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CME Objectives

After completing this CME activity, the psychiatrist should be able to:

- Review data on the risk for suicide among psychiatric patients with schizophrenia
- Examine the clinical characteristics and adequacy of antipsychotic treatment in different phases of illness among suicide victims with schizophrenia
- Consider adequacy of psychopharmacologic treatment, particularly during the active illness phase, as an important factor in suicide prevention among patients with schizophrenia

Statement of Need and Purpose

Physicians responding to articles in The Journal of Clinical Psychiatry and its related CME activities have indicated a need to know more about issues associated with the antipsychotic treatment of schizophrenia. This CME enduring material presents current information to address that need. There are no prerequisites for participating in this CME activity.

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Suicide Victims With Schizophrenia in Different Treatment Phases and Adequacy of Antipsychotic Medication

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Background: To investigate clinical characteristics and adequacy of antipsychotic treatment in different phases of illness and treatment among suicide victims with schizophrenia.

Method: As part of the National Suicide Prevention Project, a nationwide psychological autopsy study in Finland, all DSM-III-R schizophrenic suicide victims with a known treatment contact (N = 88) were classified according to the phase of illness (active/residual) and treatment (inpatient/recent discharge/other). Characteristics of victims in terms of known risk factors for suicide in schizophrenia, as well as adequacy of the neuroleptic treatment, were examined.

Results: Fifty-seven percent of suicide victims with active phase schizophrenia were prescribed inadequate neuroleptic treatment or were noncompliant, and 23% were estimated to be compliant nonresponders. Inpatient suicide victims had the highest proportion of negative or indifferent treatment attitudes (81%), whereas recently discharged suicide victims had the highest prevalence of comorbid alcoholism (36%), paranoid subtype (57%), and recent suicidal behavior or communication (74%), as well as the highest number of hospitalizations during their illness course and shortest last hospitalization.

Conclusion: Suicide risk factors in different treatment phases of schizophrenia may differ. Substantial numbers of suicide victims with schizophrenia are receiving inadequate neuroleptic medication, are noncompliant, or do not respond to adequate typical antipsychotic medication. Adequacy of psychopharmacologic treatment, particularly in the active illness phase, may be an important factor in suicide prevention among patients with schizophrenia.

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Patients with schizophrenia comprise a large proportion (31%–78%) of psychiatric hospital suicides.[1–11] Among clinical samples of suicide victims with schizophrenia, many suicides (10%–44%) have occurred during inpatient treatment.[12–16] Suicide during hospital treatment may be preceded by more severe illness and frequent suicidal behavior. Mistrust in the treatment relationship, discharge plans, and other treatment changes, particularly among long-stay patients, have been more common among suicide victims with schizophrenia than among living inpatients.[7,8,10,11,17,18]

The risk for suicide among psychiatric patients is particularly high during the recent discharge period,[19–21] especially during the first 3 months.[22] A substantial proportion (33%–55%) of suicides among clinical samples of schizophrenic patients have occurred within 3 months of discharge.[12,14] Uncontrolled studies have suggested that discharge may be experienced as an adverse life event among subjects with schizophrenia, resulting in depression or exacerbation of psychotic symptoms, and also that high levels of psychopathology and functional impairment and brief hospitalizations are associated with suicide after discharge.[23–25]

Most suicide victims with schizophrenia have been receiving antipsychotic medication at the time of suicide[12–14,26]; however, the role of such treatment in suicides remains unclear.[27] Case reports have suggested that high doses of neuroleptics may even increase the suicide risk via side effects,[28] whereas some controlled studies in living patients have shown an association with depressive states.[29]

Dose comparisons of prescribed neuroleptics between suicide victims and living patients with schizophrenia have yielded inconsistent findings; it has been suggested that victims receiving higher doses may be more severely ill, whereas lower doses in victims imply more prevalent depressive symptoms.[13,30–34] However, the adequacy of antipsychotic treatment in terms of victim's current psychopathology has not been explored.

Among factors influencing treatment outcome, noncompliance and treatment refractoriness have been little studied in the context of completed suicide in schizophrenia. Noncompliance may occur in up to 50%–75% of patients with schizophrenia[35,36] and account for at least 40% of all relapses.[37] Many factors associated with drug noncompliance are also related to suicide in schizophrenia: a negative attitude toward treatment, compulsory hospital admission, paranoid symptoms, high level of positive schizophrenia symptoms, and alcoholism.[17,35,38–43] However, the findings relating to depression in drug compliance are inconsistent.[39,40,44] Approximately 25% of patients with schizophrenia are partial or nonresponders to typical neuroleptic drugs.[45] Negative symptoms in schizophrenia, despite the many problems of definition and diagnostics, are also suggested to result in less responsiveness to typical neuroleptic treatment.[46] However, schizophrenia patients with prominent negative symptoms are reported to form a subgroup with relatively low suicide risk.[43]

The aims of this study were to examine clinical characteristics known to relate to suicide risk and treatment outcome in schizophrenia, comparing patients in different treatment phases (inpatients, patients in the high suicide risk period of recent discharge, and outpatients discharged more than 3 months ago). We hypothesized that the group in the high suicide risk period of recent discharge would also have the highest proportion of characteristics associated with suicide in schizophrenia, such as recent suicidality, depressive symptoms, alcoholism, and paranoid subtype. The antipsychotic treatment prescribed and its adequacy against the current clinical state of the suicide victim before suicide were also investigated. Our previous finding of a high proportion of active psychotic symptoms among suicide victims with schizophrenia[47] also led us to expect a high proportion of actively ill victims without adequate antipsychotic treatment.

METHOD

The National Suicide Prevention Project in Finland

This study forms part of the National Suicide Prevention Project in Finland.[48] The definition of suicide was based on the results of medicolegal examination and police investigation as required by Finnish law, but these were more detailed than usual during the research project. The official classification of suicide (ICD-9) in Finland at that time defined suicide as a death resulting from an intentional self-inflicted injury. All suicides committed in Finland between April 1, 1987, and March 31, 1988 (N = 1397), were carefully examined using the psychological autopsy method.[48,49] Ethical aspects were approved by the National Board of Health and the Ethics Committee of the National Public Health Institute. Informed consent was always requested written and documented in a structured format.

Data Collection

Data were collected by 4 types of interview: (1) The next-of-kin interview was usually conducted face-to-face at home using a structured form containing 234 items concerning the suicide process, the victim's everyday life and behavior, recent life-events, family history, alcohol and psychoactive substance use, and help-seeking behavior; (2) Interview with the attending health care professional was usually conducted face-to-face at his or her office. The structured form contained 113 items about the victim's health status, suicidal behavior, and treatment received. There was also a cross-sectional psychiatric symptom questionnaire that was filled out by the interviewer with the attending health care professional; (3) The interview with the suicide victim's last health or social care contact was based on a separate semistructured form and conducted by telephone or face-to-face; (4) Additional unstructured interviews were conducted when needed, usually by telephone. The interviewers were mental health professionals specially trained for the psychological autopsy research project.

Suicide notes and medical, social agency, police, and other records, such as hospital charts and toxicologic tests, were also utilized as data sources. Details of the methods have been published previously.[47,50]

Interview data from attending health care professionals during the last year (hospital, 84%; recent discharge, 89%; other outpatients, 71%; $\chi^2 = 3.4$, df = 2, p = .18) and with the last health care contact (hospital, 76%; recent discharge, 86%; others, 80%; $\chi^2 = 0.8$, df = 2, p = .66) were available equally for all suicide victims with schizophrenia in different treatment phases, whereas the data from next-of-kin were less often available among hospital suicides than others (hospital, 18 [72%] of 25; recent discharge, 27 [96%] of 28; other outpatients, 30 [86%] of 35; $\chi^2 = 6.3$, df = 2, p = .043). Data from psychiatric records

and the forensic examination results were available for all victims.

Diagnostic Evaluation of the Subjects With Schizophrenia

The subjects for this study were identified in 3 phases from the total of 1397 suicide victims. First, all the information collected on each victim was carefully reviewed by examining retrospectively all suspected cases with a psychotic disorder. In 578 cases, such evidence existed. The sensitivity of this first phase screening procedure was checked against the Finnish Hospital Discharge Register[51] and found to be excellent. Second, these 578 suspected cases were categorized into 3 groups, first excluding the DSM-III-R organic psychoses (N = 66) and then categorizing the remainder into either the suspected schizophrenia group (N = 233) or other psychosis group (N = 279). The suspected schizophrenia group was chosen if there was any evidence of current or lifetime history of DSM-III-R criterion A for active phase symptoms of schizophrenia. Third, the retrospective diagnostic evaluation of the 233 suspected schizophrenic subjects was made by a pair of psychiatrists according to DSM-III-R criteria by integrating all available information. The interrater reliability of these provisional diagnoses was good ($\kappa = 0.79$). Kappa values were good (i.e., 0.60 or more) for paranoid, disorganized, and residual schizophrenia subtypes (0.62, 0.60, and 0.65, respectively) and moderate (i.e., 0.41–0.59) for undifferentiated (0.45). A third psychiatrist reanalyzed all cases with diagnostic disagreement to achieve the final best estimate diagnoses. Altogether, there were 92 suicide victims with DSM-III-R schizophrenia. The diagnostic procedure was previously described in more detail.[47]

Study Subjects and Classification of Treatment Phases

After excluding victims with no treatment contact at the time of suicide (4/92; 4%), this study included 88 suicide victims with DSM-III-R schizophrenia. The current treatment phase was classified in 3 categories according to the proximity of the last psychiatric hospitalization to suicide following the previous research results of high suicide risk among patients recently discharged from psychiatric hospital[19,20,52]: (1) psychiatric inpatient care (N = 25), (2) recent discharge (≤ 3 months) from psychiatric inpatient care (N = 28), and (3) other outpatients, i.e., discharge more than 3 months ago from psychiatric ward (N = 35). The third group included 1 victim with no lifetime psychiatric hospital treatment.

Psychopathology

Illness course was classified according to DSM-III-R definitions of residual and active illness phases, the latter including acute exacerbation. The cross-sectional classification of positive and negative schizophrenia symptoms was based on all available data, but mainly on the interview of the attending health care professional that focused on the patient's last year using a 35-item structured psychosocial symptom questionnaire. Presence of positive symptoms was recorded if at least 2 of the following were noted: (1) hallucinations, (2) delusions, (3) thought disorder, or (4) bizarre behavior. At least 2 of the following were required for the recording of the presence of negative symptoms: (1) avolition, (2) anhedonia, or (3) affective flattening. DSM-III-R classification allows a diagnosis of depressive disorder with schizophrenia confined to the residual phase of the illness, i.e., as a depressive disorder NOS. We also evaluated the presence of depressive symptoms, defined as depressed mood plus at least one other symptom of DSM-III-R major depressive episode, during the active phase of schizophrenia. Current alcoholism was classified according to DSM-III-R definitions of alcohol abuse or dependence.

Attitudes Toward Treatment

Attitude toward treatment (negative, indifferent, or positive) during the last hospitalization was determined by a structured question in the interview of the attending health care professional and hospital chart data. Indifferent attitude was also classified as negative.

Suicidality During the Last 3 Months

Suicidality (suicidal ideation, communication, threats, or attempts) during the last 3 months was assessed according to all available information and primarily according to the semistructured responses of the attending health care professional.

Treatment Noncompliance

Treatment noncompliance during the last 3 months was assessed by the attending health care professional as follows: (1) appointment noncompliance (minority, or none, of appointments kept) and (2) drug noncompliance (had quit neuroleptic medication entirely or for most of the time). This classification of noncompliance was made independent of current illness symptoms. The opinion of the attending health care professional was validated against the toxicologic analyses of liver and blood (thin layer and gas-liquid chromatography) in forensic examination at the time of suicide. The finding of no neuroleptic

in toxicologic analyses despite a prescribed detectable dose referred to noncompliance only among non–drug overdose cases (55/88; 63%) in which analyses were available (47/55; 85%).

Adequacy of Antipsychotic Treatment

Adequacy of neuroleptic treatment was assessed using chlorpromazine equivalents (CPZe). These were mainly calculated according to formulas established by Baldessarini[53] and Bollini et al.[54] When conversion formulas were missing from these sources,[53,54] other formulas were used for calculating chlorpromazine equivalents, including the following: levomepromazine (75 mg = 100 mg of CPZe), melperone (50 mg = 100 mg of CPZe), pericyazine (5 mg = 100 mg of CPZe), pipotiazine (30 mg = 100 mg of CPZe), promazine (100 mg = 100 mg of CPZe), remoxipride (60 mg = 100 mg of CPZe), sulpiride (200 mg = 100 mg of CPZe), and zuclopenthixol (10 mg = 100 mg of CPZe).

An adequate dosage of antipsychotic medication for treating acute psychosis is suggested to lie between daily equivalents of 100 to 700 mg of chlorpromazine.[55–57] Following recovery from an acute episode of psychosis, doses between 300 and 600 mg/day of CPZe are usually enough to obtain benefits, whereas doses below 100 mg of CPZe may be insufficient.[54,55,57] In the present study, neuroleptic medication of at least 300 mg of CPZe was classified as adequate in the active illness phase and at least 100 mg of CPZe in the residual illness phase for maintenance treatment.

Neuroleptic Nonresponse

Suicide victims were classified as treatment nonresponders if there were current active illness phase symptoms despite prescribed amount of 700 CPZe or more according to the upper limit of recommended sufficient chlorpromazine equivalent dosage[55] at the time of suicide, and if they were taking any neuroleptic medication that had been prescribed 6 months before suicide.

Statistical Methods

Groups were compared using the chi-square test or median test. The major comparisons involved the following 2 families of variables among schizophrenic suicide victims in different treatment phases: (1) longitudinal demographic and outcome characteristics (age, number of hospitalizations/year during the illness duration, duration of last hospital treatment) and (2) cross-sectional clinical characteristics (active illness phase, acute exacerbation, positive schizophrenia symptoms, paranoid subtype, depressive syndrome, alcoholism, suicidality during last 3 months, suicide attempts during last year, compulsory treatment, negative attitude toward treatment). The significance level was set at $p < .05$. Since our study hypotheses were based on previous research, we did not consider the use of the Bonferroni inequality necessary. However, we also provide the Bonferroni inequality-adjusted alpha level,[58] which was .017 for the first family of variables and .007 for the second family of variables.

Two logistic stepwise regression analyses were performed, the first to assess the significance of independent variables (alcoholism, depressive symptoms, illness phase, positive symptoms, negative symptoms, paranoid subtype) in predicting the presence of suicidality during the last 3 months (dependent variable), and the second to assess the significance of independent variables (acute exacerbation, alcoholism, compulsory final hospitalization, depressive symptoms, paranoid subtype) in predicting the presence of drug noncompliance (dependent variable). SPSS software[59] was used.

RESULTS

Clinical Characteristics of Suicide Victims With Schizophrenia in Different Treatment Phases

Recently discharged victims had the highest number of hospitalizations during their illness duration (Table 1). They were also significantly more likely to have paranoid schizophrenia, as well as comorbid alcohol disorder or recent suicidality, than other victims (Table 2). Hospitalized suicide victims had a negative attitude toward treatment more often than other suicide victims, and their last hospitalization was more likely to be compulsory (see Table 2).

The proportion of victims with current prominent positive schizophrenia symptoms was 70% (N = 52/74), while 61% (N = 44/72) had suffered prominent positive as well as negative symptoms at the time of suicide (see Table 2). In logistic regression analysis, suicidality during the 3 months before suicide was associated with the presence of prominent positive schizophrenia symptoms (Wald $\chi^2 = 9.1$, df = 1, p = .0026; odds ratio [OR] = 6.6; 95% confidence interval [CI], 1.9 to 22.7) and depressive symptoms (Wald $\chi^2 = 7.8$, df = 1, p = .0052; OR = 5.5; 95% CI, 1.7 to 18.3).

Pharmacologic Treatment of Suicide Victims With Schizophrenia

Antipsychotic treatment was prescribed for 97% (N = 85/88) of all schizophrenia suicide victims. Medication had been discontinued in 2 cases (2%), and none was

Table 1. Illness Course–Related Characteristics of 88 Schizophrenic Suicide Victims in Different Treatment Phases

Variable	Inpatient (N = 25) Mean ± SD	Inpatient (N = 25) Median	Recent Discharge (≤ 3 mo) (N = 28) Mean ± SD	Recent Discharge (≤ 3 mo) (N = 28) Median	Other (N = 35) Mean ± SD	Other (N = 35) Median	Median Test p Value
Age (y)	38.6 ± 15.1	33.0	35.8 ± 10.5	34.0	44.1 ± 12.7	39.0	NS
No. of hospitalizations/illness duration	0.73 ± 0.80	0.43	1.1 ± 0.73	1.0	0.34 ± 0.27	0.27[b]	.0001[c]
Duration of last hospital treatment, d	1267 ± 2769	62.0	139 ± 551	24.0	108 ± 227	51.5[b]	.0067[d]

[a]Abbreviation: NS = not significant.
[b]N = 34; 1 suicide victim had not been hospitalized during her lifetime.
[c]Median = 0.429; $\chi^2 = 20.2$, df = 2; median for all suicide victims in different treatment settings.
[d]Median = 46; $\chi^2 = 10$, df = 2.

Table 2. Characteristics of 88 Schizophrenic Suicide Victims in Different Treatment Phases

Variable[a]	Inpatient N = 25 (28%) N	Inpatient N = 25 (28%) %	Recent Discharge N = 28 (32%) N	Recent Discharge N = 28 (32%) %	Other N = 35 (40%) N	Other N = 35 (40%) %	χ^2	p Value (df = 2)
Active illness phase[b]	23	92	27	96	15	48	23.7	.00001
Acute exacerbation[c]	14	56	12	43	9	28	4.6	NS
Positive symptoms[d]	21	84	20	83	11	44	12.5	.002
Paranoid subtype	3	12	16	57	11	31	12.2	.0023
Depressive symptoms[e]	20	80	16	62	16	53	4.3	NS
Alcoholism	1	4	10	36	8	23	7.9	.02
Suicide attempts during last year[f]	9	36	16	59	6	17	11.8	.0028
Suicidality during the last 3 months[g]	15	60	20	74	7	23	16.6	.00025
Compulsory final hospital treatment[h]	17	68	12	43	11	33	7.1	.029
Negative attitude toward final hospital treatment[i]	17	81	11	50	11	44	7.1	.029

[a]Lower total Ns in some groups due to missing data.
[b]Other outpatients N = 31.
[c]Other outpatients N = 32.
[d]Recent discharge N = 24, other outpatients N = 25.
[e]Recent discharge N = 26, other outpatients N = 30.
[f]Recent discharge N = 27.
[g]Recent discharge N = 27, other outpatients N = 31.
[h]Other outpatients N = 33.
[i]Hospital N = 21, recent discharge N = 22, other outpatients N = 25.

prescribed at all in 1 (1%) at the time of suicide. The mean dose of neuroleptic medication in chlorpromazine equivalents was 512 mg (median ± SD = 380 ± 506 mg; range, 25–2829 mg). Combinations of more than one antipsychotic were prescribed to 49 (56%) of 88 patients, and injectable depot antipsychotics to 26 (30%) of 88.

During the active illness phase, about half (54%) of the victims had received neuroleptics of 300 mg or more of CPZe (Table 3). Two (3%) of 65 victims received no neuroleptic medication at all in the active phase. The neuroleptic treatment prescribed during the active illness phase was more adequate, but not significantly, among hospitalized and recently discharged victims than other outpatients ($\chi^2 = 4.9$, df = 2, p = .08; see Table 3). A classification of neuroleptic nonresponder was given to 16 (18%) of 88. Among inpatients, almost half (11/25; 44%) were classified as neuroleptic nonresponders at the time of suicide. Inpatient nonresponders had stayed an average of 857 days (median = 189; range, 38–4756 days) in the hospital before suicide. Among nonresponders, 10 (63%) of 16 were receiving adjunctive anxiolytic drug treatment at the time of suicide, but none of the 88 suicide victims were receiving clozapine or lithium.

The proportion of drug noncompliers was 24 (31%) of 78 at the time of suicide, and the proportion of appointment noncompliers was 18 (23%) of 78. There was complete cessation of prescribed neuroleptic medication in 29% (7/24) of drug-noncompliant victims. In the logistic regression model, drug noncompliance was associated only with alcoholism (Wald $\chi^2 = 3.9$, df = 1, p = .049; OR = 3.0; 95% CI, 1.0 to 9.0).

Antidepressants (2 victims with sulpiride, 50 and 100 mg[60]; 4 with tricyclic antidepressants ranging from 25 mg to 75 mg; 1 with doxepin, 200 mg; 1 with trazodone, 150 mg; 1 with mianserin, 60 mg; and 1 with maprotiline, unknown dosage) were prescribed for 13% (11/88), of whom the majority (8/11; 73%) also suffered currently before suicide from active schizophrenia symptoms. Among all suicide victims, only 3 of 9 schizophrenic patients with depressive disorder in clinically stable (over 6 months since previous hospitalization) residual illness phase were currently receiving antidepressive medication (amitriptyline, 25 mg; clomipramine, 50 mg; maprotiline, unknown dosage). Overall, the prescribed antidepressant medication was inadequate. None of the 88 suicide victims had received electroconvulsive therapy (ECT) during the 3 months before suicide.

Table 3. Characteristics Related to Psychopharmacologic Treatment in Different Illnesses

	Active Phase (N = 65)		Residual Phase (N = 18)		Total (N = 83[b])	
Variable[a]	N	%	N	%	N	%
Adequate antipsychotic treatment[c]						
All victims	35	54	14	78	49	59
Inpatient (N = 25)[d]	16	70	2	100		
Recent discharge (N = 28)[e]	14	52	1	100		
Other (N = 35)[f]	5	33	11	73		
Compliance with treatment						
Drug noncompliance[g]	17	28	6	38	24	32
Adequate dose + drug compliance[h]	26	43	8	53	34	45
Compliant nonresponders[i]	14	23	0	0	14	18

[a]Lower total Ns in some groups due to missing data.
[b]The exact dosage of neuroleptics was not known for 1 victim in residual illness phase (1/19); illness phase for 4 other patients was not defined.
[c]Adequate antipsychotic treatment: active phase ≥ 300 mg of chlorpromazine equivalents (CPZe); residual phase ≥ 100 mg of CPZe.
[d]Active phase N = 23, residual phase N = 2.
[e]Active phase N = 27, residual phase N = 1.
[f]Active phase N = 15, residual phase N = 15.
[g]Active phase N = 60, residual phase N = 16.
[h]Active phase N = 60, residual phase N = 15.
[i]Active phase N = 60.

DISCUSSION

We found that schizophrenic suicide victims in different treatment phases differed significantly in their current clinical and treatment-related characteristics. Recently discharged victims were found to have a significant clustering of known risk factors for suicide. Fifty-seven percent of schizophrenic suicide victims in the active illness phase either were not prescribed adequate neuroleptic treatment or were not using it, and a further 23% were estimated to be compliant nonresponders.

The present study shares the methodologic limitations of other psychological autopsy studies: possible informant and interviewer biases, and unequal levels of information about the suicide victims.[50] The proportion of interviewed next of kin was smaller among inpatients than others, but the rates of interviewed health care professionals were similar in all treatment phases. Thus, no major bias is likely in the treatment- or psychopathology-related variables. The interview-based data collection, including information on the victim's mental state even close to the time of suicide, is a strength of our study. It allowed us to examine the adequacy of antipsychotic treatment according to the current psychopathology, in contrast to the majority of previous studies on suicides involving patients with schizophrenia based only on patient records.

The use of chlorpromazine equivalents for evaluating adequacy of antipsychotic treatment in schizophrenia is compromised by the well-known problems in defining the concept of drug equivalence.[61] The concept of compliance in our study was based on clinician interviews, which reportedly underestimate the magnitude of noncompliance.[36] However, it is not known whether this underestimation occurs in interviews of clinicians whose patients have committed suicide. The use of negative results from toxicologic analyses in classifying noncompliance among non–drug overdose suicides creates uneven information among the suicide victims, but it does increase the overall level of information. The classification of nonresponder in our study also differed from the strict classification used in the clozapine trial study for neuroleptic resistance,[62] being closer to broader definitions of treatment refractoriness.[63] Our classification was a cross-sectional estimate without the possibility of longitudinal evaluation in the quantity of symptoms. Moreover, our concept of nonresponder represents an underestimate, since it was used only if the current chlorpromazine equivalent dose was 700 mg or more, thus definitely eliminating the victims for whom adequate dosing had been prescribed previously without effect or the ones who had not yet been prescribed sufficient neuroleptic dose for maximum effect. As we were focusing on the pharmacologic treatment before suicide, we are not able to estimate the role of other, possibly important, nonpharmacologic treatments in drug response and in the suicide.

The classification of positive and negative symptoms is compromised by the cross-sectional nature of this study and does not allow conclusions regarding positive and negative types of schizophrenia. The concurrent proportion of negative symptoms among schizophrenic suicide victims may be inflated by the high rate of partly overlapping depressive symptoms. Our classification of suicidality is likely to be sensitive to any type of suicidal behavior, including acts of self-harm, rather than those with exact specificity to high suicidal intention. Lastly, the lack of a control group of living patients with schizophrenia precludes the possibility of using our results for estimating the magnitude of specific risk factors for suicide in different treatment phases of schizophrenia and the role of undertreatment of psychotic symptoms in suicide.

We found that an average of 512 mg of CPZe was prescribed for our schizophrenic suicide victims, which falls in the range of previously reported chlorpromazine equivalents (183 to 688 mg of CPZe) among suicide victims with schizophrenia.[12,32–34] However, despite the adequate average amount of the prescribed neuroleptics, only about a half (54%) of all suicide victims in the active illness phase were prescribed adequate antipsychotic

treatment according to the modest requirement of 300 mg of CPZe in our study. Further, the figure of 43% for the proportion of actively ill victims with adequate treatment who had actually taken the prescribed treatment is probably an overestimation. Since most suicides (78%) occurred during the active illness phase, we suggest that pharmacologic undertreatment of psychotic symptoms may be a serious problem in the management of suicidal schizophrenics.

One third of our suicide victims were assessed as drug noncompliant. Noncompliance was associated with alcoholism, as previously reported among living patients,[35,57] but not with other factors known to associate with both suicide and noncompliance in schizophrenia, such as negative attitude toward treatment during hospitalization, paranoid subtype, depressive syndrome, or acute exacerbations of illness. Noncompliance may not be a specific character of suicidal patients with schizophrenia, but it certainly plays an important role in schizophrenic relapse,[37] often leading to a cycle of hospital admissions and discharges, treatment phases of high suicide risk.

The majority (61%) of suicide victims in our sample suffered from both positive and negative symptoms simultaneously. In our sample, recent suicidality was strongly associated with the presence of current positive, but not negative, symptoms. This supports the findings by Fenton and colleagues,[43,64] who suggested that suicide may be more often connected with prominent positive symptoms and that among patients with only prominent negative symptoms, the suicide risk may be low. Positive symptoms are considered to respond better to antipsychotic treatment than negative symptoms,[46] emphasizing the importance of treatment of active psychotic symptoms among suicidal schizophrenic patients.

Meltzer and Okayli[65] suggest that neuroleptic-resistant patients with schizophrenia who suffer from persistent and severe positive and negative symptoms of schizophrenia, and may thus feel hopeless, have a particularly high risk for suicide. They reported that among neuroleptic-resistant patients, clozapine treatment decreased suicidality.[65] In our study, a considerable proportion of suicides occurred in the hospital among a subgroup of severely and chronically ill patients with recent suicidality. Further, we found that 44% of inpatient suicide victims were nonresponders to typical neuroleptics. However, none of the suicide victims had been prescribed clozapine before suicide. During the same period in Finland, about 1150 patients were using clozapine, as derived from defined daily dose values and approximations of the average usage time per year per patient (E. Palva, M.D., oral communication, April 1997) among the roughly 50,000 patients who had a diagnosis of schizophrenia. Lithium is also recommended for augmenting the efficacy of antipsychotic drugs in the treatment of positive symptoms among patients with schizophrenia,[66] but it was not prescribed for any of the suicide victims in our study. For suicide prevention in psychiatric hospitals, the treatment of severely ill and recently suicidal schizophrenic patients needs further study, but the use of alternative and augmenting treatment options, when typical neuroleptics in adequate dosages do not yield good response, is to be encouraged on the basis of our findings.

Unfortunately, we were not able to reliably examine the issue of neuroleptic side effects in our suicide sample due to lack of structured data on possible side effects, especially akathisia. According to all available information on the suicide victims, there were no spontaneous reports of current neuroleptic side effects. Akathisia is associated with higher neuroleptic doses in about 24% of patient samples,[67] but in our sample, the majority tended to be undertreated with neuroleptics or noncompliant, rather than receiving high doses of neuroleptics. This finding suggests that neuroleptic side effects are not a major factor in suicides among patients with schizophrenia, although they may play an important role in occasional cases.

Depression among patients with schizophrenia is common during the longitudinal course of schizophrenia, noted to be varyingly present depending on the diagnostic methods and patient samples in approximately 25% of cases and to be associated with functional impairment, morbidity, and mortality.[29] There is evidence that tricyclic antidepressants can be effective when used in conjunction with neuroleptic medication after the acute phase has resolved.[29,57] However, in our sample, only 3 of 9 depressive victims in a stable illness phase (after half a year since hospital discharge) were on antidepressive treatment at the time of suicide. Besides, the doses of prescribed antidepressants were often inadequate. The rates of the antidepressants' use have varied (12%, 47%) in previous studies,[13,33] but it is difficult to compare the treatment standards, because these studies did not report the antidepressant usage among stabilized depressive schizophrenic patients. Depressive symptoms are an important risk factor for suicide in schizophrenia,[25] but there is a lack of knowledge about the role of antidepressant treatment in suicide prevention among depressive patients with schizophrenia.

We found recently discharged schizophrenic patients to differ from others in having more suicide risk factors such as paranoid symptoms, alcoholism, and suicide attempts during their last year. Among all psychiatric patients, alcoholism has also been associated with higher suicide risk

during recent discharge than during inpatient care.[68] Unexpectedly, all suicide victims with schizophrenia in different treatment phases were similar in the proportions of depressive symptoms. Further, recently discharged victims with schizophrenia had the highest number of hospitalizations per year during their illness duration and the shortest median duration of last hospital treatment. Unfortunately, our data do not allow us to reliably estimate the total time spent in hospital during the whole illness or the exact rate of hospitalizations per year. However, this may imply that the revolving door syndrome in suicides involving schizophrenic patients may be associated with the recent discharge period. This is in line with the finding of a recent study by Rossau and Mortensen[52] that revolving door admission patterns are associated with increased suicide risk in schizophrenia. Attitudes of inpatient suicide victims toward treatment were more often negative or indifferent, and inpatients were more often treated against their will, which is similar to previous reports.[17] The disparities which emerged in this study between schizophrenic suicide victims in different treatment phases suggest the possibility of varying suicide risk among distinct subgroups of schizophrenic patients in different treatment phases. Furthermore, these disparities may suggest that longer hospital treatment could offer some protection against suicide among younger subjects who face revolving door admission patterns and other known suicide risk factors. However, these issues need to be further studied with a controlled study design. For suicide prevention, these findings imply that when discharge is planned, suicidality should be assessed carefully.

CONCLUSIONS

Most victims in high suicide risk periods of psychiatric hospitalization and recent discharge are, compared with the remainder, characterized by active illness phase, current prominent positive schizophrenia symptoms, and recently recorded suicidality. A substantial proportion of suicide victims with schizophrenia are not receiving adequate antipsychotic medication, are noncompliant, or do not respond to adequate antipsychotic medication. These findings suggest the need for better psychopharmacologic treatment of schizophrenia, especially in the active illness phase.

Inpatient suicide victims had the highest proportion of negative or indifferent treatment attitudes, whereas recently discharged suicide victims had the highest prevalence of comorbid alcoholism, paranoid subtype, and recent suicidality as well as the highest number of hospitalizations per year during their illness course and the shortest last hospitalization. These findings suggest that suicide risk factors may vary in different treatment phases among patients with schizophrenia and need to be studied further.

Drug names: amitriptyline (Elavil and others), chlorpromazine (Thorazine and others), clomipramine (Anafranil), clozapine (Clozaril), doxepin (Sinequan and others), maprotiline (Ludiomil), trazodone (Desyrel).

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The following agents mentioned in this article are not indicated for these respective uses: melperone as an antipsychotic, mianserin as an antidepressant, pericyazine as an antipsychotic, remoxipride as an antipsychotic for schizophrenia, sulpiride as an antipsychotic, and zuclopenthixol as an antipsychotic.

Instructions

Psychiatrists may receive 1 hour of Category 1 credit toward the American Medical Association Physician's Recognition Award by reading the article starting on page 200 and correctly answering at least 70% of the questions in the posttest that follows.

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1. Which patients form the largest group who commit suicide most commonly during psychiatric inpatient treatment?
a. Patients with major depression
b. Patients with bipolar disorder
c. Patients with schizophrenia
d. Patients with borderline personality disorders
e. Patients with alcoholism

2. When is the highest risk for suicide during the treatment of psychiatric patients?
a. At admission to hospital treatment
b. At the end of inpatient treatment
c. During the recent discharge (0–3 months) from hospital treatment
d. After 6 months of hospital treatment
e. None of the above

3. Which of the factors listed below has not been associated with a high risk of suicide among patients with schizophrenia?
a. Depressive symptoms
b. Negative symptoms
c. Negative attitude toward treatment
d. Paranoid symptoms
e. Positive symptoms

4. What is an adequate antipsychotic medication dosage (CPZe) in the active illness phase schizophrenia according to current opinion?
a. 100–300 mg of CPZe
b. 300–600 mg of CPZe
c. 500–900 mg of CPZe
d. 700–1200 mg of CPZe
e. ≥ 800 mg of CPZe

5. Which statement is not correct according to current knowledge for antipsychotic treatment and suggestions for suicide prevention in schizophrenia?
a. Clozapine treatment for neuroleptic-resistant patients with schizophrenia decreases suicidal behavior.
b. Suicide victims with schizophrenia have usually received too high a dose of neuroleptics.
c. Depression among patients with schizophrenia should be treated actively.
d. Suicide victims with schizophrenia are characterized by active illness phase, and thus pharmacologic undertreatment may be a serious problem among suicidal patients with schizophrenia.
e. Neuroleptic side effects may increase suicidality among patients with schizophrenia.

6. Drug noncompliance among patients with schizophrenia is associated with:
a. Alcoholism
b. Negative attitude toward treatment
c. High level of positive schizophrenia symptoms
d. Paranoid symptoms
e. All of the above

7. Which of the following statements is true with regard to suicide in patients with schizophrenia?
a. Inadequate treatment dosages of neuroleptics during the active illness phase
b. "Revolving door admission patterns"
c. Recent discharge from psychiatric hospital
d. Depressive symptoms
e. All of the above

Answers to the September 1998 CME posttest

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   B. Enabled me to examine the clinical characteristics and adequacy of antipsychotic treatment in different phases of illness among suicide victims with schizophrenia. ❑ Yes ❑ No
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