Informing patients about tardive dyskinesia: four-year follow up of a trial of patient education

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Objective: This paper evaluates the effects of an educational intervention about tardive dyskinesia on knowledge and clinical stability at long-term follow up.
Method: Fifty-six patients receiving antipsychotic maintenance completed a questionnaire assessing their knowledge about tardive dyskinesia. After random allocation to either educational intervention or control group, their knowledge, clinical stability and rates of tardive dyskinesia were reassessed after four years.
Results: Seventy per cent of patients completed the study. The patients in the educational group retained significantly more knowledge at follow up than at baseline but this knowledge was not significantly greater than that of the control group. There were no significant differences in the clinical outcomes between the groups.
Conclusion: Patients can retain a small but significant amount of information with a low risk of noncompliance. Discussion about tardive dyskinesia is necessary in the process of obtaining informed consent to treatment.
Key words: antipsychotic agents, dyskinesia drug-induced, informed consent, patient education, schizophrenia.

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Maintenance treatment with antipsychotic medication is complicated by tardive dyskinesia in 20 to 25% of patients. Patients who possess the capacity to consent to treatment should be informed of the risks and benefits of continued treatment with antipsychotic drugs [1]. A series of studies [2–5] support the use of educational information in improving knowledge about tardive dyskinesia without the risk of clinical deterioration. With the exception of one study [6], the follow-up periods have all been six months or less. This period may be of insufficient duration to test the endurance of acquired knowledge or for noncompliant patients to relapse. Chaplin and Kent found that patients who had received an educational session about the risk of tardive dyskinesia had a significantly higher knowledge of the condition at six-month follow up without increased clinical risk [5]. This study follows up that sample after four years.

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Method

Fifty-six patients participated in the original study. They were recruited from six community mental health teams and one rehabilitation team in south-west London, UK. All patients were diagnosed with a psychotic illness according to OPCRIT [7], 40 had schizophrenia, 11 schizoaffective disorder, and five bipolar disorder. They were all prescribed antipsychotic maintenance treatment and were clinically stable. Patients admitted to hospital or prescribed clozapine were excluded. They initially completed a brief interview to elicit socio-demographic information and their main symptoms when ill. Their knowledge about neuroleptic drugs was assessed using a questionnaire devised by Kleinman [2] with slight modifications (see Appendix I.). Most questions were answered 'true', 'false' or 'not sure' and the patients were asked not to guess. The questionnaire was scored by giving one point for each correct answer. The maximum score possible was 16.

Compliance was rated on a five-point scale after discussion with the key worker and by case notes, depot injection records and discussion

with the patients. Noncompliance was defined as a period of refusal to take prescribed antipsychotic medication for a period of two weeks or more over the four-year period. Antipsychotic dose was calculated in chlorpromazine equivalents for those not receiving atypical drugs and a drug increase was defined as an increase of 200 mg or more. The number of days in hospital was recorded as an indicator of relapse. Tardive dyskinesia was assessed using the Abnormal Involuntary Movement Scale (AIMS) [8] at the six-month follow up. It was defined by the presence of mild abnormal movements in at least two body areas or movements of moderate severity in one body area on the AIMS.

Patients were randomly allocated to intervention and control groups by a random number table. The socio-demographic and clinical characteristics of the sample are described in the initial study and did not differ between groups. The study group received a half-hour interactive session with RC on the risks and benefits of antipsychotic medication. In addition, they were given a printed sheet that enabled them to answer the questionnaire about side-effects. The control group received no information. The patients were reassessed after four years by CT who was blind to the allocation of the patients. He received education and training from RC who had conducted the original assessments. This included training in the use and scoring of the AIMS over a three-hour session in patients with varying degrees of movement disorder. A high level of agreement between the raters was achieved. The participants in the original study were approached to give informed consent and they completed all the assessments they had been performed at baseline. The ethics committee refused to give permission to examine the case records of those who declined to participate in the follow-up study, and therefore no details are available on their outcome.

Two outcome measures were judged to assess the success of the educational process. The first was the difference between knowledge at baseline and four-year follow up for both groups. A Wilcoxon test for two related samples was employed. The second was the differences in change of scores between the groups over the four years. A Wilcoxon test for two independent samples was employed. A power calculation revealed that for a follow-up sample size of 40 patients, the study had 80% power to detect a difference in scores of 2.4 or more between the study and intervention groups. Differences in rates of relapse and tardive dyskinesia rate were compared using chi-squared analysis with Yates' correction. The data was entered onto the programme SPSS [9].

Results

Patient recruitment

Fifty-six patients completed the educational session of whom 53 (95%) completed the six-month assessment. Forty patients (71%) were reassessed after four years. The mean follow-up periods were four years and 24 days for the intervention group, and four years and 47 days for the control group ($t = -1.09$, $p = 0.3$, not significant). These patients included 25 (89%) of the intervention group and 15 (54%) of the control group. The difference in follow-up rates between intervention and control patients was significant ($\chi^2 = 6.1$, d.f. = 1, $p = 0.013$). Three patients from the control group had died of natural causes and a further 10 patients who completed the six-month follow-up study declined to participate. Only one patient had been discharged to primary care.

Knowledge about tardive dyskinesia

The two groups at baseline achieved almost identical mean scores in their knowledge about tardive dyskinesia. The intervention group scored a mean of 6.3 from a possible total of 16, and the control group scored a mean of 6.4 ($Z = -0.17$, $p = 0.86$). At six-month follow up both groups made significant gains in their knowledge. The intervention group gained significantly more knowledge with a mean score 9.6 than the control group which had a mean score of 7.5 ($Z = -4.0$, $p = 0.000$). At four-year follow up, the gains in knowledge had diminished. The mean score of the intervention group was 7.5 with a mean gain of 1.2. This score was significantly higher than the initial score ($Z = -2.0$, $p = 0.043$). The mean score of the control group was 7.0 with a mean gain of 0.6. This score was not significantly higher than the initial score ($Z = -3.92$, $p = 0.7$). The changes in knowledge scores did not differ significantly between the groups ($Z = -1.0$, $p = 0.3$) (see Table 1).

Clinical outcome

Clinical stability did not vary between the two groups after four years and was measured by compliance, hospital admissions and the need for antipsychotic dose increase. The key workers' mean ratings of compliance were 4.6 from a possible total of 5 for the intervention group and 4.4 for the control group, indicating a high overall level of compliance. Noncompliance for two weeks or more was recorded in four (16%) of the intervention group patients and two (13%) of the control group patients. The mean number of days spent in a psychiatric hospital were 39 for the intervention group and 49 for the control group. Change in dose of antipsychotic drugs in chlorpromazine equivalents was measured for the 33 (83%) of patients who were not prescribed atypical antipsychotic drugs. Two (10%) of the intervention group and 5 (36%) of the control group had their antipsychotics increased by 200 mg or more chlorpromazine equivalents. There was a mean decrease in dosage by 172 mg in the intervention group and 42 mg in the control group. The overall rate of relapse was calculated

Table 1. Knowledge about tardive dyskinesia scores from a maximum of 16

	Intervention group	Control group
Baseline score	6.3	6.4
6 months score (change)	9.6 (+ 3.3) p = 0.000	7.5 (+ 1.1) p = 0.0013
4 years score (change)	7.5 (+ 1.2) p = 0.043	7.0 (+ 0.6) p = 0.7

as a combination of the above three measures. Nine (36%) of the intervention group and six (40%) of the control group experienced a relapse. None of these results indicated a significantly different outcome for either group at the 5% level. There were insufficient numbers of patients in the study to examine the differential contributions of diagnosis, AIMS rating and socio-demographic factors to the gain in knowledge.

Tardive dyskinesia

There was an overall decrease in the AIMS scores and rates of tardive dyskinesia for both groups. AIMS scores decreased from a mean of 4.3 to 2.1 in the intervention group and 3.5 to 1.1 in the control group. The decrease was significant in the intervention group ($Z = -2.4$, $p = 0.016$) but not in the control group ($Z = -1.5$, $p = 0.14$). At four-year follow up, four patients received a diagnosis of tardive dyskinesia (three in the intervention group and one in the control group). Two patients received a new diagnosis, seven patients recovered and two patients had persistent cases of tardive dyskinesia from the total of 40 patients. All the patients who recovered had lower initial AIMS scores than those with persistent tardive dyskinesia. One of the patients who recovered had been withdrawn from her antipsychotic medication while the others had no obvious reasons for recovery.

Discussion

Comparison with other studies

This study, to our knowledge, achieves the longest follow-up period after an educational session about tardive dyskinesia. This is particularly important as it allows adequate time to assess clinical outcome. At six-month follow up, clear improvements in knowledge about tardive dyskinesia persisted in the intervention group, and to a lesser extent in the control group. This knowledge could have resulted in an increased risk of non-compliance and relapse following the end of the initial study; however, the four-year follow-up data indicate this was not the case and it lends further weight to the clinical safety of the informing process. The study by Kleinman [6] found similar results at two-year follow up in terms of relapse rates and noncompliance, suggesting the safety of education. This study differed as it did not contain a placebo control group. Instead, a group of patients which received a single educational session was compared with one which received an additional session four weeks later. The group with the extra educational session required significant increases in their antipsychotic dose while our study found a non-significant trend towards dose reduction.

Follow-up rate

Nearly 30% of patients who were enlisted in the initial study failed to participate in the four-year follow up. Three had died and a further 11 patients who completed the six-month follow-up study later dropped out. Possible reasons for this result may have included the following: a different researcher conducting the study, key workers' reluctance for their patients to participate, and the failure to mention the long-term follow-up study to the patients at the initial study phase. The difference in follow-up rates between the intervention and control groups deserves comment. The local ethics committee did not allow access to the case-notes of the non-respondents so data on the non-respondents is missing. A possible reason for this differential response rate arises from impracticality of blinding the patients to their allocation to either intervention or control groups. Those patients who received the intervention may have been more favourably disposed towards further participation in the study. The greater follow-up rate of those who received the education could indicate the usefulness of engaging the patient in a discussion of treatment benefits and risks in enhancing the therapeutic alliance. The high (89%) follow-up rate of the intervention group does enable interpretation of their results with some confidence although the fate of the other 11% is unknown. It cannot be discounted that they may have had a less favourable outcome.

Changes in knowledge

Both the intervention and control groups showed improved knowledge at the end of four years and there was no statistically significant difference between the improvements of the two groups. In the intervention group this improved knowledge reached statistical significance compared with the baseline. In the control group the improved knowledge did not reach statistical significance. It cannot be said whether the modest improvement in knowledge in the control group was due to chance or whether they sought information independently. The lack of a significant difference between gains in knowledge of the two groups could have occurred due to the lack of blinding of the patients to their allocation or the control patients not receiving a placebo intervention. Patients in the control group were hence alerted about the existence of tardive dyskinesia for the first time by the knowledge questionnaire.

Outcome of patients with tardive dyskinesia

Tardive dyskinesia decreased in rate and severity through the study. This could have been an artefact of longitudinal rating by two different researchers, which is recognized using the AIMS [10]. The condition, however, has more recently been described as less

pessimistic than originally thought, including the tendency in some patients to remit [11]. These results therefore do conform to other research findings on the outcome of tardive dyskinesia. They do however, contradict some of the education that the patients were given in the study about its likely prevalence rate and its persistence. Although there was a trend for antipsychotic doses to be reduced and some patients transferred to atypical drugs, this could not explain most of the recoveries.

Atypical antipsychotic drugs

The original educational package did not include data on the relative risks of tardive dyskinesia associated with atypical and standard antipsychotic drugs. At the time of the design of the trial in 1995, there was no convincing data demonstrating a lower risk with atypical drugs with the exception of clozapine. It was not appropriate to mention this lower risk with clozapine in the educational session as most patients were stable and free from tardive dyskinesia, and therefore they would have been extremely unlikely to have been prescribed it. Further educational studies and information given to patients in the clinical situation should inform patients of a lower risk of tardive dyskinesia now known to be associated with atypical drugs. This study also provides useful naturalistic follow-up data on patients who are stable and diagnosed with psychotic illness over a period of massive change in antipsychotic prescribing habits. Most patients were not transferred to newer drugs despite there being no local restrictions on their prescription. Tardive dyskinesia therefore remained a risk for this group of patients although this risk did not in fact materialize.

Clinical implications

Although only one of the two outcome measures reached statistical significance, it is important to consider the knowledge gain in a clinical context. The intervention group's average gain of one correct question about their treatment after a period of four years could be construed as clinically relevant especially when viewed in the context of the overall safety of the intervention. The capacity of patients with chronic psychotic illness has been called into question with particular reference to schizophrenia and affective disorders [12]. Although the numbers of patients in each diagnostic category are too small to look at separately, this study adds to the increasing body of evidence to support the competency of many patients with chronic mental illness to consent to their treatment [13]. Furthermore, the assessment of capacity and methods of enhancing it could be viewed as essential skills which psychiatrists need to possess. Psychiatrists increasingly need to have the confidence and ability to discuss potentially negative treatment outcomes with patients. Patients in turn are becoming better informed about their treatment and are more likely to reject the paternalistic approach of many psychiatrists who protect them from such information [14]. A collaborative approach to the therapeutic relationship is therefore encouraged. This study also highlights that the information which is given to patients needs to be updated in terms of the latest research, as is especially so with tardive dyskinesia. In conclusion, the persistence of knowledge about tardive dyskinesia without increased clinical risk in this study should encourage further research aimed at the enhancing of capacity in other clinical groups of patients.

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Appendix I.

Tardive dyskinesia knowledge questionnaire

Answer: true, false, not sure, or select from multiple choice given. Do not guess.

1. Psychotherapy is the best treatment to stop you becoming ill again or relapsing.
2. Getting better quickly from (symptoms the patient has when ill) is best done by: (antipsychotics/talking treatment/occupational therapy/not sure).
3. People who completely stop their antipsychotic drugs have a high risk of becoming ill again or relapsing.
4. Side-effects like stiffness and shakes get better with procyclidine (also known as kemadrin) and orphenadrine (disipal).
5. Abnormal movements of the tongue, lips and mouth and other parts of the body are called tardive dyskinesia. These get better with side-effect tablets (procyclidine, orphenadrine).
6. How many patients who take antipsychotic drugs for a long time get tardive dyskinesia? (0%, 5%, 20%, 50% 100%, not sure).
7. In some patients, the abnormal movements of tardive dyskinesia will remain with them for the rest of their lives.
8. Younger patients are more at risk of developing tardive dyskinesia.
9. Doctors can tell exactly which patients will develop tardive dyskinesia.
10. In some patients, the abnormal movements of tardive dyskinesia get better if their antipsychotic drugs are stopped.
11. In some patients, the abnormal movements of tardive dyskinesia will get worse after stopping antipsychotic drugs.
12. The best way to make the abnormal movements of tardive dyskinesia disappear is to detect the condition early and stop the antipsychotic drugs.
13. Patients who take their tablets or injections as directed will not develop tardive dyskinesia.
14. Please choose the answer that applies to you: you will (definitely/might/never/not sure) develop tardive dyskinesia.
15. Patients may have the abnormal movements of tardive dyskinesia but may not be aware of it themselves.
16. Before today, has anyone ever told you about tardive dyskinesia?