Intermittent Medication for Schizophrenic Outpatients: Who Is Eligible?

by John A. Chiles, Denise Sterchi, Tom Hyde, and Marvin I. Herz

Abstract

The Medication Clinic of a large, urban Mental Health Center was screened for schizophrenic patients eligible for an intermittent medication approach. A total of 112 patients were evaluated, and 39, or 34.8 percent of the sample, met our basic inclusion criteria. No sex or age differences were found for eligibility. Sufficient eligible patients were found to make the intermittent medication approach a useful part of a comprehensive psychopharmacological program for schizophrenia, if the efficacy of the approach is demonstrated in clinical trials.

Herz et al. (1982), Carpenter and Heinrichs (1983), Carpenter et al. (1987), and Hirsch et al. (1985) have reported pilot data that indicate that some patients with schizophrenia may be effectively treated with intermittent antipsychotic medication. This approach involves establishing criteria for patient selection, tapering off medication, careful monitoring for prodromal signs of exacerbation, and restarting medication when indicated by early signs of relapse. This treatment was developed in part because of concern about harmful medication side effects, especially tardive dyskinesia. As these authors have noted, there are additional empirical bases for an intermittent medication approach derived from the literature on schizophrenia. For many schizophrenic patients, severe psychotic symptoms are episodic. The most common outcome for these patients is a deficit state characterized by blunted affect and apathy, a state not usually responsive to currently available antipsychotic drugs. In these patients, the major function of antipsychotic drugs may be to prevent relapse (Hogarty et al. 1973). Psychotic relapse usually occurs in stages, with a prodromal period preceding the onset of florid psychosis (Donlon and Blacker 1973; Docherty et al. 1978; Herz and Melville 1980; Heinrichs and Carpenter 1985). Thus, by careful observation, a relapse in an unmedicated patient can be heralded by the appearance of certain types of nonpsychotic symptoms or an increase in psychotic symptoms (Donlon and Blacker 1973; Heinrichs and Carpenter 1985), and medication can be resumed at that point to prevent full relapse.

If the efficacy of this approach is demonstrated in larger, controlled clinical trials, questions remain as to what proportion of the schizophrenic population might be considered good candidates for intermittent schedules. Sufficient numbers of schizophrenic patients need to be eligible for intermittent treatment to make implementation worthwhile. Herz et al. (1982), in the initial investigation of the usefulness of this approach, specified the following criteria for inclusion: (1) age 19–60; (2) a DSM-III (American Psychiatric Association 1980) diagnosis of schizophrenia; (3) maintenance of outpatient status; (4) remission; (5) stable symptoms and role functioning; and (6) no evidence of organic brain syndrome, serious medical illness, or suicidal or assaultive behavior during the previous 2 years. These are similar to criteria specified by Carpenter et al. (1987). As part of a
multisite study funded by the National Institute of Mental Health, we have examined these criteria, along with some others, in a schizophrenic population in treatment at a mental health center to determine who would be eligible for an intermittent approach and, if not, why not.

Method

The University of Washington Harborview Community Mental Health Center is a large, comprehensive urban center serving the city of Seattle. Our Medication Clinic handles 600 to 700 patient visits a month and follows a number of individuals with schizophrenia. Each patient is evaluated by an experienced staff psychiatrist using the criteria of DSM-III. A thorough general medical history is taken, appropriate laboratory tests are obtained, and referrals are made to the general medical clinics of Harborview Medical Center when appropriate. Our sample consists of all patients, aged 19–60, with a DSM-III diagnosis of schizophrenia, taking antipsychotic medication, seen in this clinic during a 4-month period. Each patient in the sample was evaluated by chart review and interview with the pharmacotherapist for eligibility for intermittent medication.

Results

A total of 112 patients with schizophrenia were identified, 68 males and 44 females. The sample had a mean age of 39.3 years. Criteria for eligibility were as follows: (1) Baseline hallucinations or delusions that interfere with function. Forty-eight patients had such symptoms despite various medication strategies to control them. (2) Unstable outpatient course in the past 3 months. This was rated positive if a patient had a medication increase to control symptoms or a chart note indicating increased behavioral problems in this time period. Forty-two patients were so rated. (3) Current stressful life event. We looked at whether a patient was undergoing a current major stress such as death or serious illness in the family, divorce or separation, or loss of job. Twelve patients were found to have a current stress. (4) Hospitalization in the past 3 months. Five patients had been so hospitalized. (5) Routinely uncooperative. Noncompliance with medication and/or scheduled appointments occurring repeatedly over a period of at least 6 months defined “routinely uncooperative”; 37 patients were so rated. (6) Use of other psychiatric medication in the past 3 months—antidepressants, minor tranquilizers, lithium, or sleep medications—was noted in 21 patients. (7) Suicidal or assaultive behavior within the past 2 years was documented for 18 patients. (8) A diagnosis of alcohol or drug abuse in the past 2 years was present for 15 patients. (9) A serious medical illness requiring concurrent treatment that might be jeopardized by an exacerbation in psychotic symptoms was found in six patients. For example, one patient had diabetes, and an increase in schizophrenic symptoms might interfere with the patient’s treatment and monitoring of that illness. (10) Organic brain syndrome. Of the 112 patients, 5 had a diagnosis, made by laboratory testing and neurological evaluation, of some facet of organic brain disease. (11) The availability of a significant other person was inquired about because of the usefulness of such a person in identifying prodromal characteristics and occurrence of symptoms. This person needed to have at least two face-to-face contacts with the patient during most weeks. Of the 112 patients, 75 identified such a person. The identified significant other, reported as the nearest full percent, was mother (30 percent), sibling (18 percent), child (16 percent), friend (10 percent), father (6 percent), other counselor (6 percent), spouse (6 percent), extended family member (4 percent), and church member (2 percent). (12) Travel problems significant enough to prevent patients from keeping weekly appointments were present in nine cases. (13) Disabling condition, defined as a condition such as blindness, deafness, language difficulties, or other disability that would interfere in reporting one’s developing symptoms and completing rating interviews, was present in six patients. All six were not fluent in English.

There are at present no established, empirically derived criteria for identifying candidates for an intermittent neuroleptic approach in patients with schizophrenia. Sensible sets of conservative criteria have been developed, such as those articulated by Herz et al. (1982) for an open pilot study and a controlled all-blind efficacy trial. Intrinsically to the published reports of this approach, however, are the conditions that eligible patients must have a recent history of illness stability, must not have troubling positive symptoms of schizophrenia, and must not have a significant current life stress, a situation known to exacerbate schizophrenia. Such patients have a reasonable possibility of being in a quiescent phase of their illness without an increased risk for imminent relapse: that is, they are intermittent approach candidates.
Table 1. Contraindications to the use of intermittent medication

<table>
<thead>
<tr>
<th>Contraindications</th>
<th>Percent positive (n)</th>
<th>Percentage cumulative exclusion (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basic contraindications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interfering baseline symptoms</td>
<td>43 (48)</td>
<td>43 (48)</td>
</tr>
<tr>
<td>Unstable outpatient course</td>
<td>38 (42)</td>
<td>62 (69)</td>
</tr>
<tr>
<td>Current stress</td>
<td>12 (13)</td>
<td>65 (73)</td>
</tr>
<tr>
<td>Hospitalized in past 3 months</td>
<td>5 (5)</td>
<td>65 (73)</td>
</tr>
<tr>
<td><strong>Relative contraindications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Routinely uncooperative</td>
<td>33 (37)</td>
<td>70 (78)</td>
</tr>
<tr>
<td>Other psychiatric medication</td>
<td>19 (21)</td>
<td>72 (81)</td>
</tr>
<tr>
<td>Suicidal or assaultive</td>
<td>16 (18)</td>
<td>75 (84)</td>
</tr>
<tr>
<td>Alcohol/drug abuse</td>
<td>13 (15)</td>
<td>75 (84)</td>
</tr>
<tr>
<td>Medical problems</td>
<td>5 (6)</td>
<td>76 (85)</td>
</tr>
<tr>
<td>Organic brain syndrome</td>
<td>4 (5)</td>
<td>78 (87)</td>
</tr>
<tr>
<td><strong>Management contraindications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence of a significant other</td>
<td>33 (37)</td>
<td>86 (96)</td>
</tr>
<tr>
<td>Travel problems</td>
<td>8 (9)</td>
<td>87 (97)</td>
</tr>
<tr>
<td>Disability</td>
<td>5 (6)</td>
<td>87 (97)</td>
</tr>
</tbody>
</table>

For these reasons, we made criteria 1–4 basic contraindications to choosing patients for this form of treatment. Criteria 5–10 were relative contraindications (discussed below) requiring individual patient assessment. Criteria 11–13 were management contraindications, reflecting conditions a clinic might not be able to meet to provide this approach and thus precluding its use.

Table 1 shows percent positive (to the nearest whole percent) for each contraindication, with the actual number of patients excluded provided in parentheses. The cumulative exclusion column shows how many additional patients were excluded as each contraindication was added in.

Out of our sample of 112, 39 or 34.8 percent, met our basic inclusion criteria. Baseline symptoms and unstable outpatient course accounted for most (95 percent) of the patients not meeting the basic conditions. These two conditions are not associated ($\chi^2 = 0.85, df = 1, p < .36$). There were no age or sex differences in meeting the basic criteria. Twenty-four of the 68 males would qualify for inclusion (35.3 percent), as would 15 of the 44 females (34.1 percent). We looked at this sample by age for those age 30 and under (20 patients) versus those over age 30 (92 patients), and those age 40 and under (58 patients) versus those over age 40 (54 patients). In both cases no significant difference was found on percentages of patients that would be excluded (age 30: $\chi^2 = .19, df = 1, p < .66$; age 40: $\chi^2 = .14, df = 1, p < .71$). We looked at each of the 13 criteria by age and sex. All the serious medical illnesses and organicity were in patients over 40, and the medically ill tended to be female ($\chi^2 = 3.26, df = 1, p < .07$). More males had suicidal or assaultive behavior over the past 2 years ($\chi^2 = 7.22, df = 1, p < .02$). No other significant differences were found.

**Discussion**

Relative contraindications require individual patient assessment. The largest category here is routinely uncooperative ($n = 33$). These patients were so labeled because of noncompliance with medication or missed appointments. Insofar as some of them might be noncompliant because of dysphoric drug side effects, they might be ideal candidates for an intermittent approach. Patients in this category showed considerable overlap, however, with the first two basic contraindications. The null hypothesis that routine uncooperativeness is operating independently is rejected with both baseline symptoms ($\chi^2 = 9.62, df = 1, p < .002$) and unstable outpatient course ($\chi^2 = 5.21, df = 1, p < .03$). There are currently no data on whether the use of other psychiatric medication should preclude an intermittent approach. Suicidal/assaultive behavior, alcohol/drug abuse, other medical illness, and organicity are not problems intrinsic to schizophrenic illness. Along with other medication use, these factors should be evaluated individually before it is decided that they preclude an intermittent strategy.

Management contraindications are factors that might make early identification of prodromal symptoms difficult, but which could be addressed by changes in appointment frequency, programs,
therapist skills. The need for a significant other person would not be pertinent if therapist contacts are frequent (probably at least weekly), or if the patient demonstrates competence to recognize prodromal symptoms. Travel difficulties might be met by an outreach program. Disabling conditions might make communication more difficult, but arrangements (e.g., an interpreter or bilingual therapist) could overcome this.

Of all 13 factors, only 1, organic brain syndrome, is a long-term contraindication. All others might change with time, and several, like hospitalization in the past 3 months or an increase in current stress, would definitely change over time. Thus, a clinic using this approach would need to make periodic reassessments of schizophrenic patients’ eligibility.

These criteria were part of a research design, and 15 patients (13.4 percent) met all 13 of the inclusion requirements. Of these 15 patients, 5 consented to participate in a controlled, all-blind efficacy trial.

If our basic criteria are applied, intermittent medication for the treatment of schizophrenia is a strategy that can be instituted in approximately 35 percent of our sample. Thus, our main conclusion is that this treatment is applicable to enough patients to make it a practical part of a clinical approach to schizophrenia, if its efficacy is demonstrated.

Clinical staff initially felt that almost all patients at this inner-city clinic would be found to have drug or alcohol abuse, lack of a significant other, or high baseline symptom levels. While our data confirm that many patients have baseline levels of symptomatology that exclude an intermittent approach, the majority of patients could name a significant other and relatively few would be excluded for drug or alcohol abuse. Preliminary research has shown that an intermittent medication regimen is efficacious in treating schizophrenia, and current research is continuing to examine the effects of this approach on symptom control and side-effect reduction. This study demonstrates that there exists a relatively stable group of individuals with schizophrenia for whom an intermittent alternative to maintenance medication may be considered, with the aim of improving the quality of their lives.

References


Acknowledgments

This research was supported in part by USPHS grant MH–150–2693, from the National Institute of Mental Health (Marvin Herz, M.D., Principal Investigator). The authors acknowledge the contributions of Robert Waters, M.D., John Brinkley, M.D., David Dunner, M.D., Ilene Stein, R.N., M.S.W., and Pamela Stern, B.A.
The Authors

John A. Chiles, M.D., is Associate Professor of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, WA. Denise Sterchi, M.S.W., is Mental Health Practitioner, Community Support Program, Harborview Community Mental Health Center, Seattle, WA. Tom Hyde, Ph.D., is Research Assistant Professor of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, WA. Marvin I. Herz, M.D., is Professor and Chair of Psychiatry, State University of New York at Buffalo, Buffalo, NY.

Announcement

The Theodore and Vada Stanley Foundation is pleased to announce the initiation of the New Support Program for Research on Serious Mental Diseases. The program will consist of Stanley Fellowship Awards—the purpose of which is to enhance research opportunities for those already in the field and to attract new researchers to the field. Special attention will be paid to neuroscience investigators with innovative approaches not funded by traditional research support mechanisms and to established investigators in other areas of medicine or neuroscience who wish to undertake research on diseases such as schizophrenia and bipolar disorder.

Stanley Fellowships will pay the researcher up to $50,000 per year, plus $20,000 per year in research costs for up to 3 years. Between three and five new awards will be given each year. The announcement of the first awardees will take place at the national convention of the National Alliance for the Mentally Ill in Cincinnati in July 1989.

Nominations for the awards will be made by members of the Selection Committee. Suggestions are welcome from senior researchers in the form of a one-page letter to the address listed below. A small group of nominees will then be invited to submit plans for the use of such an award.

For further information, please contact:

E. Fuller Torrey, M.D.,
Chairperson
Stanley Research Foundation Awards Program
National Alliance for the Mentally Ill
2101 Wilson Blvd., Suite 302
Arlington, VA 22201