CLINICAL MONITORING OF PATEINTS ON CLOZAPINE

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ABSTRACT

Objective: To find out if the Maudsley Guidelines for clinical monitoring of the patients on Clozapine has been followed or not and association of Clozapine with Diabetes Mellitus and Hyperlipidemia.

Design: Descriptive observational study.

Place & Duration of Study: Study was carried out at Three Bridges Unit Ealing Hospital West London Mental Health NHS Trust London .The data was collected between Dec 2005 & Jan 2006.

Subjects & Methods: Study includes all the in-patient at the time of Data Collection started on Clozapine since Sept 1999.Pateints details were obtained from Clozapine Clinic at Three Bridges Unit Ealing Hospital .Data was collected by looking at patient's blood results retrospectively via an access to Central Path Lab Data system at Ealing Hospital.

Results: The total number of patients was 60 out of which 52 were males and 8 were females. 3.33% of the sample was less than 25 years old, 45% were between 25-40, 48.3% were between 40-60 and 3.33% were above 60 years of age. There were 41.67% white British, 13.33% Black British, 10% British Asians while the rest 35% were of miscellaneous ethnic origin. The results signify the importance of following the Maudsley guide lines in clinical monitoring of patients on Clozapine. It also supports the previous established studies of association of Clozapine with Hyperglycemia[1].

Conclusion: All patients receiving Clozapine should be regular monitored for changes in weight, lipid, and glucose levels so that appropriate preventive and therapeutic measures can be initiated.

Key words: Clinical monitoring, Clozapine, Diabetes mellitus, Hyperlipidemia.

INTRODUCTION

Clozapine has been known to be associated with high blood sugar and raised lipid level, as like any other second generation Anti-psychotic drugs[1]. Study consistent with previous established data suggests that Olanzapine, Clozapine and some conventional antipsychotics appear to increase the risk of acquiring or exacerbating type 2 diabetes and the effect may vary with drugs[2]. Hyperglycemia and type 2 diabetes mellitus are more common in schizophrenia than in general population. Glucoregulatory abnormalities have also been associated with the use of antipsychotic medications themselves. Clozapine –treated patients have significant glucose elevation at fasting and 75 minutes after load in comparison with patients receiving typical antipsychotics and untreated control subjects[3]. Reports from a 10 year naturalistic study support the hypothesis that Clozapine-treated patients appears to be at risk fro death from cardiovascular disease secondary to Clozapine associated medical disorders such as obesity , diabetes , hypertension and Hyperlipidemia[4].

Increasing numbers of reports concerning diabetes,ketoacidosis, hyperglycemia, and lipid dysregulation in patients treated with second generation(or atypical) antipsychotics have raised concerns about the possible association between these metabolic effects and treatment with these medication. Atypical antipsychotics offer significant improvements over older, conventional antipsychotic agents. However, recently the newer agents have been linked to medical morbidity including hyperglycaemia, diabetes mellitus, bodyweight gain and abnormal lipid levels. Even more concerning, because of a significant risk of death, there have been numerous case reports of patients treated with Clozapine or Olanzapine developing diabetic Ketoacidosis shortly after initiation of the drug. Much of the information concerning the medical morbidity of diabetes mellitus is based on case reports, retrospective chart reviews, naturalistic studies and cross-sectional stud-

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ies. While definitive studies have yet to be reported, mounting evidence suggests that the atypical antipsychotic agents, particularly Clozapine and Olanzapine, may significantly impair glucose metabolism and increase the risk of diabetes in patients with schizophrenia. Diabetic Ketoacidosis, although it appears to be uncommon, is of great concern secondary to the risk of death[5].

Lindenmayer et al found that Clozapine, Olanzapine, and Haloperidol were associated with an increase in plasma glucose level, and Clozapine and Olanzapine were associated with an increase in cholesterol level[1].

In view of these concerns the regular monitoring of these parameters is suggested by various guidelines for the patients on atypical antipsychotics. Maudsley Guidelines also require monitoring the lipid and sugar levels for those on Clozapine. A clinical audit was initiated at R.S.U (Regional Secure Unit) Ealing Hospital to find out the adherence to Maudsley Guide Lines in clinical monitoring of in-patients started on Clozapine since Sept 1996 and also the point prevalence of Hyperlipidemia as well blood glucose abnormalities among these patients.

SUBJECTS AND METHODS

The total number of in-patients who were started on Clozapine at Regional Secure Unit Ealing Hospital West London Mental Health NHS Trust since Sept 1996 was 60. Details of the patient were obtained from On-Site Clozapine Clinic which facilitate the regular blood monitoring of patients on Clozapine .Access to the patient blood results was arranged through Path Lab Ealing Hospital .The Path Lab at Ealing Hospital has the blood results of all the patient on their Data system since Sept 1996. Blood results were searched on the system with help of patient's demographic details which included age, gender, date of birth, hospital number and date they were started on Clozapine.

Maudsley Guidelines was laid down as base for Clinical Monitoring of patients on Clozapine. Table 1 shows Maudsley Guidelines for clinical monitoring of patients on Clozapine.As data was collected from the Path Data System, So Ethic Committee approval was not sought .Data was collected in an anonymous way and analysed.

RESULTS

The data showed that all of the patients F.B.C was analysed before they were started on Clozapine. According to the national guide lines all the pharmacists and physicians were registered .As part of the baseline monitoring, none of the patient fasting blood sugar was requested while in 10% of the cases random blood sugar was requested which was with in the reference range. HBA1C and lipid level was requested in 2% and 5% of the cases respectively which were with in the reference range. In 24% of the patients started on Clozapine LFTs & U&E was requested, as part of the baseline due to lack to motivation and insight monitoring.

Table 1

Maudsley Guide lines for Clinical Monitoring of Patients on Clozapine.

Base Line Monitoring:	Prescriber & Pharmacist must be registered .Full Blood Count, HBA1C, Blood Pressure recording, ECG (optional) LFTs, Blood Lipid Level, Weight
Monitoring at 1st Month:	Fasting Plasma Glucose, HBA1C, Blood Pressure 4hrly titration, ECG (optional).
Monitoring at 3rd Month:	Blood Lipid Level
Monitoring at 6th Month	LFTs, Fasting Plasma Glucose, HBA1C.
Monitoring at 9th Month:	Blood Lipid Level.
Monitoring at 12th Month:	Blood Lipid Level, LFTs, Fasting Plasma Glucose, HBA1c

At the first month only 5% of the patient blood sample was sent for random blood sugar and were reported to be in the normal range.

At three months since started on Clozapine only 1.6% of the patient's blood was analysed for the lipid level. The results were norma5% of the patients lipid level was requested at 6th month and all of them had raised lipid level which supports the previous establish studies of association of Clozapine with increase cholesterol level(Lindenmayer et all JP 2003) .Two patients HBA1C was requested, and one of them was diagnosed with diabetes mellitus.

At ninth month only 13.33 % of the patient's lipids level were requested and out of those 77.5% were reported to be suffering from Hyperlipidemia.

After a year since started on Clozapine two patients blood were requested for lipid level. Both of them were reported back with Hyperlipidemia .Three patients' blood was requested for glycated Haemoglobin, and one of them was reported to be diagnosed with diabetes mellitus. Liver function Test was requested in only 25% of the patients.

DISCUSSION

Although Maudsley guidelines require regular monitoring of patients blood glucose and other a parameters at regular intervals, in this study a surprisingly low level of adherence to these guidelines was found.

None of the patients had fasting blood levels. Similarly in the first month only 5% of the patient blood sample was sent for random blood sugar. At three months since being started on Clozapine only 1.6% of the patient's blood was analysed for the lipid level. Considering the extent of lipid and glucose abnormalities found in the patients on Clozapine adherence to the Guideline is vitally important. This lack of adherence may be due to lack of awareness or the practical difficulties associated with adherence to guidelines in clinical practice. This needs to be considered in future formulation of such guidelines

This study also highlights the importance of adhering clinical guidelines. We found significant number of lipid and blood glucose abnormalities in those tested for these. Although the numbers are very small, more than two third of the patients had hyperlipidemia and one in three patients tested for glycated Haemoglobin had diabetes Mellitus. Our data seem to support the already established studies on association of Clozapine with diabetes mellitus and Hyperlipidemia. Although not scientifically proven, available evidence seems to indicate Clozapine and Olanzapine may have a high propensity to induce diabetes compared with other atypical antipsychotic drugs[6]. As we didn't try to find out about other possible risk factors for diabetes mellitus and Hyperlipidemia in our patient sample, but the data does signify the importance of clinical monitoring of patients on Clozapine for diabetes mellitus and Hyperlipidemia. In a comparative study, both nonobese Clozapine & Olanzapine treated groups displayed significant insulin resistance and impairment of glucose effectiveness compared with risperidone treated subjects[7]. In a retrospective study done at department of Veterans Affairs Out patient mental health clinic in the Mid-Atlantic region, Of the Clozapine cases without a history of diabetes/ hyperglycaemia, 27.7% developed diabetes after initiation of Clozapine[8]. As Clozapine is usually initiated to treat the patients with Schizophrenia after they have been tried on other antipsychotics , it becomes more important to closely monitor these patients for any metabolic dysregulation . Exposure to multiple second generation antipsychotics or Clozapine or Quetiapine significantly increased the risk of treatment emergent diabetes mellitus[9].

CONCLUSION

The data signify the importance of following the Maudsley Guidelines for clinical monitoring of patients on Clozapine .All patients receiving Clozapine should be regular monitored for changes in weight , lipid, and glucose levels so that appropriate preventive and therapeutic measures can be initiated .This is specially important in psychiatric services as the patient with mental illness often fail to communicate their symptoms with the health professionals due to lack to motivation and insight. It is vital for the treating physician to monitor their patients for any potential health problems.

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