A Cross-Sectional Study of Patients' Perspectives on Adherence to Antipsychotic Medication: Depot Versus Oral

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Background: Antipsychotic depot medications improve medication adherence by reducing covert nonadherence, but some clinicians believe that they are unacceptable to patients. This cross-sectional study investigated patients' perspectives on factors influencing adherence to antipsychotics, from both those taking depots and those taking tablets in ongoing voluntary outpatient care. The study is novel in also encompassing such factors as injection phobia and perceived coercion regarding medication in relation to self-reported adherence.

Method: Seventy-three patients with schizophrenia/schizoaffective disorder (ICD-10 criteria) completed structured clinical interviews that included the Rating of Medication Influences (ROMI) scale as well as instruments that assessed patients' functioning, psychopathology, insight, extrapyramidal symptoms, quality of life, needle anxiety, experience of coercion, and beliefs about medication.

Results: Participants taking depot (vs. oral) medication had higher ROMI noncompliance mean scores (15.7 vs. 14.4, p = .019). Predictive factors for influences on noncompliance included certain beliefs regarding medication (concern and overuse) but not extrapyramidal symptoms. There were no differences between the 2 formulation groups on the ROMI compliance subscale. Further predictive factors associated with influences on compliance included perceived necessity.

Conclusions: Previously, side effects were considered to be a reason for nonadherence to depot more than for oral medications, but our findings do not support this. Rather, beliefs and attitudes are more important than side effects in predicting self-reported adherence and influencing factors thereof. Prescribing a depot medication to enhance relapse prevention will not in itself ensure adherence and therefore must also be accompanied by discussion regarding adherence and associated personal benefits.

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In schizophrenia, poor treatment adherence (noncompliance) to antipsychotic drugs is the main reason why these drugs are seen to perform better in controlled drug trials (drug efficacy) than in routine clinical practice (drug effectiveness).[1] Nonadherence rates for antipsychotics are generally reported to be 40% to 60% and are associated with higher risk of relapse and resultant increased clinical and economic burden for health services.[2–5] Factors predictive of nonadherence include poor insight, negative attitudes to medication, and previous nonadherence, while sociodemographic factors, symptom severity, side effects, drug class (typical vs. atypical), and formulation (oral vs. depot) have been found not to be consistent predictors.[4,6]

Depot antipsychotics are believed to afford early detection of overt nonadherence and eliminate the possibility of covert nonadherence, thereby enhancing adherence and reducing relapse rates.[7–10] Indeed, nonadherence rates for depots are 24% (range, 0%–54%), which is lower than that for orals.[11,12] While some clinicians claim that depots are underutilized,[13] others concede that depots are stigma-

tizing and are less acceptable to patients.[14–18] To study this systematically, we conducted a cross-sectional questionnaire study on attitudes regarding antipsychotics in 222 outpatients with schizophrenia/schizoaffective disorder. We found that current formulation (i.e., whether the patient was taking depot or orals) predicted preference (depot vs. oral) but not attitudes to treatment which, in turn, were more influenced by illness duration, extrapyramidal symptoms, and insight.[19] However, to explore this more fully, it is necessary to carry out in-depth interviews with patients that cover beliefs and attitudes as well as a clinical examination for extrapyramidal symptoms and psychopathology.[20,21] Previous studies have looked at the impact on adherence when treatment is switched from oral to depot antipsychotic medication at discharge from hospital[22] and others have looked at ethnicity differences and depot adherence in the community,[23] but we specifically investigated the difference in attitudes to adherence and influencing factors in more symptomatically stable and voluntarily treated patients in the community. Our study is novel in using a geographically defined clinical sample of patients receiving oral or depot medication and encompassing such factors as injection phobia, perceived coercion, and insight in relation to attitudes to adherence.

Aim and Hypotheses

This study aimed to test the following hypotheses: (1) patients' general attitudes to their current medication, levels of insight, and side effects would be similar regardless of whether they were receiving depots or orals; (2) insight would be identified as a significant positive influence on adherence; and (3) the presence of side effects would be identified as a significant influence for nonadherence.

METHOD

Design

This article reports the results of the second stage of a 2-stage cross-sectional study.[19] The study was approved by the local ethics committee, and research governance procedures were adhered to.

Sample

For the larger study,[19] 222 participants with schizophrenia or schizoaffective disorder receiving maintenance antipsychotics (approximately 33% were receiving depots) were recruited from 2 geographically defined clinical populations: (1) inner city London (Norwood and Brixton) served by the South London and Maudsley NHS Foundation Trust and (2) Bromley, a suburban region on the outskirts of Greater London and served by Oxleas NHS Foundation Trust. These 2 areas were chosen as they had different socioeconomic profiles and so that, combined, the study would cover a reasonably representative sample. To meet inclusion criteria, participants had to be aged ≥ 18 years and to be voluntary outpatients; those with learning disability or substance abuse disorder were excluded. Of the 222 participants, 102 were randomly selected (using predetermined tables) and of these 73/102 (72%) consented to take part in further in-depth interviews. The study was conducted from October 2003 through October 2006. Those consenting did not differ from the remainder in age, gender, education, employment, and length of illness but comprised a slightly higher proportion of those from ethnic minority groups (consenters, 52%; nonconsenters, 24%; $\chi^2 = 4.91$, $p = .027$).

Variables and Instruments

Sociodemographic factors included age, gender, level of education, employment, and ethnicity.[24] Clinical factors included age at illness onset, number of admissions in previous 12 months, antipsychotic medication history, and main psychiatric diagnosis (*International Classification of Diseases, 10th Revision* [ICD-10][25]). Other measures were also used:

- Rating of Medication Influences (ROMI) scale.[26] This 20-item scale was the main outcome measure, and it measures the influence of factors on medication adherence. Each item is rated according to degree of influence on medication-taking behavior: none (1), mild (2), and strong (3). It has 2 subscales—compliance factors (7 items: e.g., your relationship with your prescribing doctor influences you; you are pressured or forced to take medication) and noncompliance factors (13 items: e.g., you believe medication does not help you feel better; someone whose opinion is important to you is against your taking the medication). The ROMI is closely related to the Drug Attitude Inventory (DAI),[27] which, in turn, is a good predictor of actual adherence.[26,27] The ROMI compliance subscale positively correlates ($r = 0.56$, $p < .001$) and the noncompliance subscale inversely correlates ($r = –0.47$, $p < .001$) with the DAI, as would be expected.[26] Thus, it is not unreasonable to assume that the attitudes measured by the ROMI are directly related to adherence behavior, rather than mere stated intent (see also Weiden et al.[22] for similar relationship with another adherence behavior measure). However, the ROMI is a more extensive instrument than the DAI as it covers aspects particularly important to outpatient care, such as the influence of family.
- Beliefs about Medicines Questionnaire (BMQ).[28] The first part, BMQ-Specific, rates the named medication with subscales on necessity and con-

cerns. The second part, BMQ-General, rates general beliefs about medication with subscales on overuse and harm. Higher reported adherence correlates positively with the necessity subscale, and inversely with the other 3 subscales.

- Medication Experience Survey (MES)[29] adapted from the MacArthur Admission Experience Survey Short Form 1.[30] The 3 main subscales for the MES are perceived coercion, negative pressures, and voice. Systematic simple word substitutions were made to adapt the original scale into a form that addresses coercion regarding medication. Items in the perceived coercion subscale include the following: "I feel free to do what I want about taking medication," "I choose to take medication," and "I have more influence than anyone else on whether I take the medication."
- Blood-Injection Symptom Scale (BISS).[31] This scale was used to measure blood and injection phobia (needle anxiety) with 17 items in 2 subscales: fear and faintness.
- Positive and Negative Syndrome Scale (PANSS).[32] This scale was used to measure psychopathology symptom severity.
- Schedule for the Assessment of Insight-expanded (SAIE).[33,34] This scale provided a clinician rating of insight and patient compliance levels.
- Extrapyramidal Symptom Rating Scale (ESRS).[35] This scale was used to objectively measure side effects by using 3 main subscales: parkinsonism, dystonia, and (dyskinetic) movements.
- Manchester Short Assessment of Quality of Life (MANSA).[36]
- Global Assessment of Functioning (GAF).[37]

Procedure

Written informed consent was obtained at the beginning of the in-depth interview. All of the above scales (including self-rating scales) were completed during the interview. The participant's clinician provided the medication history and diagnosis (ICD-10) with reference to the case notes.

Analyses

The main relationships between current formulation (depot vs. oral) and ROMI compliance and noncompliance subscales were analyzed using SPSS (SPSS Inc., Chicago, Ill.) and STATA (StataCorp, College Station, Tex.) computer packages. Relationships between current formulation and symptomatology, functioning, quality of life, and beliefs and the 2 ROMI subscales were explored by using mean differences (2-tailed t tests) and proportional differences (χ^2 test, Fisher exact test). Relationships between baseline instruments and the 2 ROMI subscales were identified by using Pearson correlations, univariate regression, and multiple linear regression.

RESULTS

Baseline

Among participants, 24/73 (33%) were currently receiving typical depot antipsychotics and 49/73 (67%) were currently taking oral antipsychotics, of whom, 42 (86%) were taking atypicals, 3 (6%) were taking typicals, and 4 (8%) were taking clozapine. There were no group differences for sociodemographic characteristics, baseline clinical factors (Table 1), and mean scores on the PANSS, BISS, SAIE, ESRS, BMQ, MANSA, and GAF. However, MES total scores were significantly higher for patients taking depot versus oral medication (mean, 4.39 vs. 2.80; $t = 2.26$; $p = .027$) as were perceived coercion and negative pressures subscale scores. No significant differences were found for the voice subscale (Table 2).

Main Outcome

Participants taking depot medication scored significantly higher mean scores on the ROMI noncompliance factors (depot, 15.75; oral, 14.37; $t = 2.41$; $p = .019$); there were no group differences for ROMI compliance factors (Table 2). Item-by-item analysis revealed only 1 significant difference: "no perceived daily benefit" was more commonly rated as a reason for personal nonadherence for patients taking depot than those taking oral (33% vs. 10%, $p = .015$), but this finding would not survive correction for multiple testing. Common reasons for compliance included fear of rehospitalization (oral, 47%; depot, 67%) and relapse prevention (oral, 78%; depot, 71%). Common reasons for noncompliance included denial of illness (oral, 33%; depot, 14%) and deeming the medication unnecessary (oral, 24%; depot, 42%). For the total sample, ROMI noncompliance scores did not significantly correlate with ROMI compliance scores ($r = –0.12$, $p = .321$); thus, the 2 subscales were not interrelated and were measuring separate factors.

Relationship Between ROMI Compliance and Other Measures

ROMI compliance scores positively correlated with total SAIE scores, BMQ necessity subscale (regarding participants' antipsychotic medication) and, curiously, ESRS total score, but did not correlate with MES, PANSS, BISS, GAF, and MANSA (Table 3). Univariate regression confirmed these findings. When we adjusted for other factors using multivariate linear regression, ROMI compliance scores remained positively associated with ESRS and the BMQ necessity subscale, but the association with SAIE was lost and formulation (oral vs. depot) was not predictive (see Table 3). This model predicted 33.8% of the variance in ROMI compliance scores.

Table 1. Sample Characteristics According to Formulation of Current Medication

Characteristic	Depot N	Depot %	Oral N	Oral %	Total[a] N	Total[a] %	Test Statistic
Gender[a]							
Male	14	58.3	29	59.2	43	58.9	$\chi^2 = 0.01$
Female	10	41.7	20	40.8	30	41.1	p = .945
Age, y[a]							
18–34	6	25.0	10	20.4	16	21.9	$\chi^2 = 0.59$
35–44	9	37.5	16	32.7	25	34.3	p = .743
≥ 45	9	37.5	23	46.9	32	43.8	
Ethnicity[b]							
White	10	52.6	20	46.5	30	48.4	$\chi^2 = 0.20$
Other	9	47.4	23	53.5	32	51.6	p = .657
Black/Black British	7	36.8	19	44.2	26	41.9	
Asian/Asian British	1	5.3	3	7.0	4	6.5	
Chinese/other	0	0.0	1	2.3	1	1.6	
Mixed	1	5.3	0	0.0	1	1.6	
Education[c]							
No qualifications	10	43.5	16	33.3	26	36.6	$\chi^2 = 0.69$
Some qualifications	13	56.5	32	66.7	45	63.4	p = .406
GCSE level or equivalent (age 16)	8	34.8	18	37.5	26	36.6	
A level or equivalent (age 18)	5	21.7	11	22.9	16	22.6	
University degree	0	0.0	3	6.3	3	4.2	
Employment status[a]							
Not working/studying	21	87.5	40	81.6	61	83.6	Fisher
Working/studying	3	12.5	9	18.4	12	16.4	p = .739
Studying only, no work	2	8.4	4	8.2	6	8.2	
Some work +/– studying	1	4.1	5	10.2	6	8.2	
Main diagnosis[a,d]							
Schizophrenia	22	91.7	43	87.8	65	89.0	Fisher
Schizoaffective disorder	2	8.3	6	12.2	8	11.0	p = .713
Illness duration, y[a]							
< 15	10	41.7	27	55.1	37	50.7	$\chi^2 = 3.55$
15–29	13	54.2	16	32.7	29	39.7	p = .170
≥ 30	1	4.1	6	12.2	7	9.6	
Recent admission (12 mo)[e]							
No	12	52.2	26	63.4	38	59.4	$\chi^2 = 0.77$
Yes	11	47.8	15	36.6	26	40.6	p = .380
Only 1 admission	9	39.1	14	34.2	23	35.9	
2 or more admissions	2	8.7	1	2.4	3	4.7	

[a]N = 73.
[b]Ethnicity (N = 62) was categorized using a standard classification system.[24]
[c]N = 71.
[d]Psychiatric diagnoses were categorized according to *International Classification of Diseases, 10th Revision*.[25]
[e]N = 64.
Abbreviation: GCSE = General Certificate of Secondary Education.

Relationship Between ROMI Noncompliance and Baseline Measures

ROMI noncompliance (1) positively correlated with PANSS total, MES total scores, and the BMQ concern, harm, and overuse subscales; (2) negatively correlated with total SAIE scores and the BMQ necessity subscale; and (3) did not correlate with BISS, GAF, and MANSA (Table 4). Univariate regression confirmed these findings as well as the relationship between formulation and ROMI noncompliance (oral group had lower ROMI noncompliance scores than depot group, $\beta = -1.38$, p = .018). Using multivariate linear regression, ROMI noncompliance scores (1) remained positively associated with certain beliefs regarding medication (BMQ concern and overuse); (2) lost the initially significant positive association with psychotic symptomatology, coercion, and beliefs about harmfulness of medication (PANSS total, MES total, and BMQ harm subscale); (3) lost the negative association with beliefs about the necessity of the specific medication (BMQ necessity); and (4) kept the negative association with total SAIE scores. Taking oral medication (vs. depot) remained inversely associated with ROMI noncompliance ($\beta = -1.05$, p = .043) when these other factors were taken into consideration; in other words, participants receiving depot scored more highly on ROMI noncompliance than did participants receiving oral (see Table 4). This model predicted 51.5% of the variance in noncompliance (ROMI) scores.

DISCUSSION

This study investigated patients' perspectives on adherence and nonadherence to antipsychotics, from both those taking depots and those taking tablets, with in-depth clinical interviews in a cross-sectional study.

Table 2. Formulation Group Comparisons for Symptomatology, Functioning, Quality of Life, Adherence, and Beliefs

	Overall Group (N = 73)			Depot (N = 24)		Oral (N = 49)			95% CI			
Scale	Mean	SD	Range	Mean	SD	Mean	SD	Mean Difference	Lower	Upper	t	p Value
PANSS												
Positive	16.01	5.10	7–29	16.17	5.52	15.94	4.93	0.23	–2.32	2.78	0.18	.860
Negative	18.04	6.10	7–36	18.25	6.39	17.94	6.02	0.31	–2.74	3.36	0.20	.840
General	35.36	8.23	19–51	34.63	8.56	35.71	8.13	–1.09	–5.20	3.02	–0.53	.599
Total	69.41	17.00	34–106	69.04	18.13	69.60	13.31	–.055	–9.05	7.95	–0.13	.898
SAIE												
Total	17.50	6.04	3–27	15.88	6.37	18.30	5.77	–2.43	–5.40	0.53	–1.63	.107
Item C	5.18	1.15	3–7	5.17	1.13	5.18	1.17	–0.02	–0.59	0.56	–0.06	.953
ESRS												
Parkinsonism	6.00	4.02	0–19	5.75	2.59	6.12	4.58	–0.37	–2.38	1.64	–0.37	.713
Dystonia	0	0	0–0	…	…	…	…	…	…	…	…	…
Movements	0.99	2.42	0–12	0.71	1.63	1.12	2.73	–0.41	–1.62	0.79	–0.68	.496
Total	6.99	5.68	0–27	6.46	3.48	7.24	6.51	–0.79	–3.62	2.05	–0.55	.582
GAF Total	54.38	12.11	24–82	54.38	2.40	54.10	1.77	0.27	–5.79	6.33	0.090	.929
MANSA Total, mean	4.22	1.02	1.67–6.33	4.17	1.06	4.24	1.01	–0.07	–0.58	0.43	–0.29	.776
BISS[a]												
Fear, mean	0.22	0.26	0–1	0.17	0.24	0.23	0.27	–0.06	–0.19	0.07	–0.91	.366
Faintness, mean	0.14	0.19	0–0.56	0.13	0.20	0.15	0.19	–0.02	–0.11	0.08	–0.34	.731
MES[a]												
Perceived coercion	1.99	1.53	0–5	2.52	1.47	1.73	1.51	0.79	0.03	1.54	2.08	.041
Negative pressures	0.60	1.30	0–6	1.17	1.83	0.33	0.85	0.85	0.22	1.47	2.70	.009
Voice	0.72	0.95	0–3	0.70	0.97	0.73	0.95	–0.04	–0.52	0.44	–0.16	.872
Total	3.31	2.87	0–13	4.39	3.50	2.80	2.39	1.60	0.19	3.00	2.26	.027
BMQ												
Necessity	16.28	5.05	5–25	15.42	5.64	16.69	4.74	–1.28	–3.79	1.23	–1.01	.314
Concern	14.58	4.02	5–24	14.71	4.65	14.53	3.72	0.18	–1.83	2.19	0.12	.861
Overuse	11.92	2.93	4–19	11.21	3.08	12.27	2.82	–1.06	–2.50	0.39	–1.46	.149
Harm	11.92	2.38	4–17	10.63	2.65	10.73	2.26	–0.11	–1.30	1.07	–0.18	.855
ROMI												
Compliance	12.57	2.95	7–20	12.5	2.34	12.61	3.23	–0.11	–1.59	1.36	–0.15	.880
Noncompliance	14.82	2.38	13–28	15.75	3.38	14.37	1.54	1.38	0.24	2.53	2.41	.019

[a]One of the patients receiving depot medication did not complete the scale.
Abbreviations: BISS = Blood-Injection Symptom Scale, BMQ = Beliefs About Medicines Questionnaire, ESRS = Extrapyramidal Symptom Rating Scale, GAF = Global Assessment of Functioning, MANSA = Manchester Short Assessment of Quality of Life, MES = Medication Experience Survey, PANSS = Positive and Negative Syndrome Scale, ROMI = Rating of Medication Influences, SAIE = Schedule for the Assessment of Insight-expanded.

Table 3. Exploratory Correlation and Regression for Predicting Compliance (ROMI)

		Unadjusted (univariate regression) for ROMI Compliance				Adjusted (multivariate regression) for ROMI Compliance			
Variable	Correlation	Coefficient	SE	t	p Value	Coefficient	SE	t	p Value
Oral medication (current)[a]	…	0.112	0.74	0.15	.880	–0.277	0.72	–0.38	.703
PANSS total	–0.09	–0.016	0.02	–0.78	.438	–0.045	0.04	–1.26	.213
SAIE total	0.25*	0.120	0.06	2.14	.036	0.045	0.08	0.57	.570
ESRS total	0.26*	0.137	0.60	2.31	.024	0.157	0.06	2.42	.019
GAF total	–0.04	–0.009	0.03	–0.32	.752	–0.032	0.05	–0.70	.486
MANSA total, mean	–0.07	0.201	0.34	–0.59	.559	–0.123	0.39	–0.32	.751
BISS									
Fear, mean[b]	0.21	2.357	1.31	1.80	.076	2.267	1.69	1.34	.185
Faintness, mean[b]	0.20	2.985	1.79	1.67	.099	–0.367	2.27	–0.16	.872
BMQ									
Necessity	0.43***	0.253	0.06	4.05	< .001	0.203	0.08	2.62	.011
Concern	0.06	0.043	0.09	0.50	.621	–0.029	0.09	–0.31	.755
Overuse	–0.09	–0.088	0.12	–0.74	.461	–0.132	0.16	–0.81	.420
Harm	–0.07	–0.092	0.15	–0.62	.535	0.145	0.20	0.73	.468
MES total[b]	0.14	0.147	0.12	1.20	.234	0.202	0.12	1.64	.106
Constant	…	…	…	…	…	12.339	6.53	1.89	.064

[a]Current oral medication is compared to the baseline of current depot medication.
[b]One of the patients receiving depot did not complete the scale.
*p < .05.
***p < .001.
Abbreviations: BISS = Blood-Injection Symptom Scale, BMQ = Beliefs About Medicines Questionnaire, ESRS = Extrapyramidal Symptom Rating Scale, GAF = Global Assessment of Functioning, MANSA = Manchester Short Assessment of Quality of Life, MES = Medication Experience Survey, PANSS = Positive and Negative Syndrome Scale, ROMI = Rating of Medication Influences, SAIE = Schedule for the Assessment of Insight-expanded.

Table 4. Exploratory Correlation and Regression for Predicting Noncompliance (ROMI)

		Unadjusted (univariate regression) for ROMI Noncompliance				Adjusted (multivariate regression) for ROMI Noncompliance			
Variable	Correlation	Coefficient	SE	t	p Value	Coefficient	SE	t	p Value
Oral medication (current)[a]	…	–1.383	0.57	–2.41	.018	–1.047	0.51	–2.07	.043
PANSS total	0.24*	0.034	0.02	2.09	.040	0.019	0.02	0.78	.440
SAIE total	–0.51***	–0.200	0.04	–4.96	< .001	–0.139	0.06	–2.52	.015
ESRS total	0.02	0.010	0.05	0.16	.871	0.002	0.05	0.03	.973
GAF total	–0.13	–0.026	0.02	–1.12	.268	0.032	0.03	1.02	.311
MANSA total, mean	0.14	–0.348	0.27	–1.27	.208	–0.036	0.27	–0.14	.893
BISS									
Fear, mean[b]	0.13	1.136	1.07	1.06	.292	1.060	1.18	0.90	.373
Faintness, mean[b]	–0.01	–0.164	1.47	–0.11	.911	–0.603	1.59	–0.38	.706
BMQ									
Necessity	–0.38***	–0.180	0.05	–3.50	.001	–0.062	0.05	–1.15	.255
Concern	0.38***	0.224	0.06	3.45	.001	0.169	0.06	2.66	.010
Overuse	0.37***	0.299	0.09	3.35	.001	0.244	0.11	2.15	.036
Harm	0.25*	0.253	0.11	2.21	.031	–0.237	0.14	–1.71	.092
MES total[b]	0.35**	0.289	0.09	3.10	.003	0.117	0.09	1.36	.179
Constant	…	…	…	…	…	12.647	4.56	2.77	.008

[a]Current oral medication is compared to the baseline of current depot medication.
[b]One of the patients receiving depot did not complete the scale.
*p < .05.
**p < .01.
***p < .001.
Abbreviations: BISS = Blood-Injection Symptom Scale, BMQ = Beliefs About Medicines Questionnaire, ESRS = Extrapyramidal Symptom Rating Scale, GAF = Global Assessment of Functioning, MANSA = Manchester Short Assessment of Quality of Life, MES = Medication Experience Survey, PANSS = Positive and Negative Syndrome Scale, ROMI = Rating of Medication Influences, SAIE = Schedule for the Assessment of Insight-expanded.

Formulation

Participants receiving depot antipsychotics (vs. oral) scored more highly on ROMI noncompliance factors. Depots are often advocated to promote medication compliance, yet the evidence for this is scant.[4] This observation endorses findings by Weiden et al.,[22] who found an initial benefit in adherence attitudes and behavior for those discharged from hospital and taking depot (vs. oral) but which was not maintained at 12 months. For our study, participants who were more likely to nonadhere may have subsequently been prescribed depots, but their reasons for nonadherence would not have changed. That said, depots may enhance relapse prevention because they allow the clinician to differentiate between lack of efficacy and nonadherence.[12,13,38] It is also particularly noteworthy that our 2 groups did not differ in baseline measures of sociodemographic characteristics and clinical factors of diagnosis and duration of illness and evidence of recent admission. This would suggest that that those prescribed depots are not selected differentially by clinicians for such factors. Thus it could be taken as evidence in support of the notion that the only difference between those taking depots and those taking oral medication is that there are problems with adherence. Certainly in the United Kingdom, prescribing of depots is far more prevalent than in other countries such as the United States and, at the time of the study, more first-generation typical antipsychotic depots were used as risperidone long-acting injection had only just been made available. That said, prescribing of antipsychotics in the United Kingdom is still mostly for atypical oral antipsychotics, which is endorsed by national guidelines.

Extrapyramidal Symptoms

Extrapyramidal symptoms were not predictive of the number of factors influencing noncompliance as measured by the ROMI noncompliance subscale. This is in keeping with some, but not all, studies that have found extrapyramidal symptoms to be associated with negative attitudes to antipsychotics.[4,39–41] Paradoxically, we noted a positive association with ROMI compliance scores and extrapyramidal symptoms; perhaps parkinsonism and other extrapyramidal symptoms are a proxy measure for actual medication adherence. However, we note too that akathisia is perhaps not sufficiently assessed by the ESRS, and this can be subjectively very distressing, thereby also adversely effecting adherence.

Coercion

Voluntary patients, who perceived others unduly pressuring them to adhere, also stated more reasons for noncompliance as measured by the ROMI noncompliance subscale. However, this apparent association between increased coercion and ROMI nonadherence scores did not hold when other factors were considered. Here, formulation (i.e., depot) is the likely explanatory factor, with significant associations with both coercion and ROMI nonadherence scores. A relationship between coercion and adherence has been previously identified (1) to be inverse for coercion regarding inpatient admission,[42] (2) to be

positive for perceived coercion only in forensic outpatients on parole,[43] and (3) to be inverse for untoward influence from family or spouse or peer pressure.[44]

Other Factors

Symptomatology, function, and quality of life were predictive of neither ROMI compliance nor noncompliance, which endorses findings by others.[4,21] Thus, discussions between clinician and patients regarding the benefits of adherence should also include other aspects, such as achievement of personal future goals. A novel finding was that scores for blood and injection phobia (BISS) were consistently higher for the oral group and some scored highly, suggesting true phobia and a reason why depots are not a viable option for some patients.[31,45]

Insight and Beliefs

Insight was predictive of ROMI noncompliance scores but not of compliance scores, which partially conflicts with our hypothesis. Due to the multidimensional nature of insight, patients with no insight into illness may still accept and derive benefit from medication.[4,41,42,46] Alternatively, beliefs about the necessity of the specific medication may be more pertinent than other aspects of insight for adherence. Thus, helping patients to accept a mental illness label is not essential for adherence.[41,47] Participants who believed medications in general are overused, or had specific concerns about their antipsychotics, also had higher ROMI noncompliance scores, suggesting that they were less likely to adhere. Paradoxically, those who thought medications in general were harmful did not have higher ROMI noncompliance scores; this suggests that they were not more likely to be nonadherent (which is not in keeping with previous literature[4,28]). This finding may be due to patients feeling more freely able (or empowered) to state their concerns regarding harmfulness within a therapeutic alliance or simply a dissociation between the general concept and the specific personal reality.

The Health Belief Model is an explanatory model for adherence that emphasizes the patient's subjective cost-benefit analysis of a treatment within the context of the patient's personal goals and priorities.[47,48] The model is underpinned by relationships between nonadherence and insight and by negative beliefs and side effects, which are not fully supported by our findings. Further, our findings suggest that there are different factors that predict adherence and nonadherence. That said, Health Belief Model–based interventions do provide credence for the model as they are more effective at improving adherence and clinical outcomes than are simple psychoeducational strategies.[49,50] Alternatively, Day et al.[42] proposed a model for attitudes to antipsychotics, based on data from acute inpatients, which did not include side effects but suggested that positive relationships with clinicians and insight predict more positive attitudes. Our findings on insight and beliefs suggest that modifications to the model are required to encompass nonacute outpatients.

Limitations

This article reports the results of a naturalistic study rather than a randomized controlled trial, so comparison of attitudes and beliefs between groups of patients is liable to various biases. Hence, all inferences must be judged in this light. Selection bias is a problem for all attitude studies since patients who are more compliant in general are more likely to participate in research studies. This study was about patients receiving maintenance antipsychotic treatment in the community, and, as such, it did not focus specifically on nonadherence in an acute phase of psychotic illness. That said, we did achieve some representation of those with negative attitudes evidenced by relatively high noncompliance scores. However, some might also argue that clinicians who made the original treatment decision to prescribe depot medication to some of the patients may have been correct in their identification of patients less likely to have positive feelings and, therefore, lower adherence independent of their experience receiving the depot. Secondly, we were particularly interested in attitudes so chose a subjective rather than objective method of measurement for measuring adherence and associated factors. That said, there is no completely accurate measure of adherence that can be readily used. Biological measures of antipsychotic medication adherence are invasive, pill counts/prescription refill data do not necessarily reflect the amount or frequency of medication actually taken, and "objective" clinician measures of patient adherence are deemed less accurate than "subjective" patient self-reported adherence measures. However, some believe that only plasma levels of the drug can count as a true "gold standard" measure of adherence, even though variation is seen in plasma levels for the same dose given to different people. Alternatively, categorically knowing that the medication has been taken is perhaps the best measure of all, e.g., by administering an injection oneself. Finally, atypical and typical oral antipsychotics and clozapine were considered together as a single group and were compared to those receiving typical depot antipsychotics. The study took place before long-acting risperidone became widely available.

CONCLUSIONS

This study was motivated in part by the need to understand the proposed underutilization of depot or long-acting antipsychotics. When patients who are currently voluntarily maintained with antipsychotics are asked detailed questions about their attitudes regarding current medication adherence, stated reasons for nonadherence were more evident in patients taking depot than those taking oral. This confirms that prescribing a depot must be

accompanied by discussion regarding adherence, or reasons for nonadherence may convert into actual nonadherent behavior, if they have not already done so. Previously, side effects were associated more with depots than with orals and were seen as a reason for depot nonadherence, but our findings do not support this belief and emphasize instead beliefs about medication and lack of insight. This study endorses findings of others, both in 2 smaller studies on established schizophrenia[51,52] and also in 1 on first-episode schizophrenia.[53] However, even when predictive factors for nonadherence are absent, some patients miss taking medications as prescribed.[54] Thus, it is imperative that clinicians continue to strive to understand their patients' individual perspectives—including the opportunity to express concerns regarding the use of force during voluntary treatment and beliefs, regardless of how accurate they may be—about medication. In so doing, it is hoped that the adverse clinical and economic impact of treatment nonadherence in schizophrenia may be further reduced.

Drug names: clozapine (Clozaril, FazaClo, and others), risperidone (Risperdal).

REFERENCES

1. Patel MX, David AS. Medication adherence: predictive factors and enhancement strategies. Psychiatry 2007;6(9):357–361
2. Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. Psychiatr Serv 1998;49:196–201
3. Lindstrom E, Bingefors K. Patient compliance with drug therapy in schizophrenia: economic and clinical issues. Pharmacoeconomics 2000;18:106–124
4. Lacro JP, Dunn LB, Dolder CR, et al. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. J Clin Psychiatry 2002;63(10):892–909
5. Zygmunt A, Olfson M, Boyer CA, et al. Interventions to improve medication adherence in schizophrenia. Am J Psychiatry 2002;159:1653–1664
6. Dolder CR, Lacro JP, Dunn LB, et al. Antipsychotic medication adherence: is there a difference between typical and atypical agents? Am J Psychiatry 2002;159:103–108
7. Hogarty GE, Schooler NR, Ulrich R, et al. Fluphenazine and social therapy in the aftercare of schizophrenic patients: relapse analyses of a two-year controlled study of fluphenazine decanoate and fluphenazine hydrochloride. Arch Gen Psychiatry 1979;36(12):1283–1294
8. Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. Schizophr Bull 1997;23:637–651
9. Schooler NR. Relapse and rehospitalization: comparing oral and depot antipsychotics. J Clin Psychiatry 2003;64(suppl 16):14–17
10. Tiihonen J, Wahlbeck K, Lonnqvist J, et al. Effectiveness of antipsychotic treatments in a nationwide cohort of patients in community care after first hospitalisation due to schizophrenia and schizoaffective disorder. BMJ 2006;333:224–227
11. Young JL, Zonana HV, Shepler L. Medication noncompliance in schizophrenia: codification and update. Bull Am Acad Psychiatry Law 1986; 14(2):105–122
12. Young JL, Spitz RT, Hillbrand M, et al. Medication adherence failure in schizophrenia: a forensic review of rates, reasons, treatments and prospects. J Am Acad Psychiatry Law 1999;27(3):426–444
13. Patel MX, David AS. Why aren't depots prescribed more often, and what can be done about it? Advances in Psychiatric Treatment 2005;11: 203–213
14. Glazer WM, Kane JM. Depot neuroleptic therapy: an underutilized treatment option. J Clin Psychiatry 1992;53:426–433
15. Davis JM, Matalon L, Watanabe MD, et al. Depot antipsychotic drugs: place in therapy. Drugs 1994;47:741–773
16. Walburn J, Gray R, Gournay K, et al. A systematic review of patient and nurse attitudes to depot antipsychotic medication. Br J Psychiatry 2001;179:300–307
17. Patel MX, Nikolaou V, David AS. Psychiatrists' attitudes to maintenance medication for patients with schizophrenia. Psychol Med 2003;33:83–89
18. Patel MX, De Zoysa N, Baker D, et al. Depot antipsychotic medication and attitudes of community psychiatric nurses. J Psychiatr Ment Health Nurs 2005;12:237–244
19. Patel MX, De Zoysa N, Bernadt M, et al. Depot and oral antipsychotics: patient preferences and attitudes are not the same thing [published online ahead of print June 26, 2008]. J Psychopharmacol.doi: 10.1177/0269881108092124
20. Rogers A, Pilgrim D. Service users' views of psychiatric treatments. Sociol Health Illn 1993;15(5):612–631
21. Hofer A, Kemmler G, Eder U, et al. Quality of life in schizophrenia: the impact of psychopathology, attitude toward medication, and side effects. J Clin Psychiatry 2004;65(7):932–939
22. Weiden P, Rapkin B, Zygmunt A, et al. Postdischarge medication compliance of inpatients converted from an oral to a depot neuroleptic regimen. Psychiatr Serv 1995;46(10):1049–1054
23. Tunnicliffe S, Harrison G, Standen PJ. Factors affecting compliance with depot injection treatment in the community. Soc Psychiatry Psychiatr Epidemiol 1992 Oct;27(5):230–233
24. Office for National Statistics. The Census of England and Wales. Available at: http://www.statistics.gov.uk/census2001. Accessed June 30, 2008.
25. World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva, Switzerland: World Health Organization; 1992
26. Weiden P, Rapkin B, Mott T, et al. Rating of Medication Influences (ROMI) scale in schizophrenia. Schizophr Bull 1994;20(2):297–310
27. Hogan TP, Awad AG, Eastwood R. A self-report scale predictive of drug compliance in schizophrenics: reliability and discriminative validity. Psychol Med 1983;13:177–183
28. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. Psychol Health 1999;14:1–24
29. Patel MX, de Zoysa N, Bernadt M, et al. Voluntary outpatients and coercions: depot versus oral antipsychotics. Schizophr Bull 2007;33:452
30. Gardner W, Hoge SK, Bennett N, et al. Two scales for measuring patients' perceptions for coercion during mental hospital admission. Behav Sci Law 1993;11(3):307–321
31. Page AC, Bennett KS, Carter O, et al. The Blood-Injection Symptom Scale (BISS): assessing a structure of phobic symptoms elected by blood and injections. Behav Res Ther 1997;35(5):457–464
32. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull 1987;13:261–276
33. Kemp R, David A. Insight and compliance. In: Blackwell B, ed. Treatment Compliance and the Therapeutic Alliance in Serious Mental Illness. Amsterdam, The Netherlands: Harwood Academic Publishers; 1997: 61–84
34. Sanz M, Constable G, Lopez-Ibor I, et al. A comparative study of insight scales and their relationship to psychopathological and clinical variables. Psychol Med 1998;28:437–446
35. Chouinard G, Ross-Chouinard A, Annable L, et al. The extrapyramidal symptom rating scale. Can J Neurol Sci 1980;7:233
36. Priebe S, Huxley P, Knight S, et al. Application and results of the Manchester Short Assessment of Quality of Life (MANSA). Int J Soc Psychiatry 1999;45(1):7–12
37. Frances A, Pincus HA. The Global Assessment of Functioning scale (GAF). In: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association;1994
38. Keith SJ, Kane JM. Partial compliance and patient consequences in schizophrenia: our patients can do better. J Clin Psychiatry 2003; 64(11):1308–1315
39. Van Putten T, May PRA, Marder SR, et al. Subjective response to antipsychotic drugs. Arch Gen Psychiatry 1981;38:187–190
40. Castle D, Morgan V, Jablensky A. Antipsychotic use in Australia: the patients' perspective. Aust N Z J Psychiatry 2002;36:633–641
41. Freudenreich O, Cather C, Evins AE, et al. Attitudes of schizophrenia outpatients toward psychiatric medications: relationship to clinical

variables and insight. J Clin Psychiatry 2004;65(10):1372–1376
42. Day JC, Bentall RP, Roberts C, et al. Attitudes toward antipsychotic medication: the impact of clinical variables and relationships with health professionals. Arch Gen Psychiatry 2005;62:717–724
43. Farabee D, Shen H, Sanchez S. Program-level predictors of antipsychotic medication adherence among parolees. Int J Offender Ther Comp Criminol 2004 Oct;48(5):561–571
44. McPhillps M, Sensky T. Coercion, adherence or collaboration? Influences on compliance with medication. In: Wykes T, Tarrier N, Lewis S, eds. Outcome and Innovation in Psychological Treatment of Schizophrenia. Chichester, England: John Wiley & Sons; 1998:161–177
45. Hepburn T, Page AC. Effects of images about fear and disgust upon responses to blood-injury phobic people. Behav Ther 1999;30:63–77
46. David AS. Insight and psychosis. Br J Psychiatry 1990;156:798–808
47. Hughes I, Hill B, Budd R. Compliance with antipsychotic medication: from theory to practice. J Ment Health 1997;6:473–489
48. Perkins DO. Adherence to antipsychotic medications. J Clin Psychiatry 1999;60(suppl 21):25–30
49. McDonald HP, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication prescriptions. JAMA 2002;288(22):2868–2879
50. Nosé M, Barbui C, Gray R, et al. Clinical interventions for treatment non-adherence in psychosis: meta-analysis. Br J Psychiatry 2003;183:197–206
51. Donohoe G, Owens N, O'Donnell C, et al. Predictors of compliance with neuroleptic medication among inpatients with schizophrenia: a discriminant function analysis. Eur Psychiatry 2001;16(5):293–298
52. Rettenbacher MA, Hofer A, Eder U, et al. Compliance in schizophrenia: psychopathology, side effects, and patients' attitudes toward the illness and medication. J Clin Psychiatry 2004;65:1211–1218
53. Mutsatsa SH, Joyce EM, Hutton SB, et al. Clinical correlates of early medication adherence: West London first episode schizophrenia study. Acta Psychiatr Scand 2003;108:439–446
54. Osterberg L, Blaschke T. Adherence to medication. New Engl J Med 2005;353:487–497

