Medication Noncompliance in Adolescents with Psychiatric Disorders

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ABSTRACT: The purpose of the study was to estimate prevalence of medication noncompliance among adolescents, following discharge from hospital. A second purpose was to identify predictors of such noncompliance. Seventy-one adolescents, who had been prescribed a medication during psychiatric hospitalization, were interviewed by telephone, 6–8 months post-hospitalization. Medication noncompliance was defined as discontinuing medication without the recommendation of the treating physician. Twenty-four subjects (33.8%) were noncompliant with medication. Age, race, gender, SES, diagnosis, type and number of medications, severity of depression, and family living arrangement did not predict noncompliance. We concluded that noncompliance with psychotropic medications was relatively common and difficult to predict in adolescents who had been hospitalized to a psychiatric inpatient unit; the majority of them suffered from depression. Clinicians should be aware that medication noncompliance may be common and a relatively unpredictable phenomenon.

KEY WORDS: Adolescence; Medication; Noncompliance.

Introduction

Medication compliance among adolescents with psychiatric disorders is an understudied area. Studies involving medically ill patients have indicated that adolescents, compared to other age groups, may be at the highest risk for medication noncompliance.[1,2] A medication noncompliance rate of 60% has been reported in a mixed preadolescent and adolescent group of 54 outpatients with attention deficit hyperactivity disorder.[3,4] A more recent study of adolescents, a large number of whom were substance abusers (47%), found a 62% noncom-

pliance rate at 14 months following discharge from psychiatric hospitalization. With the exception of a few recent studies, most studies of noncompliance among child psychiatric populations have focused on psychotherapy as a treatment modality and noncompliance with medication has been left largely unexplored.[5,6] Although findings from psychosocial treatments may generalize to other treatment modalities, study of psychotropic medication noncompliance is likely to have distinct clinical implications.

The definition of noncompliance and study-methods used for its estimation are fraught with controversy. Compliance has been defined as "the extent to which the patient's behavior coincides with the clinical prescription."[7] Study-methods employed to measure compliance and treatment follow-through have included direct estimation of medication in body fluids, pill count, self-report interview, estimation based on treatment outcome, and estimation based on assessment of the treating physician. Each method has advantages and disadvantages.[8,9] For instance, body fluid measurement is costly and impractical. Pill count method is susceptible to multiple problems such as patient failure to bring the pill container, errors caused by the pharmacist, and the fact that the patient may discard pills prior to the visit.[8] The pill-count method, compared with body fluid estimates, was found to over-estimate medication compliance by approximately 10%.[9] Self-report interview techniques have the advantage of being the least expensive method, those who report noncompliance rarely lie, and this method may identify those noncompliant individuals most susceptible to interventions for improving compliance.[7] However, this technique has the disadvantage of over-estimating compliance.[10]

To our knowledge, medication noncompliance in the post-hospitalization period among adolescents with psychiatric disorders has never been examined with the exception of a recent study which involved a large number of patients with substance abuse disorders.[4] In the present study, we examined the influence of psychiatric diagnosis, number of medications prescribed, type of prescribed medication, severity of depression, and demographic variables. The present study involved a structured telephone follow-up questionnaire. This was the most feasible approach because study participants were recruited from a university hospital with a large catchment area (majority of follow-up care was provided in outlying centers) which precluded a more direct measurement (i.e. pill count; body fluid level estimation). It should be noted that previous studies have documented comparable findings from telephone and in-person interviews using a structured instru-

ment.[11] Finally, we believed that adolescents might find a self-report telephone interview relatively nonthreatening. We hypothesized that adolescents who had been psychiatrically hospitalized at a university medical center would be at high risk for noncompliance with psychotropic medications. Noncompliance was defined as discontinuing medication without the recommendation of the treating physician. Conversely, compliance was defined as either continuing medication at the time of the follow-up, or discontinuing medication based on recommendation of the treating physician.

Methods

Subjects were 71 adolescents (Table 1) who had been hospitalized to the Adolescent Psychiatry Inpatient Program at a university hospital and were prescribed a psychotropic medication. Majority of patients, 31 (54.9%), were recommended one medication. Many patients had failed treatment prior to hospitalization resulting in frequent use of mood stabilizers and neuroleptics. The small numbers of stimulants prescribed in the present study reflect that attention deficit disorder was rarely the presenting problem. Subjects were distributed across social classes I-IV.[12] Each subject received a comprehensive diagnostic evaluation: a clinical interview; a computerized diagnostic interview using the Diagnostic Interview Schedule for Children (DISC-2.3).[13] psychoeducational evaluation; milieu observation; and routine laboratory investigations. Standardized rating scales completed during assessment were the Children's Depression Rating Scale-Revised (CDRS);[14] Reynolds Adolescent Depression Rating Scale (RADS);[15] and Suicidal Ideation Questionnaire (SIQ-JR).[16] Admission CDRS-R = 52.6 ± 14.3; admission SIQ-Jr = 26.4 ± 25.1; admission RADS = 71.8 ± 17.4; and follow-up RADS = 67 ± 16.8; follow-up SIQ-Jr = 21.2 ± 18.8. Prior to discharge, parental written consent and assent of the adolescent were obtained for a follow-up telephone interview.

The sections in the follow-up interview pertinent to the study were: 1) name of the medication; 2) whether the medication was discontinued on recommendation of a physician; 3) reason for discontinuation (side-effects, recovery from illness, perceived lack of efficacy); and 4) current living situation. Questions were administered to both the parent (or a responsible adult) and the adolescent. Final answers were based on clinical judgment, using information from both respondents.

Because of sample size limitations, diagnostic and medication categories were created for the analyses. Diagnostic categories were based on DSM-III-R (APA, 1987);[17] medication categories were consistent with standard classification principles used in psychopharmacology. Depressive Disorders (DD: major depression, dysthymia, depressive disorder-NOS), Anxiety Disorders (AD: panic disorder with/without agoraphobia, simple phobia, social phobia, OCD, PTSD, generalized anxiety disorder, separation anxiety disorder), Disruptive Behavior Disorders (DBD; attention deficit hyperactivity disorder, conduct disorder, oppositional defiant disorder, alcohol and substance use disorders).

Table 1
Demographic and Clinical Characteristics of Subjects

n	*71*
Gender	F = 40, M = 31
Mean age	14.9 ± 1.4 years
Race	Caucasian = 62(87.3%) African American = 7(9.9%) Other = 2(2.8%0
Mean number of medications per patient	1.5 ± 0.6
Length of hospitalization	23.1 ± 12.4 days
Interval from discharge to follow-up	6–9 months
Living arrangement	Biological parents = 27(37.7) Single parents = 15(14.4%) Biological + step = 15(21.7%) Non-parent = 14(20.2%)
*Diagnosis	Depressive Disorders = 55(77.5%) (depression with comorbid anxiety/ behavior disorders = 44, depression with no comorbid anxiety or /disruptive behavior = 11) Disruptive Behavior = 40(56.3%) Anxiety Disorder = 32(45.7%)
*Medications prescribed	Antidepressants = 58 (62%) Mood stabilizers = 16(17%) Neuroleptic = 18(19%) Stimulants = 2(2%)

*Many subjects received more than one diagnosis and were prescribed more that one medication

In addition, the Depressive Disorders group was subcategorized into Depression with Comorbidity and Depression Without Comorbidity (DEP-nocomorbid) subgroups. Because of a relatively small sample size and preliminary nature of the study, it was not feasible to analyze compliance for all possible diagnostic or medication subgroups. Therefore, we compared subjects with depression versus those who did not have depression, anxiety disordered patients versus those who did not have an anxiety disorder, disruptive behavior disordered patients versus those with no disruptive behavior disorders, and depression with comorbid anxiety/behavior disorder versus depression without comorbid disorders (no comobid anxiety or behavior disorder). Comorbidity was common and diagnoses per subjects were 1.79 ± .81 (mean ± SD). Medication categories compared were Antidepressants (serotonin reuptake inhibitors, tricyclic antidepressants, tetracyclics, bupropion, venlafaxine,

trazodone) versus no antidepressants, Mood Stabilizers (lithium, valproate, carbamazepine) versus no mood stabilizers, Neuroleptics versus no neuroleptics, Tricyclic (TCA) antidepressants versus no TCAs, and non-tricyclics (Non-TCA; included selective serotonin reuptake inhibitors) to those not on non-TCAs.

Noncompliance was defined categorically as discontinuation of medication without recommendation of a physician. Compliance was defined as either continuing treatment with the medication, or discontinuing it on a recommendation made by a physician. Noncompliant subjects were compared with compliant subjects using chi-square, t-test, or analysis of variance as appropriate. Variables examined were age, race, gender, SES, diagnoses, severity of depression, length of hospitalization, type and number of medications, and family living arrangement (both biological parents, single parent, one step and one biological parents, a non-parent).

Results and Discussion

Out of the entire group of 71 patients, 42 (59.2%) subjects had discontinued their medication at the time of follow-up. But only 24 (33.8%) subjects met criteria for noncompliance as defined for this study, i.e. the medication was stopped without recommendation of a physician. Therefore, the noncompliance rate was 33.8%. All references to noncompliant patients involved this sub-group. Since the majority of subjects in our sample suffered from some type of depressive disorder, our findings are most relevant to this patient population. Reasons given by the noncompliant group were side-effects = 30%(7), perceived recovery = 10%(2), perceived lack of efficacy = 20%(5), and other = 40%(10). The mean number of medications recommended per patient was = 1.5 ± 0.6. The interval between discharge and follow-up was approximately 6–8 months (mean in weeks = 30.4 ± 6.7). Mean number of follow-up appointments with a psychiatrist/family physician for medication management was 5.4 ± 6.

In the overall sample, noncompliance could not be predicted based on diagnosis, type of medication, number of medications, severity of depression, age, race, gender, SES, or family living arrangement. Absence of an association between demographic variables and noncompliance is consistent with previous studies.[7] The present study design did not measure patient-attitude toward psychotropic medications which may significantly influence medication compliance.[19] Also, parent-child relationship factors could not be evaluated; findings from other studies indicate that absence of hostility and affective-relatedness with a parent may significantly improve medication compliance.[18,10]

Lack of association with depression severity was probably a result of high mean depression score for the entire group.

In comparison to subjects without depressive disorders, the fifty-five patients (77.5%) diagnosed with a Depressive Disorder were prescribed significantly fewer number of medications. The Depressive Disordered group was prescribed a significantly fewer number of medications compared to non-depressed subjects (mean = 1.4 vs. 1.8; $t(df = 18.7) = -1.8$, $p < .05$). However, the proportion of noncompliant subjects in the two groups did not differ. There was also no difference in the noncompliance rate between the two distinct sub-groups: depression with comorbidity versus DEP-nocomorbid.

Thirty-two (45.7%) patients were diagnosed with one or more Anxiety Disorders, which was usually comorbid with another Axis I disorder (30 out of 32 were comorbid). There was no difference in the number of medications prescribed for this group, and the noncompliance rate did not differ when compared with subjects with no anxiety disorders.

Forty (56.3%) subjects met diagnostic criteria for a Disruptive Behavior Disorder. There was no difference in the number of medications prescribed for this group, and no difference in the noncompliance rate compared with patients without a Disruptive Behavior Disorder. Although we had anticipated a greater noncompliance rate in the DBD, this was not found to be true. We believe that because of high prevalence of comorbidity, the impact of individual disorders could not be fully elicited. The effect of bipolar mood disorder and schizophrenia could not be examined because of the small number of subjects (4 and 2 respectively).

Our findings have several clinical and research implications. First, because we used a conservative definition of noncompliance, the actual rate of noncompliance may far exceed the one reported here. Second, there appears to be a lack of relationship between type of medication and noncompliance, therefore, the issue of noncompliance must be addressed for all types of medication efficacy studies involving psychotropic medications. Third, when lack of response to a psychotropic agent is encountered in clinical practice, the high possibility of noncompliance and methods to improve adherence to medication must be considered before implementing any medication changes. Finally, given the unpredictability of medication noncompliance behavior, preventive measures to ensure greater compliance must be directed at all psychiatrically ill adolescents.

Drawbacks of the present study include a relatively small sample

size; reliance on patient self-report measure of noncompliance and lack of direct methods for confirming medication compliance (examination of body fluids); variability induced by different treating clinicians and treatment settings at the time of follow-up; a variable time interval between discharge from hospital and follow-up; a relatively homogeneous diagnostic group which did not allow for comparison with other diagnoses; patient attitude toward medication was not measured, and the relationship between the adolescent and an adult living in the home could not be measured. Despite these drawbacks, findings of the present study are an important contribution to an understudied area of psychopharmacology. Based on our findings, it would thus appear that noncompliance with psychotropic medications is common and difficult to predict. A high index of suspicion for noncompliance is warranted and methods known to be associated, at least anecdotally, with higher compliance rates (i.e., patient education and least effective dosing to minimize side-effects) should be universally incorporated in medication management of all adolescent psychiatric patients. Future research on medication compliance should include direct methods for estimation of medication compliance, measurement of patient and parental attitudes toward medication, and measurement of factors, which reflect parent-child relationship.

Summary

Using telephone follow-up method, we found that a little over a third of adolescents hospitalized 6–9 months earlier to an acute psychiatry inpatient unit were noncompliant with their psychotropic medications. Noncompliance was defined as discontinuing a medication without input from a treating physician. Majority of patients suffered from a Depressive Disorder, therefore, the study findings are most relevant to this group. Given the conservative nature of our definition of noncompliance, a higher noncompliance rate may be expected in clinical practice. Demographic variables, diagnoses, severity of depression, or the type and number of prescribed medications could not predict noncompliance. We concluded that noncompliance with psychotropic medications is common, difficult to predict, preventive measures should be directed at all psychiatrically ill adolescents, and should be suspected when encountering lack of response to a psychotropic agent. Implications for clinical practice and future study direction are discussed.

References

1. Korsch BM, Fine RN, Negrete VF: Noncompliance in children with renal transplants. *Pediatrics* 61:872–876, 1978.
2. Smith SD, Rosen D, Trueworthy RC, et al: A reliable method for evaluating drug compliance in children with cancer. *Cancer* 43:169–173, 1979.
3. Sleator EK, Ullmann RK, von Neumann A: How do hyperactive children feel about taking stimulants and will they tell the doctor? *Clinical Pediatrics* 21:474–479, 1982.
4. Lloyd A, Horan W, Borgaro SR, Stokes JM, Pogge DL, Harvey PD: Predictors of medication compliance after hospital discharge in adolescent psychiatric patients. *Journal of Child and Adolesc Psychopharmacology*, 8,2,133–141, 1998.
5. Webster-Stratton C: Predictors of treatment outcome in parent training for conduct disordered children. *Behavior Therapy* 16:223–243, 1985.
6. Dumas JE, Wahler RG: Predictors of treatment outcome in patient training: Mother insularity and socioeconomic disadvantage. *Behavioral Assessment* 5:301–313, 1983.
7. Haynes RB, Sackett DL, Gibbon ES, et al: Improvement of medication compliance in uncontrolled hypertension. *Lancet* 1:1265–1268, 1976.
8. Fletcher SW, Pappius EM, Harper SJ: Measurement of compliance in a clinical setting. *Arch. Int. Med.*, 139:635–638, 1979.
9. Bergman AB, Werner RJ: Failure of children to receive penicillin by mouth. *New Eng J. Med.*, 268:13334, 1963.
10. Gordis L, Markowitz M, Lilienfeld A: Why patients don't follow medical advise: A study of children on long-term antistreptococcal prophylaxis. *Journal of Pediatrics* 75:957–68, 1969a.
11. Aneshensel CS, Freichs RR, Clark VA, & Yokopenic PA: Measuring depression in the community: A comparison of telephone and personal interviews. *Public Opinion Quarterly*, 46, 110–121, 1982.
12. Hollingshead AB, Redlich F: Social class and mental illness. New York: Wiley, 1958.
13. Costello EJ, Edelbrock CS, Costello AJ: Validity of the NIMH Diagnostic Interview Schedule for Children: A comparison between psychiatric and pediatric referrals. *Journal of Abnormal Child Psychology* 13:579–595, 1985.
14. Poznanski E, Mokros HB, Grossman J, et al: Diagnostic criteria in childhood depression. *American Journal of Psychiatry* 142:1168–1173, 1985.
15. Reynolds WM: Reynolds Adolescent Depression Scale: Professional Manual. Odessa, Florida: Psychological Assessment Resources, 1987.
16. Reynolds WM: Suicidal Ideation Questionnaire: Professional Manual. Odessa, Florida: Psychological Assessment Resources, 1988.
17. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 3rd edition-revised (DSM-III-R). Washington, DC: American Psychiatric Association, 1987
18. King CA, Hovey JD, Brand E, et al (1997): Prediction of positive outcomes for adolescents psychiatric inpatients hospitalized adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry* 36:10,1434–1442.
19. Williams RA, Hollis HM, Benoit K: Attitudes Toward psychiatric medications among incarcerated female adolescents. *J. Am. Acad. Child Adolesc. Psychiatry*, 37:12, 1301–1307, 1988.