeping the management of diabetes unchanged. The patients were reviewed after 6 weeks from date of initial assessment and blood glucose were repeated. The study concluded as 47%of the patients started on Tab. Escitalopram showed lower fasting and post lunch blood sugar values on follow up which was clinically and statistically significant. The prevalence of depression with/without anxiety in the study was 39%. Among depressed patients stressors were found in 84% of patients with social and interpersonal stressors as the more prevalent types. The socio-economic profile showed a female preponderance, lower to middle socioeconomic and educational status and majority were married.

[5]**SINEAD M O'BRIEN,***et al.*, (2006); conducted a study on "Anti-Depressant Therapy and CRP." This study was done to examine the levels of C-reactive protein in Depression and to evaluate the impact of SSRI (Selective Serotonin Reuptake Inhibitor) therapy on CRP. The study was done in two parts. In the first part, CRP was measured in 32 patients with a history of depression (20 depressed, and 12 euthymic) and all the subjects were on SSRI treatment. Part two included 20 patients with major Depression and CRP levels were measured before and after SSRI (Selective Serotonin Reuptake Inhibitor) treatment. The results showed that, there were no difference in the levels of CRP in patients already on SSRI treatment but there was a significant drop in the CRP in the part two subjects after the SSRI treatment and hence from this study it was concluded that following SSRI treatment for major depression there is a significant
drop in C-reactive protein concentrations whether or not the depression resolves. These findings indicate that antidepressants induce an anti-inflammatory response independent of antidepressant action.

[6]**PATRICK J LUSTMAN,***et al.*, (2000);conducted a study on "Fluoxetine for Depression In Diabetes – A Double Blind Placebo Controlled Trial." This was an open labelled randomised study. In this study, 60 patients diagnosed with Diabetes (type 1, n=26; type 2, n=34) with moderate to severe depression entered into an 8 week randomised placebo controlled double blind

trial. Patients were given daily doses of Fluoxetine (upto40mg daily). The results showed a reduction in depression symptoms was significantly greater in patients treated with Fluoxetine compared with those receiving placebo and a greater reduction in FBS. In obese patients with Type 2 Diabetes Mellitus, Fluoxetine produced moderate improvements in glycemic control and significant decrease in required insulin levels, In this diabetic sample, Fluoxetine was a safe and effective therapeutic agent for symptoms of major depression.

[7]**JEAN- CLAUDE** et *al*., (1996); conducted a study on the "Usefulness Of Fluoxetine In Obese Non-Insulin Dependent Diabetics: A Multicenter Study." In this study, 82 patients- obese non-insulin dependent type 2 Diabetes Mellitus patients were enrolled in the study as per the inclusion and exclusion criteria. The patients were given for an 8 week period , either placebo or Fluoxetine and the patients were instructed to keep the same dosage of their usual hypoglycemic agent. FBS decreased in Group taking Fluoxetine after 3 weeks and 8 weeks. HbA1c decreased from 8.5 % to 7.7% in Fluoxetine group and 8.6% to 8.3 % in placebo group. In conclusion, the addition of Fluoxetine to the usual oral hypoglycaemic agent therapy might be beneficial in obese non-insulin dependent diabetes atleast on a short term basis.The results demonstrated weightreduction, better glycemic control in 31 type 2 obese patients receiving60 mg fluoxetine daily during 8 weeks. This improvedmetabolic control was obtained with significantly lowerserum insulin levels.

CONCLUSION

The better antidepressant which can be suggested in case of Type2 Diabetes Mellitus as comorbidity in Psychiatric illness and the comparatively better anti-depressant in reducing the risk of inflammation can be analyzed

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