Suicide risk in schizophrenia – a follow-up study after 20 years

Part 2: Symptomatology and pharmacotherapy

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Objective. This study followed up, after a period of 20 years, a group of patients with schizophrenia who were considered to be at high risk for suicide. In Part 1 we reported on outcome and associated social factors, and in this paper we discuss re-evaluated suicide risk in these patients and investigate symptomatology and pharmacotherapy over the past two decades.

Method. The subjects were interviewed and a questionnaire evaluating suicide risk was completed. The Beck Hopelessness Scale (BHS) was administered and ratings were compared with those from the original study. The Calgary Depression Scale for Schizophrenia (CDSS) was also administered. Cross-tabulations were then performed to identify factors associated with increased suicide risk. For those subjects who had committed suicide since the original study, a psychological autopsy was performed.

Results. Fourteen of the original 33 high-suicide-risk schizophrenia patients were traced. Three subjects had committed suicide during the 20-year period. Among the living subjects, risks for suicide were found to be lower than those 20 years ago. Hopelessness and depressive symptoms correlated with independently evaluated suicide risk. Social withdrawal, blunting of affect and delusions were also associated with elevated risk. Good insight into illness and a history of previous suicide attempts coincided with high suicide risk. Cannabis abuse and poor or periodic adherence to treatment, as well as weight gain, akathisia and parkinsonian adverse effects, were also associated with an increase in risk of suicide. Formal thought disorder, avolition and cognitive impairment were associated with a lower risk of suicide.

Conclusion. Hopelessness, depression, certain positive symptoms and adverse effects of medication found to be associated with suicide risk in patients with schizophrenia in this study are in accord with those reported in the literature. Despite current knowledge about this subject, suicide remains notoriously and ominously unpredictable in patients with schizophrenia.

Despite extensive research into the symptoms of schizophrenia that may be associated with an increased risk of suicide, and the search for and implementation of more effective treatment interventions for schizophrenia, rates of completed suicide have increased in the modern era.[1] Suicide rates of 0.5% between 1875 and 19241 and 3% between 1947 and 1960[2] have been reported. These pre-chlorpromazine-era suicide rates for patients with schizophrenia are significantly lower than those reported in recent studies. Possible reasons for this increase that have been suggested include: (*i*) the drive towards deinstitutionalisation, leading to shorter periods of hospitalisation; (*ii*) less time available to the clinician to establish a rapport, leading to the patient's reluctance to report suicidal thoughts; (*iii*) greater patient awareness of the impairments, course and prognosis of schizophrenia; (*iv*) psychopharmacology creating the opportunity for restored insight after a psychotic episode; and (*v*) adverse effects of antipsychotics (especially parkinsonian adverse effects and akathisia).[1]

In this paper we report on the current suicide risk in the study cohort and its association with the following factors: (*i*) the course of depressive and psychotic symptomatology; (*ii*) psychiatric pharmacotherapy – adverse effects of and compliance with pharmacotherapy and its influence on symptomatology; and (*iii*) the effect of cannabis abuse and insight into illness.

Method

The previous paper described the details of the methodology of this study.

As part of evaluation of the symptomatology and treatment, the Calgary Depression Scale for Schizophrenia (CDSS)[3] and the Beck Hopelessness Scale (BHS)[4] were administered.

The severity of psychotic symptoms was evaluated using the Positive and Negative Symptom Scale for Schizophrenia (PANSS),[5] which was adapted for this study. The complete PANSS was not performed, as parts of the scale require personal observation, and it was anticipated that many of our consultations would be telephonic.

Previous and current psychiatric pharmacotherapy, treatment response, adverse effects and adherence to treatment were investigated by means of a questionnaire, after clinical interviews and perusal of patient records.

Results

Psychotic symptomatology

Delusions

Of the 10 living subjects, 7 currently suffer from delusions, 4 of them to a severe degree. Five of these individuals have frequently experienced severe delusions over the past two decades. All of the 3 subjects who committed suicide had frequently been experiencing severe delusions before and at the time of suicide.

Of all 14 subjects, only 3 had total remission of their delusions on treatment, all of whom are still alive. Three subjects showed no response to treatment, and 2 of these committed suicide. The remainder had partial remission on antipsychotics and showed higher CDSS scores than those who obtained complete remission (means 10.67 v. 3; standard deviations (SD) 6.77 and 3.61). The BHS scores showed a similar pattern (means 8.83 v. 3.33; SD 6.40 and 4.16).

The BHS scores were significantly higher in subjects who had suffered from mild delusions over the past two decades compared with those with moderate to severe delusional severity (means 1 v. 9.67 and 6.60; SD 1.41 v. 6.03 and 6.47). The CDSS scores showed a similar pattern (means 2.50 v. 13.67 and 5.80; SD 0.71 v. 4.73 and 6.77).

Current persecutory, referential and nihilistic delusions tended to coincide with increased hopelessness as shown by the BHS scores. Frequent persecutory delusions predicted more hopelessness, depression and suicide attempts. Predictably, subjects with current nihilistic delusions had vastly higher CDSS scores than those without (means 18 v. 4.88; SD 1.41 and 4.29).

Hallucinations

Eight of the 10 living subjects currently experience hallucinations and have done so over the past two decades, and 5 of these are afflicted to a severe degree. Hallucinations were also present before and at the time of death in 2 of the 3 victims of suicide, and were only partially responsive to treatment. Of the 8 living subjects who suffered from hallucinations, only 3 achieved complete remission on treatment.

The BHS and CDSS scores showed a slight increase with hallucinatory severity and a decrease with treatment response. In keeping with this trend, both auditory and visual hallucinations increased both hopelessness and depression, where auditory hallucinations tended to have a greater impact on hopelessness and visual hallucinations on depression.

Formal thought disorder

Half of the sample interviewed displayed formal thought disorder. These symptoms tended to be chronic, and at various stages showed some response to treatment in 7 of the subjects.

Subjects without formal thought disorder scored higher on the BHS (mean 9; SD 7.14) compared with those mildly (mean 3.33; SD 4.16) and severely (mean 4.5; SD 4.95) afflicted. This finding was echoed in the CDSS scores, which showed a mean of 11.6 (SD 7.44) for those without symptoms and 3.4 (SD 2.07) for the affected individuals. Supporting data were provided by the high numbers of lifetime suicide attempts among subjects without thought disorder. This trend is further supported by the data on treatment response, where complete remission was associated with higher levels of hopelessness (BHS mean 7.25 v. 4.5; SD 6.90 and 4.95) and depression (CDSS mean 10.25 v. 3.4; SD 7.85 and 2.07) and with more frequent suicide attempts than in subjects who experienced no response to treatment.

Negative symptoms

All the subjects in the study were found to have at least one negative symptom. The presence of blunted affect and social withdrawal coincided with increased BHS and CDSS scores. The converse is true for avolition and cognitive impairment. Absence of cognitive impairment was also found in the 3 individuals who had the most lifetime suicide attempts and in all 3 who committed suicide.

Depressive symptomatology

The mean CDSS score for this study was 7.5 (SD 6.72), with the lowest score being 0 and the highest 19. Half of our subjects obtained a score above the critical cut-off of 6, indicating an 85% probability of the presence of a major depressive episode. All the subjects had had depressive symptoms during the past two decades, of which half were of severe intensity. These symptoms were of a chronic nature in half of the subjects.

In response to antidepressant medication, 4 subjects demonstrated a partial response and 2 achieved total remission. The 3 subjects who took their own lives all experienced severe depressive symptoms. Two of these showed no response to antidepressant therapy, while the other only achieved partial remission.

Unsurprisingly, the BHS scores increased with depression severity and decreased with responsiveness to treatment. The mean score for those with total remission of depressive symptoms was 0.5 (SD 0.71), compared with 11.25 (SD 5.85) for those who achieved only partial remission.

As expected, chronic severe depressive symptoms and antidepressant resistance were found to be associated with more frequent suicide attempts.

Anxiety symptoms

Half of the subjects reported experiencing anxiety symptoms during the course of their illness. Severe anxiety symptoms were known to plague one of the suicide victims.

Insight into illness

One of the major difficulties in the treatment of schizophrenia was highlighted by the fact that only 3 subjects currently showed good insight into their illness. Five had partial insight and 2 no insight whatsoever. The BHS scores increased proportionally with the amount of insight, with a mean of 4 (SD 5.66) among those without insight versus 8.67 (SD 7.02) for those with good insight. Two of the 3 subjects who committed suicide had no insight into their condition.

Cannabis use

Seven of the subjects interviewed denied cannabis use during the preceding 20 years and 3 admitted to occasional use, with 2 of these having a history of frequent suicide attempts. Among those who committed suicide, one occasionally and one habitually abused cannabis. Increased use of cannabis coincided with increased current suicide risk and higher scores on both the BHS (mean no use 5.43 v. occasional use 8.67; SD 5.74 and 7.51) and the CDSS (mean no use 6 v. occasional use 11; SD 5.89 and 8.54).

Psychopharmacology

Antipsychotics

Current psychopharmacology, or psychopharmacology at time of death, was evaluated according to the following drug categories: typical antipsychotics, atypical antipsychotics, and depot preparations. The following findings are of interest:

1. Both subjects on trifluoperazine and all 4 subjects on fluphenazine depot had no risk of suicide at the time of evaluation. Furthermore, the BHS and CDSS scores for subjects on both these drugs were lower than the scores for those who were not.

2. The 4 subjects on flupentixol depot had higher mean BHS (8.25 v. 5.17; SD 6.55 and 6.01) and CDSS (8.75 v. 6.67; SD 6.95 and 7.09) scores than those who were not.

3. The 7 subjects on haloperidol oral treatment had higher mean scores on both the BHS (8 v. 6; SD 11.31 and 5.32) and the CDSS (9.5 v. 7; SD 13.44 and 5.56) than those who were not.

4. The only subject currently on clozapine presented with suicidal ideation. None of the 3 subjects who had committed suicide had been on clozapine at the time.

Antidepressants

The antidepressants most commonly used by our study subjects were selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TADs). Five of the subjects were on an antidepressant at the time of evaluation or of their death. In these 5 subjects there is no evidence that the use of antidepressants was associated with a decrease in suicide risk, hopelessness or depressive symptomatology. In fact, the 2 subjects on fluoxetine had higher scores on the CDSS (means 11 v. 6.63; SD 1.41 and 7.31) than those who were not.

Lithium

Only one of the subjects interviewed was on lithium, and was found to be free of suicide risk. Two had used it during the preceding 20 years and attempted suicide less frequently than the rest. None of the deceased subjects had used lithium prior to their deaths.

Benzodiazepines

Both the BHS and CDSS scores were slightly higher for those subjects currently on benzodiazepines than for those who were not.

Adverse effects of medication

Eight of the 10 living subjects experienced one or more adverse effects of medication. All 4 deemed to be at risk of suicide had adverse effects. All 3 of the subjects who had committed suicide were known to have had adverse effects at the times of their deaths. Furthermore, the presence of adverse effects coincided with a higher number of suicide attempts during the 20-year follow-up period, as well as with higher BHS scores (means 7.75 v. 1; SD 6.07 and 1.41) and CDSS scores (means 8.75 v. 2.5; SD 7.01 and 0.71).

The most commonly experienced adverse effects were, in descending order, parkinsonism, sedation, akathisia and weight gain.

Weight gain proved to be a notable risk factor for suicide, as demonstrated by the higher BHS scores in those who experienced this adverse effect (means 13.67 v. 3.29; SD 4.04 and 3.5). The CDSS scores confirmed this finding (means 16 v. 3.86; SD 3.61 and 3.44). Weight gain was not only associated with increased current suicide risk, but also with the number of prior suicide attempts.

Those subjects currently experiencing akathisia were found to have attempted suicide more often and had higher mean BHS (10.25 v. 3.83; SD 7.23 and 3.92) and CDSS (10.25 v. 5.67; SD 9 and 4.76) scores than those who did not experience this adverse effect.

All 3 of the subjects who committed suicide experienced parkinsonian adverse effects. In the living subjects the mean BHS (8.2 v. 4.6; SD 7.76 and 3.85) and CDSS (9 v. 6; SD 8.63 and 4.64) scores were higher in those who exhibited parkinsonism than in those who did not.

Sedation did not significantly add to suicide risk.

Treatment adherence

Two-thirds of the subjects who committed suicide had poor adherence to their prescribed treatment. Among the living subjects, periodic adherence was associated with a higher risk of suicide than good adherence. This was further supported by the fact that the BHS scores for subjects with periodic adherence were higher than the subjects with good treatment adherence (means 8.25 v. 4.6; SD 6.55 and 6.54). The CDSS scores showed a similar trend (means 8.5 v. 6.8; SD 8.66 and 6.61).

Discussion

Psychotic symptoms were found to contribute to suicide risk in our subjects. Those who experienced delusions were at higher risk and delusional severity was found to be proportionate to suicide risk. Delusions of persecution, reference and nihilism can all lead to negative emotional states, and subjects who experienced these delusions were found to be at high risk of suicide. According to the literature, the paranoid subtype of schizophrenia carries a higher risk of suicide.[6]

Resistance of delusional symptoms to medication was common and associated with higher suicide risk. Delusions can contribute to poor treatment adherence and therefore to treatment resistance. Hallucinatory symptoms were also found to be somewhat resistant to treatment. Severity of hallucinations was less convincingly associated with suicide risk than severity of delusions.

The presence of formal thought disorder coincided with a lower suicide risk in this sample. Disordered thought was associated with lower BHS and CDSS scores, both of which increased in response to treatment of the thought disorder. Subjects without formal thought disorder had much higher levels of depression and hopelessness and attempted suicide more frequently. It is possible that the presence of formal thought disorder shields patients against the realisation of the implications of their illness.

Contrary to some of the literature on the subject,[7] the presence of negative symptoms per se was not found to be associated with decreased suicide risk. This was only found to be true of two specific negative symptoms, avolition and cognitive impairment, which were, incidentally, absent in all 3 patients who committed suicide.

Blunting of affect and social withdrawal were, in fact, associated with increased suicide risk. The diminished motivation of avolition could, for example, lead to a decreased suicidal drive while social withdrawal could lead to loneliness and demoralisation, increasing the risk of suicide.

The findings in this study underline the fact that depressive symptoms are common in schizophrenia, and some even consider them to be part of the symptom dimensions of the illness.[8] The presence of a depressed mood is known to increase suicide risk in this population,[9-11] and it is noteworthy that all the subjects in

the study had suffered from depressive symptoms over the past 20 years. Half of these subjects still experience severe depressive symptoms that are resistant to treatment.

Half of the subjects experienced anxiety symptoms. These symptoms were not investigated in great detail in this study. For the prevalence of anxiety symptoms in schizophrenia, the co-morbidity of the various anxiety disorders and the possible relationship between anxiety and depressive symptoms in this population, the reader is referred to some existing literature on the subject.[12-19]

Insight into the illness remains a problem in patients with schizophrenia. This was also found in the current study, in which increasing amounts of insight caused increased levels of hopelessness. Insight gained therapeutically, according to the International Suicide Prevention Trial (InterSePT), does not increase suicidal ideation but, paradoxically, decreases it.[20]

A history of cannabis abuse was found in half of the subjects. This is a substantial increase from the prevalence among the same subjects 20 years ago, when only 3% abused cannabis.[21] Abuse of cannabis was found to coincide with both higher current suicide risk and frequency of suicide attempts, as well as depressive symptoms and feelings of hopelessness. Increased abuse of cannabis may be due to the increased need to self-medicate as negative and depressive symptoms associated with schizophrenia increase in severity during the course of the illness. The increase in suicide risk and suicidal behaviour may be due to more frequent and severe psychotic symptoms secondary to cannabis abuse.

In evaluating the previous and current pharmacotherapy of the 14 subjects in this study, it was found that the medications prescribed varied greatly, which made it difficult to generalise and draw conclusions about the possible effects of individual medications on suicidality and various symptoms experienced by the subjects.

Wilkinson and Bacon found a lower likelihood of suicide attempts in patients receiving antipsychotic drugs, although the rates did not markedly differ between different drugs.[22]

Of note is that all the subjects currently on the antipsychotic trifluoperazine, and those on fluphenazine depot, were found to be at low suicide risk and had low BHS and CDSS scores. These medications were prescribed more frequently a couple of decades ago. The symptoms of these subjects might have been relatively well controlled on these drugs, resulting in their continued prescription and an accompanying decrease in suicide risk. This finding was in contrast to that for flupentixol depot, which was unexpectedly found to be associated with higher BHS and CDSS scores. Similarly, subjects currently on oral haloperidol were also found to experience more severe depressive symptoms and feelings of hopelessness. This may be due to dysphoria, a known adverse effect of haloperidol.

The InterSePT study highlighted the efficacy of clozapine in reducing suicide rates.[23]

It is interesting that none of the 3 subjects in our study who committed suicide was taking clozapine at the time of their suicide. Five subjects had previously been on clozapine, including one who subsequently committed suicide. The reason for discontinuation of the drug in each case was not determined. The only subject currently on clozapine was found to be at high risk for suicide, presenting with suicidal ideation, which is probably why the drug was prescribed. Nevertheless, it is surprising that so few subjects have had a trial of or are currently on clozapine, not only because of their increased risk of suicide, but also because many of the subjects were found to be treatment resistant, and clozapine is a drug used for the treatment of treatment-resistant schizophrenia.

Notwithstanding lithium's effect of reducing suicidal behaviour and all-cause mortality in mood disorders,[24] evidence for its efficacy in psychotic disorders (alone or in combination with an antipsychotic) is either weak or absent, even though it appears to have some benefit in schizo-affective disorder.[25] With this in mind, it is interesting to note that only 3 subjects in the study had ever been prescribed lithium, and that none of these had committed suicide.

Regarding the concomitant use of antidepressants, imipramine might be useful,[26] but SSRIs have yielded mixed results.[27] Consistent with literature on the subject, antidepressants were not found to consistently reduce depressive symptoms[25] or hopelessness, and did not decrease suicide risk. Current protocol suggests that antidepressants should only be prescribed for patients with schizophrenia whose depressive symptoms do not respond to an atypical antipsychotic.[25]

Adverse effects of medication were common among the study subjects, particularly in those with higher suicide risk, BHS and CDSS scores, and those who attempted suicide more frequently during the 20-year follow-up period. All 3 subjects who committed suicide experienced adverse effects on their medication.

The importance of avoiding parkinsonian adverse effects is demonstrated by the American Psychiatric Association's practice guidelines recommending that in individuals with suicidal

behaviour the use of first-generation antipsychotics be reserved for those needing depot preparations.[1,28] In line with these findings, the presence of akathisia, as well as parkinsonism, was associated with an increased risk of suicide among the subjects interviewed.

In this study it was found that weight gain was also a notable risk factor for suicide. This has important implications for schizophrenia sufferers, who are increasingly being treated with atypical antipsychotics that are associated with weight gain and metabolic syndrome.[29]

There is as yet no literature addressing the value of cognitive behavioural therapy (CBT) for suicidality in schizophrenia.[30] CBT and other psychosocial interventions have, however, established efficacy in improving adherence and alleviating depression and hopelessness.[25]

As predicted, and in line with findings in the literature,[31] poor as well as periodic adherence to treatment was associated with an increased risk of suicide among the subjects.

The major limitation of this study is its small sample size of 14 subjects, resulting from the difficulty in finding a known group of subjects 20 years after initial evaluation. However, small sample sizes are not uncommon among prospective studies investigating suicide in schizophrenia. In one of the few prospective studies on the subject, found and reviewed by Hawton *et al.*,[32] Cohen *et al.*[33] prospectively followed up only 8 patients. The small sample size limits the use of statistical processing of data and causes the captured data usually not to reach statistical significance. Tendencies and associations could be identified, but sometimes with difficulty because of the small sample size. Another limitation is that because so many symptoms were being evaluated, not all of them could be measured using rating scales. Furthermore, the method of psychological autopsy is of necessity retrospective and, therefore, introduces recall bias.

One of the strengths of our study, like that of Cohen *et al.*,[33] is that relevant data were also retrospectively collected for the period of time between evaluations, which enabled fluctuations in symptoms and suicide risk to be captured. This method differs from that used in many prospective studies that capture data and evaluate subjects initially and then again only after a certain period of time when the subjects are followed up. Another strength of the current study is the 20-year period over which the data were collected. Few studies follow patients up over such a long period of time. Casadebaig and Philippe,[34] for instance, in another study reviewed by Hawton *et al.*,[32] followed patients up prospectively after a period of only 3 years. In our study, a questionnaire was also designed to evaluate suicide risk and capture all relevant data that may contribute to the risk, resulting in a vast number of factors that could influence suicide risk being evaluated.

Conclusion

Blunting of affect, social withdrawal, depressive symptoms, feelings of hopelessness and the presence of severe delusions were associated with an elevated suicide risk. Good insight into illness, previous suicide attempts, cannabis abuse, akathisia, parkinsonian adverse effects, weight gain and both poor and periodic adherence to treatment all coincided with an increased risk of suicide. These findings are mostly in keeping with the literature on the subject. Factors associated with a lower risk of suicide include formal thought disorder, avolition and cognitive impairment. Despite knowledge of the factors that influence suicide risk, however, suicide remains notoriously and ominously unpredictable among patients with schizophrenia.

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