

A Clinical Study to Review Treatment Options for Irish Patients of Schizophrenia

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Objectives: To review various treatment options for the schizophrenic patients in order to improve effectiveness of treatment and to minimize side effects.

Study Design: This is an Interventional Prospective study.

Period: From July 2006 to June 2007 (one year).

Setting: This study was carried out in a Depot. Injection Out-patient Clinic of St. Brendan's Hospital, Dublin Ireland.

Methods: (Patients and processes). A group of seventy patients (45 male and 25 female) were included in this study. Their age group was between 20y to 65y. All of them were attending the out-patient clinic regularly to receive a Depot. injection. Except one all of them were on Typical Antipsychotic medication. All patients were thoroughly assessed by one author (KU. Gill) to confirm their diagnosis. Their blood investigations were carried out in one laboratory to record their Full Blood Count, LFTs. TFTs, Blood Glucose (random and fasting), Urea and Electrolytes, Serum Prolactin levels. Recommendations on the basis of their biochemical and other investigation results were made to the patients regarding a switching their treatment either from Depot injection to oral preparation or from typical to atypical antipsychotic medication. From here patients were divided into two groups, those who accepted to switch their treatment were followed up 6 weekly and the rest were followed up 3 monthly.

Results: Twenty seven patients out of 70 had gross liver function abnormalities, 2 female patients had underactive thyroid, 4 patients were suffering from diabetes and 18 patients had very high prolactin levels. The group of patients who opted for a change in their medication i.e. from Depot to either oral atypical antipsychotic or from typical to atypical antipsychotic showed a decrease in their prolactin levels also by reducing the total dose LFTs were improved and same was found in cases of diabetes.

Conclusion: The results of this study suggest that depot patients on typical antipsychotic may benefit from medication review to consider use of atypical antipsychotics and also to review patients on regular basis enhance patients care. However, matching a patients clinical and biochemical profile with that of the drug's pharmacological actions to achieve optimum outcomes remains a challenge.

Key Words: Depot. Injection, Typical Antipsychotics, Atypical Antipsychotics.

Introduction

During the last 10-15 years there has been considerable progress in Psycho-pharmacological options for the patients who suffer from schizophrenia. This clinical study was initiated with an aim to address current issues in mental health service provision in one of the out-patient clinics of St. Brendan's Hospital, Dublin. In this particular out-patient clinic nearly all of the patients were on any of the long acting Depot. Injections (e.g. Flupenthixol). For more than four decades conventional anti-psychotics held the monopoly for depot injection, an atypical antipsychotic (Respiredone consta) is now available in depot form as well.^{1,2}

During this clinical study this was borne out of concern that patients with schizophrenia were not receiving the option of Atypical antipsychotic treatment, from which they may benefit from a reduced incidence of drug-induced side-effects, such as sedation, weight gain, extra-pyramidal symptoms, metabolic disturbances, etc.etc.^{3,4} Conventional antipsychotic depot medication, treatment switches and monitored adverse effects associated with the original depot

treatment are reported in this study. This study aimed to encourage other clinicians to review their clinical practice in order to maximize patient care decreasing the likelihood of unwanted effects of the older antipsychotics.

Methods

Setting:

The study was carried out at the depot clinic that is part of St. Brendan's Hospital, Dublin. The said hospital provides psychiatric care to a catchment area of a population of about 150,000 with by and large Irish people who have a wide-ranging socio-economic backgrounds.

Patients and Process:

A protocol was determined that all outpatients with a reported diagnosis of schizophrenia attending the depot clinic would, in accordance with current guide-lines, have full psychiatric and physical reviews. This prospective interventional study was commenced in July 2006 and was terminated in June 2007. Information leaflets that fully explained

the treatment review process were given to the patients, who were then asked to provide informed consent to a clinical review. For each patient results of the study were collated and a recommendation regarding their future treatment was made based on the findings of the clinical reassessment done by one clinician (K.Gill) and physical health check. So treatment was switched on the basis of an individual patient's symptoms, side effects, and test results, e.g. a patient who was symptomatic on a typical antipsychotic but overweight was not prescribed an antipsychotic with the potential to lead to significant weight gain, or the need for other medication, e.g. antiparkinsonian drugs for extra-pyramidal side-effects.

Table 1: Characteristics of patients included in this study.

No. of patients Assessed	Total N (%) 70	Males N (%) 45	Females N (%) 25
Gender	70	64.3%	35.7%
Age Range:			
20 y to > 25y	7 (10)	5 (7.1)	2 (2.8)
25y to > 35y	9 (12.87)	6 (8.5)	3 (4.2)
35y to > 45y	15 (21.43)	11 (15.7)	4 (5.7)
45y to > 55y	24 (34.29)	13 (18.5)	11 (15.7)
55y to > 65y	15 (21.4)	10 (14.3)	5 (7.14)

Recommendations on the choice of drug or any change in drug regimen (Typical Vs Atypical antipsychotics; depot

Table 2: Baseline Biochemical Abnormalities.

	Total (N = 70) N (%)	Males (N = 45) N (%)	Females (N = 25) N (%)
Biochemical abnormalities:			
LFTs	27 (38.6)	17 (37.8)	10 (40)
TFTs	2 (2.9)	0	2 (8)
Urea/Creatinine	1 (1.4)	1 (1.4)	0
Glucose Abnormalities:			
Fasting Glucose abnormalities	4 (5.7)	2 (4.4)	2 (8)
Fasting Glucose abnormalities	4 (5.7)	2 (4.4)	2 (8)
+glucose in urine	3 (4.9)	1 (2.2)	2 (8)
Prolactin IU/liter			< 700 (normal)
1000-2000	14 (20.0)	4 (8.8)	10 (40)
2000-3000	4 (5.7)	1 (2.2)	3 (12)

Vs oral medication) were discussed with the patients, who were asked to give written informed consent to change or to decline a change in their treatment. Alternative treatments were offered approximately three months after baseline psychiatric and physical assessments. Patients were given a detailed information about their medication and were followed up fortnightly for six weeks. From there on two groups were defined. Patients who had changed their medication were followed up at three months and those patients who remained on their existing medication were followed up at six months. Characteristics of patients included in the study are presented in table 1.

Assessment Procedures:

In order to confirm the diagnosis of Schizophrenia the ICD-10¹² criteria was strictly obeyed. Side effect profile such as extra-pyramidal symptoms, were assessed within the Schizophrenia Quality of Life questionnaire.¹⁰ The physical review included the height/weight, blood pressure, body temperature, pulse rate, ECG, hematology, urine analysis, LFTs, TFTs, fasting and random blood sugar and Serum prolactin levels. All the physical and bio-chemical tests were done in the same centre and laboratory. The results are presented using descriptive statistics in table 2.

Results

Baseline bio-chemical abnormalities:

Out of seventy patients a total of 27(38.6%); 17(37.8%) males and 10(40%) females had abnormal liver function tests which is understandable keeping in view that they had been on long term antipsychotic medication. Only two female patients were detected having abnormal thyroid function, both had underactive thyroid and were treated for the same reason in its own right appropriately (see Table 2). Seven patients (10%), three (6.7%) men and 4 women (16%) had glucose abnormalities (see Table 2). All patients were on typical antipsychotics, particularly Flupenthixol Decanoate. The treatment was changed in only three patients, all were switched to Risperidone long-acting injection. Eighteen patients (25.7%) were found having Hyperprolactinaemia and it was particularly notable in women both in terms of number of patients and severity (see Table 2). Five (11.1%) of 45 men and 13 (52%) of 25 women had Hyperprolactinaemia. Most of these patients were receiving Flupenthixol Decnoate Or Zuclopenthixol Decanoate. Treatment was changed for eleven of these patients. They were mainly switched over to Risperidone Long-acting injection, oral Olanzapine or Quetiapine. The rest of patients opted to reduce the dose of their original medication.

Cardiovascular abnormalities:

Out of 45 men, with baseline data, 9 (20%) had hypertension and 4 (16%) out of 25 women had the same problem, almost all of them were heavy smokers and obese. All of them were receiving Flupenthixol Decanoate. About 25% of all of patients had abnormal ECGs which were nonspecific and it was decided to refer them to specialist cardiology services to sort them out and a regular liaison was developed with the cardiologist with an open option to change the medication of those patients, if deemed necessary.

Medication before review process:

All the 70 patients were taking a depot medication before the review, of whom 69 (98.5%) patients were on conventional (typical) Antipsychotic depot preparation and only one (1.5%) was on Atypical Antipsychotic i.e., Risperidone Consta which is a long-acting in injectable form. Among 98.5% nearly two-thirds of patients (46) were on Flupenthixol Decanoate, 8 (11.4%) were on Zuclopenthixol Decanoate, 10 (14.2%) were on Fluphenazine Decanoate and 5 (7.1%) were on Haloperidol Decanoate.

Medication after review process.

Following the review 50 (71.4%) patients opted for a medication in depot injection form and 20 (28.6%) patients went for an oral form of medication. Those who preferred a Depot Injectable form 41 (82%) received Typical Antipsychotic and 9 (18%) preferred to switch over to Risperidone long acting injection. Those who went for oral preparation were mostly on Atypical Antipsychotics e.g., Olanzapine, Risperidone, Quetiapine and Aripiprazole. This constituted a change in medication for 29 (41.4%) and 41 (58.6%) remained on the same medication. Of the 41 patients who continued on the same medication, 7 tried another antipsychotic before returning to their original medication, (loss of efficacy was the main reason for the decision to change patients back to the original medication), 3 had a change in dose and 1 patient had a change in dose frequency.

Discussion

Unless medication is reviewed periodically many patients suffering from Schizophrenia are likely to continue to receive their current antipsychotic medication regardless of its effectiveness or side effects. Following medication review this study showed that in this non-specific cohort of patients on typical antipsychotic depot medication, nearly two-thirds continued on the same medication. In a few patients, this was after a change in dose level or frequency, or after unsuccessful trials of other medications. Most patients (59%) were treated with Flupenthixol Decanoate before medication review, which was the treatment of choice for almost 40% of patients following review. However over one-third of patients were switched to either Risperidone long acting injection or an oral Atypical antipsychotic. A significant number of patients remained on the same medication despite blood, biochemical and cardiovascular abnormalities. Con-

cerns regarding patient selection and the process of starting treatment with atypical antipsychotics may have limited a switch. Depot antipsychotics guarantee the delivery of a known quantity of medication by requiring the person to attend for injection at a specific clinic, and may confer a small benefit over oral drugs on global outcome. Comparisons have shown no convincing advantages for one typical depot antipsychotic drug over another. However, if initiated appropriately, switching to atypical antipsychotic medication should not compromise patient's functioning; indeed, there are long-term benefits of switching from typical to atypical antipsychotics from a patient's perspective, including psychological functioning and quality of life. In this respect, Risperidone long-acting injection may confer the advantages of atypical medication as well as those of depot preparations. Moderate hyper-prolactinaemia is a common side effect of typical antipsychotics and is associated with the high D₂ receptor occupation on anterior pituitary mammothrophic cells.^{4,5} Our study revealed abnormalities in prolactin levels in almost one-third of patients. Atypical antipsychotics may also cause hyperprolactinaemia to varying degrees. However a switch to an atypical antipsychotic drug may be effective in reducing elevated prolactin levels, and individuals with schizophrenia who previously received oral risperidone therapy have shown a reduction in prolactin levels after a switch to the long acting injection.²

In our study, patients who showed raised prolactin-related side-effects were offered a change in medication. It is of significance that the majority of patients showing raised prolactin levels were asymptomatic. Ten percent patients of this study population receiving mainly depot typical antipsychotics had disturbances in glucose levels, while over 40% had other biochemical abnormalities including hyperlipidaemia. Patients with schizophrenia have a high prevalence of risk factors for cardiovascular disease, such as diabetes and obesity, which are around 1.5 – 2.0 times greater than in general population⁶. Use of some antipsychotics may result in dyslipidaemia, glucose dysregulation, obesity, and the metabolic syndrome, which, in turn, exacerbate the risk of cardiovascular disease and diabetes in these patients.⁴ Rates of hyperlipidaemia and hyperglycaemia with resultant type 2 diabetes associated with antipsychotic use vary between specific antipsychotic medications. According to a recent overview, the risks of disturbances in lipid and glucose metabolism is least with haloperidol and other high-potency typical agents (and also with the atypical agents aripiprazole, risperidone and ziprasidone) and greatest with olanzapine and olanzapine. Using the British Hypertension Society guidelines⁶ this study showed that Hypertension requiring drug treatment may be present in more than 1/3 of a non-specific cohort of patients a depot clinic. Only 1/3 of the observed population had optimal values of blood pressure as defined by the British Hypertension Society. This is of concern because of the increased risk of heart disease and stroke with high blood pressure, and may explain the high rate of abnormal electrocardiograms in a population asymptotic

matic for cardiovascular disease.⁶ It may therefore be prudent to consider a change in these patients' medication to remove this as a possible cause of hypertension and the need for antihypertensive drugs. Antipsychotic medication switching is necessary for patients who achieve suboptimal symptom response or who are experiencing intolerable or high-risk side-effects.

Conclusion

The results of this study suggest that depot patients on typical antipsychotic may benefit from medication review to consider use of atypical antipsychotics. The possibility now exists to switch patients to a long-acting injection of an atypical antipsychotic, should the clinical profile of the patient and their preferences benefit from such a formulation. The health implications of long-term therapy with agents that cause morbidity are of growing concern, and the findings of this study suggest that health monitoring maybe prudent in patients with schizophrenia on typical depot medications. Clinicians need to determine which patient is likely to benefit from medication change, and tailor management to the needs of the individual patient. However, matching a patients clinical and biochemical profile with that of the drug's pharmacological actions to achieve optimum outcomes remains a challenge.

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