age and length of illness to higher chlorpromazine equivalent prescription. This may relate to the possibility that as a psychotic illness progresses, neuroleptic dose is frequently increased by a succession of different doctors, but is less often reduced — on the basis that 'they must be on that dose for a good reason'. Having age and length of illness as significant predictors for chlorpromazine equivalent prescription indicates that patients accumulate higher doses of medication as an index of time rather than the severity of their illness.

The logistic regression clearly confirmed previous findings that history of violence predicts higher neuroleptic prescription (Krakowski et al, 1993; Chaplin & McGuigan, 1996), but did not demonstrate any contribution of disturbed behaviour during the last week on neuroleptic prescription, unlike previous studies (Krakowski et al, 1993; Chaplin & McGuigan, 1996; Peralta et al, 1994). This suggests that patients' reputation and history influences neuroleptic prescription far more than their current presentation. The only other significant predictor of high neuroleptic prescription was a positive history of larger than 5-years' neuroleptic prescription. Again this supports the notion that over time the dose of neuroleptic is frequently increased to limit patients' undesirable behaviour and is not then subsequently lowered for fear of the behaviour returning, as previously suggested (Van Putten et al, 1992). An alternative explanation is that patients with longer illnesses are on higher doses because there was a previous trend to prescribe higher doses, which they have remained on. If this was the case it still supports the argument that regular review and education of neuroleptics does not occur.

In summary this study shows three things: certain consultants prescribe higher doses of neuroleptics than others; patients with a history of aggression get prescribed higher doses of neuroleptics; and third, patients who have been on neuroleptics longer than 5 years get prescribed higher doses. As our study did not look at patients over time it is possible that patients with a history of aggression had previously not responded to lower doses of neuroleptics and subsequently responded to higher doses. However, the alternative explanation is that psychiatrists are prescribing on the basis of prejudice

relating to patients' previous behaviour, if this is true – then who are we treating?



# References

BALDESSARINI R. J., COHEN B. M. & TEICHER M. H. (1988) Significance of neuroleptic dose and plasma level in the pharmacological treatment of psychosis. Archives of General Psychiatry, **45**, 79–91.

BOLLINI, P., PAMPALLONA, S., ORZA, M. J., et al (1994) Antipsychotic drugs: is more worse? A meta-analysis of the published randomized control trials. *Psychological Medicine*, **24**, 307–316.

BRITISH MEDICAL ASSOCIATION & ROYAL PHARMACEUTICAL SOCIETY (1994) British National Formulary. London & Wallingford: British Medical Journal & Pharmaceutical Press.

CHAPLIN, R. & McGUIGAN, S. (1996) Antipsychotic dose: from research to clinical practice. *Psychiatric Bulletin*, **20**, 452–454.

COLE, J. O. (1982) Antipsychotic drugs is more better? *Mclean Hospital Journal*, **7**, 6–7.

FOSTER, P. (1993) Neuroleptic equivalence. *Pharmaceutical Journal*, **290**, 431–432.

KO, G. N., KORPI, E. R. & LINNOILA, M. (1985) On the clinical relevance and methods of quantification of plasma concentrations of neuroleptics. *Journal of Clinical Psychopharmacology*, **5**, 253–262.

KRAKOWSKI, M., KUNZ, K., CZOBOR, P. et al (1993) Long term high-dose neuroleptic treatment: who gets it and why? Hospital and Community Psychiatry. **44**, 640–644.

LIN, K., ANDERSON, D. & POLAND, R. E. (1995) Ethnicity and Psychopharmacology. *Psychiatric Clinics of North America*, **18**, 635–647.

NORUSIS, M. J. (1994) SPSS Advanced Statistics 6.1. Chicago, IL: SPSS Inc.

PERALTA V., CUESTA, M. J. & CARO, F. (1994) Neuroleptic dose and schizophrenic symptoms – a survey of prescribing practices. *Acta Psychiatrica Scandinavica*, **90**, 354–357.

STRAKOWSKI, S. M., SHELTON, R. C. & KOBRENER, M. L. (1993) The effects of race and comorbidity on clinical diagnosis in patients with psychosis. *Journal of Clinical Psychology*, **54**, 96–102

TABACHNICK, B. G. & FIDELL, L. S. (1989) *Using Multivariate Statistics*. California: Harper Collins.

VAN PUTTEN, T., MARDER, S. R., MINTZ, J., et al (1992) Haloperidol plasma levels and clinical response: a therapeutic window relationship. *American Journal of Psychiatry*, **149**, 500–505.

VAN TOL, H. H., WU, C. M., GUAN, H. C., et al (1992) Multiple dopamine D4 receptor variants in the human population. *Nature*, **358**, 149–152.

WORLD HEALTH ORGANIZATION (1978) The ICD-9 Classification of Mental and Behavioural Disorders. Geneva: WHO.

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# MAIRI S. MACLEOD AND DONALD M. SHARP

# Precursors of compliance with lithium treatment in affective disorders

# AIMS AND METHOD

Objective and subjective lithium compliance was investigated in 30 out-patients attending at an affective disorders clinic. Possible precursors of compliance levels were investigated; namely lithium knowledge and attitudes, patient satisfaction and dosage of lithium administered.

#### RESULT

All patients were defined as currently compliant. Patients with a previous history of non-compliance were exclusively diagnosed with manic depression. Patient satisfaction, lithium knowledge and attitudes were not good predictors of lithium compliance.

# CLINICAL IMPLICATIONS

Compliance with lithium can remain excellent in the presence of moderate lithium knowledge and poor attitudes. Poor attitude towards lithium worsens with years on medication, despite high levels of compliance. Clinicians should be aware that larger prescribed dosages of lithium may be associated with poorer compliance.



papers

Lithium is an effective therapeutic agent in the control of mood in affective disorders (Baastrup & Schou, 1967; Prien et al, 1973; Prien & Potter, 1990). However, the dramatic success of lithium has been tempered by poor levels of patient compliance (Van Putten, 1975; Bech et al, 1976; Cochran, 1984, 1986). Various factors have been associated with patient compliance in affective disorders (Jamison et al, 1979; Connelly et al, 1982). Harvey and Peet (1991) found that a controlled education programme resulted in improved reported tablet omissions and serum lithium levels, suggesting that knowledge and attitudes were related to compliance. Patient satisfaction has been claimed to increase the likelihood of medication compliance in a range of medical settings (Davis, 1968; Francis et al, 1969; Ley, 1976; Ley et al, 1982). However, little is known about the role of satisfaction in compliance in patients suffering from affective disorder.

Lithium non-compliance is a prevalent problem in patients with affective disorder (Strober et al, 1990). The current study aims to investigate the role of the following factors in compliance: patient satisfaction, lithium attitudes and knowledge and prescribed dosage of lithium. Compliance will be examined using a wide range of measures. By evaluating the possible precursors of lithium compliance, this might bring us closer to identifying and managing lithium non-compliance more effectively.

# The study

Patients eligible for study entry had a clinical diagnosis of affective illness, were in attendance at a lithium maintenance clinic and had been prescribed with lithium or carbamazepine. Patients with schizoaffective disorder were excluded from the study. A total of 42 patients were approached. Thirty patients gave informed consent (28 lithium, 2 carbamazepine) and comprised 14 women and 16 men whose mean age was 45.3 years (s.d.=12.4; range 25-64 years). Eighteen patients were clinically diagnosed with manic depression and 12 with major depression. The mean age of onset of the affective disorder was 30.4 years (s.d.=12.6; range, 13-60 years). Patients had been taking lithium for an average of 7.7 years (s.d.=9.4; range, 5 months-30 years). Thirty per cent of patients had received formal psychological or psychiatric counselling of significant duration. Twenty-four patients were receiving additional medication (range, 1-9). Data were not available for the 12 patients who declined to give consent to participate.

A staff psychiatrist saw all patients at the lithium maintenance clinic and invited those willing to participate to sign a patient consent form. Ethical approval from the local health board was granted for the study. Questionnaires were administered by an independent assessor during a single appointment, under the supervision of a research clinical psychologist. The following measures were taken.

# Compliance assessments

- (a) Objective the most recent serum assays were inspected. The number of missed appointments and the percentage of acceptable assays during the previous 12 months were recorded.
- (b) Subjective patients were asked, "How good do you think you are at following doctor's advice for taking your tablets?" (Scale: 1 (excellent) to 7 (extremely poor).) Using the same scale, the psychiatrist rated patients on how well they followed advice for taking their tablets, and documented any history of noncompliance.

Patients were defined as non-compliant if they met both of the following criteria:

- (a) serum lithium levels below 0.4 mmol/l and/or less than 75% acceptable assays during the previous year;
- (b) patient rating of compliance below 'average' (4 or lower) and/or a psychiatrist rating of compliance below 'average' (4 or lower).

# Other measures

Patients rated the level of care they received at the clinic by completing a satisfaction questionnaire (based on Roghmann et al, 1979), with 25 statements on a scale ranging from 1 (very strongly agree) to 7 (very strongly disagree). The Lithium Knowledge Test (LKT; consisting of seven multiple choice questions) and the Lithium Attitudes Questionnaire (LAQ; 19 'yes' or 'no' statements) (Peet & Harvey, 1991) were administered by the psychiatrist to lithium patients. Prescribed dosage of lithium was also recorded

# Findings

Details of the results of the compliance assessment are shown in Table 1.

Table 1. Compliance assessment	
Compliance rating	Mean score
Patient self-report	'very good'
Clinician report	'very good'
Serum lithium level	0.66 mmol/l 'acceptable'
Previous acceptable assays over past 12 months	94.6%
Number of missed appointments over past 12 months	0.4 (75% of those who missed appointments were manic depressed)
History of any non-compliance?	seven patients with manic depression (23%)

# Subjective compliance measures

Approximately half of the patients were rated by themselves and the psychiatrist as 'excellent' at following the doctor's advice for taking their tablets. The mean overall patient response was 'very good' and this was corroborated by the psychiatrist's ratings. Although the psychiatrist rated 7% of patients as 'poor' at taking their tablets, none of the patients rated their compliance levels as 'less than average'.

## Serum levels

All patients indicated serum lithium levels above the recommended level of 0.4 mmol/l (range, 0.44—1.07 mmol/l), with the exception of two patients who showed good subjective compliance ratings. Both of the carbamazepine patients were compliant on all measures. Six patients had shown unacceptable serum assays in the past year (range, 50–89% acceptable). Although five patients met one of the two criteria required for non-compliance, none of the patients met both. Thus, according to the specified criteria employed here, all patients were defined as currently compliant.

# Missed appointments

Eight (27%) patients had missed appointments during the past year (six of these had been diagnosed with manic depression).

# History of non-compliance

The seven patients with a history of non-compliance had exclusively had manic depression (Fisher's exact test, P < 0.05) and rated their current compliance levels as significantly poorer than patients with no history of non-compliance (t=-2.1, df=29, P < 0.05). They had also been prescribed a significantly larger dose (+500 mg) of lithium (t=-2.8, df=29, P < 0.05).

## Patient satisfaction

Patients were very satisfied with the care received at the clinic, with a mean score of 1.6 ('strongly satisfied') obtained, suggesting that patients perceived the care positively, and the psychiatrist to be caring and willing to listen to their concerns. Patients were least satisfied about the waiting time before an appointment, and about doctor availability. Patient satisfaction was weakly, although not significantly, related to patient compliance ratings (r=0.28, Ns).

## Patient scores on questionnaires

Patients achieved a mean overall score of 13.1% in the LAQ (s.d.=14.04; range 0-32%), and a mean of 52.6% in the LKT (s.d.=9.38; range, 18-73%). These scores were not significantly associated with compliance measures. Patients with manic depression scored significantly worse

on the LAQ than patients with major depression (t=-2.91, df=21, P<0.01). LKT scores worsened highly significantly (r=-0.55, P<0.01) with increasing age. Lithium attitudes decreased significantly with increased years of taking lithium (r=-0.56, P<0.05), thus patients became more negative about their medication with increased years of use.



### Comment

The patients investigated in the present study were all defined as currently compliant. This finding contrasts markedly to previous research, where approximately onequarter of patients maintained on lithium regimens failed to comply with physicians' instructions (Jamison et al, 1979; Connelly et al, 1982; Cochran, 1986). It should be noted that the patients in the current study were all attending a specialist lithium maintenance clinic and this may account for the high compliance rates found here. The lack of association obtained between compliance and diagnostic category is consistent with the findings of Connelly et al (1982). However, patients who had a history of non-compliance had manic depression, were mostly male and tended to rate themselves as less compliant than those with no history of non-compliance. Thus, poor previous adherence to lithium regimens is generally predictive of poor current levels of compliance, supporting the trends observed by Frank et al (1985). Patients with a history of non-compliance had been prescribed higher doses of lithium, possibly leading to the increased presence of side-effects (Jamison & Akiskal, 1983; Gitlin et al, 1989). Also, more unstable illness may have produced both poorer compliance, causing more symptoms, and a higher subsequent prescribed dosage of lithium. Patients perceived the standard of care received at the clinic to be very high. The weak and non-significant association between patient satisfaction and compliance was inconsistent with the strong association found by Francis et al (1969). In the present study, however, any possible association may have been masked owing to the high ceiling effect for both variables. Also, our sample was small and may not have been representative of all lithium patients, as those who did not participate may have been dissatisfied. Patient knowledge about lithium was moderate and decreased with age. Attitudes toward lithium were generally poor, particularly among patients with manic depression and with increased years taking lithium. In contrast to the findings of Peet and Harvey (1991) LKT and LAQ scores were not associated with compliance. The LKT scores were similar to the community psychiatric nurse scores obtained by Peet and Harvey (1991), and also similar to the scores of Peet and Harvey's (1991) patients after their educational programme.

Cade's (1949) original claim that lithium could be described as the 'magic wand' for patients can only be supported in the presence of adequate current compliance. Patients in the current study were all currently compliant, in striking contrast to previous research. These findings collectively have clinical relevance for existing lithium clinics, and it is suggested



that educational interventions should be directed particularly towards older patients with manic depression who have been taking lithium for a number of years.

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### References

BAASTRUP, P. C. & SCHOU, M. (1967) Lithium as a prophylactic agent: its effect against recurrent depressions and manic–depressive psychosis. Archives of General Psychiatry, **16**, 162–172.

BECH, P., VENDSBORG, P. B. & RAPHAELSEN, O. J. (1976) Lithium maintenance treatment of manic melancholic patients: its role in daily routine. *Acta Psychiatrica Scandinavica*, **53**, 70–81.

CADE, J. F. J. (1949) Lithium salts in the treatment of psychotic excitement. *Medical Journal of Australia*, **2**, 349–352.

COCHRAN, S. D. (1984) Preventing medical noncompliance in the outpatient treatment of bipolar affective disorders. *Journal of Consulting and Clinical Psychology*, **52**, 873–878.

— (1986) Compliance with lithium regimens in the outpatient treatment of bipolar affective disorder. *Journal of Compliance in Health Care*, **1**, 153–170.

CONNELLY, C. E., DAVENPORT, Y. B. & NURNBERGER, J. I. (1982) Adherence to treatment regimen in a lithium carbonate clinic. *Archives of General Psychiatry*, **39**, 585–592.

DAVIS, M. S. (1968) Variations in patients' compliance with doctor's advice: an empirical analysis of patterns of communication. *American Journal of Public Health*, **58**, 274–288.

FRANCIS, V., KORSCH, B. M. & MORRIS, M. J. (1969) Gaps in doctor patient communication: patients' response to medical advice. New England Journal of Medicine, 280, 535–540.

FRANK, E., PRIEN, R. F., KUPFER, D. J., et al (1985) Implications of noncompliance on research in affective disorders. Psychopharmacology Bulletin, 21, 37–42.

GITLIN, M. J., COCHRAN, S. D. & JAMISON, K. R. (1989) Maintenance lithium treatment: side effects and compliance. *Journal of Clinical Psychiatry*, **50**, 127–131.

HARVEY, N. S. & PEET, M. (1991) Lithium maintenance. 2. Effects of personality and attitude on health information acquisition and compliance. *British Journal of Psychiatry*, **158**, 200–204.

JAMISON, K. R. & AKISKAL, H. S. (1983) Medication compliance in patients with bipolar disorder. *Psychiatric Clinics of North America*, **6**, 175–192.

—, GERNER, R. H. & GOODWIN, F. K. (1979) Patient and physician attitudes toward lithium. *Archives of General Psychiatry*, **36**, 866–869.

LEY, P. (1976) Increasing patients' satisfaction with communications. *British Journal of Social and Clinical Psychology*, **151**, 403–413.

—, BRADSHAW, P.W., KINCEY, J. A., et al (1982) Satisfaction, communication and compliance. British Journal of Clinical Psychology, **21**, 3–16.

PEET, M. & HARVEY, N. S. (1991) Lithium maintenance. 1. A standard education programme for patients. *British Journal of Psychiatry*, **158**, 197–200.

PRIEN, R. F. & POTTER, W. Z. (1990) NIMH workshop report on treatment of bipolar disorder. *Psychopharmacology Bulletin*, **26**, 409–427.

—, CAFFEY, E. M. & KLETT, C. J. (1973) Prophylactic efficacy of lithium carbonate in manic depressive illness. Archives of General Psychiatry, **28**, 337–341

ROGHMANN, K. L., HENGST, A. & ZASTOWNY, T. R. (1979) Satisfaction with medical care: its measurement and relation to utilization. *Medical Care*, **27**. 461.

STROBER, M., MORRELL, W., LAMPERT, C., et al (1990) Relapse following discontinuation of lithium maintenance therapy in adolescents with bipolar 1 illness: a naturalistic study. American Journal of Psychiatry, 147, 475–461.

VAN PUTTEN,T. (1975) Why do patients with manic–depressive illness stop their lithium? *Comprehensive Psychiatry*, **16**, 179–182.

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