Case-Control Study of the Relationship of Depressive Symptoms to Suicide in a Community-Based Sample of Individuals with Schizophrenia in China

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Abstract

Backgound—Suicide is the leading cause of premature death among people with schizophrenia. Most studies on suicide and schizophrenia report an associated depression history, but they are based on clinical samples from mostly western countries.

Methods—We conducted a secondary analysis of 74 suicides (cases) and 24 accidental deaths (controls) among persons with schizophrenia identified in a national psychological autopsy study in mainland China using the Chinese version of the Structured Clinical Interview for DSM-IV. A 'depression symptom severity score' based on number, severity, and persistence of depressive symptoms 2 weeks before death was derived from psychiatric interviews with 2 informants; determination of a 'dysfunction due to depressive symptoms score' was based on informants' reports about effects of depressive symptoms on decedents' functioning in the month before death. In addition, the mean number of negative life events was determined along with the effect of the events on the decedent. Comparison of the measures made for cases and controls were made by univariate analysis followed by adjustments using the False Discovery Rate.

Results—Compared to persons with schizophrenia who died by accident, those who died by suicide were more likely to have a recent DSM IV diagnosis of major depression, the symptom of depressed mood, thoughts of death and a prior suicide attempt. In addition, those who died by

suicide were more likely to have a higher overall depression severity score and greater dysfunction due to depressive symptoms.

Discussion—This community-based study of individuals with DSM-IV schizophrenia who died by suicide in a non-western culture extends findings from clinical studies in western cultures providing data on the importance of depressive symptoms as risk factors for suicide in schizophrenia in a low income rural setting. These findings underline the importance of routine screening for depressive symptoms among patients with schizophrenia.

Keywords

depression; suicide; schizophrenia; China; psychological autopsy

Introduction

Suicide is one of the causes of premature death among persons with schizophrenia. Among persons with schizophrenia 40%-50% report suicidal ideation at some point in their lives and 4%-13% eventually die by suicide (Montross et al 2005). Schwartz and Cohen (2001) found that depressive symptoms accounted for nearly 50% of the suicidal intent reported by 267 patients with schizophrenia. Fenton (2000) found that suicide in persons with schizophrenia is highly correlated with the number of depressive symptoms, and a 17-year follow-up study of 7,217 Finnish community members found that having schizophrenia with accompanying depressive symptoms is associated with elevated risks for both natural and unnatural mortality (Joukamaa et al 2001; Heila et al 1997). A review by Hawton et al (2005) reported that death by suicide among persons with schizophrenia is associated with a history of depression, symptoms of agitation or motor restlessness, worthlessness or low self esteem, hopelessness, a family history of depression and recent losses.

The relevance of these findings for low-income countries such as China remains uncertain. Ran et al reported a 4.5% 10-year risk of suicide in subjects with schizophrenia in China-- similar to the rates in western samples reported by Palmer et al (2005). Zhang and Xiao (2002) found that among 177 Chinese inpatients with schizophrenia, approximately 50% reported suicidal ideation and 16% attempted suicide. Ran and colleagues (2004) reported that the lifetime prevalence rate of suicidal ideation alone was 11% and that for suicide attempts was 27.6%. And Phillips et al (2004) reported a 0.7% annual incidence of suicide and a 24-fold relative risk for suicide (compared to the general population) among persons with schizophrenia in China.

Little is known about suicide risk factors in Chinese patients with schizophrenia. Li and colleagues (2008) found that 64 inpatients with schizophrenia who committed suicide endorsed greater depressive mood, guilt, suicidal ideation and suicide attempts compared with a randomly selected group of inpatient controls without suicidal intent or behaviors. Ran et al (2005) reported that community-based suicide attempters with schizophrenia in rural China had greater depressed mood, hopelessness, and rates of positive symptoms compared to those who did not attempt suicide. Similarly, among 74 patients with psychosis and schizophrenia in a rural community, suicide attempts were significantly associated with depression and hopelessness (Ran et al, 2003). Yim and colleagues (2004) found that among 73 Chinese patients with schizophrenia, past suicide attempts, suicidal ideation, unemployment and maternal mental illness were significant predictors of suicide shortly after discharge. Research from Hong Kong revealed that significant suicide risk factors among 92 inpatient suicides included a diagnosis of schizophrenia, depressive symptoms, past deliberate self-harm and stress related to work or living situation (Kan et al, 2007; Dong et al, 2005). Despite these studies from China, most lacked representative samples and no

study has used a control group of deceased patients with schizophrenia with the psychologic autopsy method.

To systematically assess the role of depressive symptoms and other risk factors for suicide among persons with schizophrenia in China we conducted a secondary analysis of 74 suicides (cases) and 24 accidental deaths (controls) among persons with schizophrenia identified in a national community-based psychological autopsy study of suicide in mainland China (Phillips et al 2005). Our goal was to test four hypotheses. Compared to persons with schizophrenia in China who die of other methods, those who die of suicide are more likely to 1) have experienced recent thoughts of death and to have a past history of suicide attempt, 2) have experienced recent symptoms of depression, 3) have a past history of depression and a family history of depression, and 4) have recently experienced a major negative life event.

Methods

Sample

The national psychological autopsy study, conducted in 23 geographically representative locations around China, has been described in detail in previous reports (Phillips et al 2002, 2004; Yang et al 2005). Briefly, deaths of persons over 10 years of age in which the cause of death recorded on the death certificate was suicide, accidental causes, undetermined injury, or mental illness that occurred in 3 of the sites from 1 August 1995 to 31 August 2000 and in the other 20 sites from 1 January 1997 to 31 August 2000 were reported to the research group at 3-month intervals. All deaths with suicide or an undetermined injury as the recorded cause of death and a random selection of those with other accidents as the recorded cause of death were selected for detailed investigation. Trained mental health professionals took 2–3 hours to complete separate interviews with the decedents' family members and close associates. At the time of the study, written consents were not required in China, partly because many rural informants were illiterate. We read the informants a standard statement about their rights to refuse to participate and to stop the interview at any point. They were then asked for their oral consent and, if given, the interview proceeded. The number of refusals to participate was minimal relative to the sample size and is provided in a previous publication of these data (Phillips et al, 2002).

Measures

Diagnoses were assessed using an expanded and adapted version of the Structured Clinical Interview for DSM-IV (SCID). The SCID was translated, back-translated and revised for use with proxy informants. The section on depression was expanded to make it more sensitive to the Chinese methods of describing depressive affect and symptoms; with the exception of the item on agitation, 1 to 3 culture-appropriate probes were added for each symptom of depression and asked after the standard SCID probe(s) unless responses to the standard probe(s) indicated that the symptom was definitely present for at least 14 days prior to death. Other modifications included: 1.) For each depressive symptom that was definitely present or considered 'sub-threshold' the number of days the symptom was continuously present prior to death was recorded; 2.) all 9 symptoms of depression were assessed even if depressive affect and anhedonia were absent; 3.) the social and psychological effect of the depressive symptoms in the month prior to death was assessed by asking about how distressed the individual was by the symptoms and about the effect the symptoms had on the individual's work, daily activities, spirits, social interactions and self-care (each of the 6 items was scored 0 to 3, none to severe); and 4) the presence and degree of hopelessness (on a 0-100 point scale) in the 14 days prior to death was assessed. The inter-rater reliability for this version of the SCID has been reported previously (Phillips et al 2002); the intra-class

correlations coefficients for affective disorders, substance abuse, psychotic disorders and other mental disorders were respectively 0.87, 0.94, 0.83 and 0.71."

Several other measures were included in this analysis. The severity of illness in the month before death was assessed as defined by Phillips et al (2007). In addition, an interview-based life event scale was specifically developed for suicides in China (Phillips et al 2007): for each negative life event that occurred in the year before death or that occurred earlier but continued to have a psychological effect in the year before death, the respondent indicated the time the life event occurred, the respondent's perception of what effect the negative life event had on the deceased, the time over the last year of life that the psychological effect lasted, and the magnitude of the psychological effect (from none to very severe, coded as 0–4). To assess quality of life in the month before death, we asked respondents to rate six characteristics of the deceased (physical health, psychological health, economic circumstances, work, family relationships, and relationships with non-family associates) on a scale of 1 (very poor) to 5 (excellent); the sum of the 6 scores was then converted to a scale of 0–100 (Phillips et al 2007).

Statistical methods

SPSS (version 11.0) software was used to conduct the analysis. Descriptive statistics were obtained for all variables, including distributions, means, medians, variances and standard deviations. Comparisons between cases and controls used Chi square tests, Fisher's exact tests (for nominal data) or t-tests (for continuous variables). Because of the large number of univariate analyses, we subjected the data to further analyses using the False Discovery Rate method (Benjamini and Hochberg, 1994). All analyses used a two-tailed alpha (p=0.050) as the level of statistical significance.

This study was approved by the institutional review boards of the Beijing Hui Long Guan Hospital and the Chinese Academy of Preventive Medicine.

Results

Table 1 summarizes subjects' characteristics. There were no differences between cases and controls in age, gender or rural versus urban residence. Compared to individuals with schizophrenia who died by accident, those who died by suicide were more likely to have had a greater mean effect of negative life events in the prior year—despite having a similar number of chronic and acute negative life events. There were no differences between the groups in the age of onset of schizophrenia, in the proportion who had a positive family history for psychosis or depression or in the proportion who had been treated with antipsychotics or antidepressants in the month before death. Furthermore, there were no differences between the groups in terms of the severity of illness in the month before death, in overall quality of life in the month before death or whether they had prior mental health treatment.

Table 2 compares the prevalence of different psychotic and depressive symptoms between the two groups. There were no differences between the groups in the prevalence of different psychotic symptoms over the month prior to death. In addition, none of the accidental controls met DSM-IV criteria for major or minor depression while 20 of 74 suicide decedents met full criteria for DSM-IV major or minor depression; this difference was statistically significant. Furthermore, the group that completed suicide was more likely to have had a past suicide attempt, to have recently experienced the symptom of depressed mood, and thoughts of death (see Table 2). In addition, the overall severity of the depressive symptoms and the effect of the depressive symptoms on functioning were significantly higher in those who died by suicide.

Discussion

The results support three of our four *a priori* hypotheses. Compared to persons with schizophrenia who die of accidental causes, those who died by suicide are more likely to have recent suicidal ideation, have a past suicide attempt, have higher levels of depressive symptoms at the time of death, and to have experienced greater stress due to negative life events over the year prior to death. Contrary to our hypotheses, cases were not more likely to have had prior episodes of depression nor to have a family history of depressive illness.

The methods of the psychological autopsy method cited here are widely accepted and has been used in the past with patients with schizophrenia (Heila et al 1997; Cavanagh et al 2003; Hawton et al 1998; Isometsa 2001). Limitations of the study include the fact that there was a small number of accidental deaths among persons with schizophrenia (n=24). Furthermore, the samples were not matched. In addition, we attempted to reduce recall bias —a problem common to all psychological autopsy studies--by using two proxy informants for each decedent. The informants who participated included a co-resident family member and a non-co-resident associate. As described previously, we "coded up," meaning that if is a symptom is reported by either informant, it is considered present. In using accidental deaths as controls we also reduced differential recall bias between cases and controls.

Based on Phillips (2002), in many locations in China there was a high rate of suicide among those whose death has been attributed to an undetermined accident and this is often classified as an open case. In addition, there were often frequent misclassifications of suicides as well as other types of accidents which lead to an overall under-reporting of suicides. Clearly, restriction of the study of suicide to those whose death certificate specifies suicide can decrease the representativeness of the sample deaths by suicide. In this study, this was avoided by reclassifying the cause of death of all accidental and undetermined deaths by using detailed information about the circumstances of the death. These were provided by the informants. Reclassification, in turn, can also introduce bias since the decision about cause of death could be influenced by the presence or absence of postulated risk factors. Furthermore, we should point out there was no important difference between the results of the analysis that used the cause of death recorded on the death certificate and those based on their final decision about cause of death.

Our study adopted a novel approach to increase sensitivity to cultural differences in the manifestation and experience of depressive symptoms. We retained the core structure and diagnostic criteria of the SCID interview for DSM-IV; all subjects were asked about all nine symptoms of depression and we added culture-sensitive probes for depressive symptoms. A previous report by Phillips et al (2007) found that this expanded-probe method identifies a substantial number of depressed subjects not identified by the standard SCID interview. Developing and assessing such probes is a lengthy process and their inclusion in structured questionnaires adds to respondent burden, but we believe it to be an essential step to improving the validity of psychiatric epidemiological studies in non-western cultures.

Culture-bound syndromes are, in general, rare and as a result they were not specifically assessed in this study. This was the case particularly because our informants were proxies and not the subjects themselves. This issue of culture bound syndromes is relevant to disorders such as neurasthenia, a disorder which overlaps with somatic symptoms (Kleinman, 1986). With regards to somatic symptoms in this sample, there were no differences between the 2 groups noted; this includes symptoms such as appetite change and insomnia.

Extensive research with DSM-IV criteria (Widiger and Coker, 2003) highlights the limitations of the categorical diagnostic system, the problem of high levels of co-morbidity

and the lack of clarity between diagnostic boundaries. Several authors suggest that a dimensional classification of psychopathology may be more valid, particularly for affective and anxiety spectrum conditions (Watson, 2005). The Nomenclature Work Group for DSM V has specifically considered various methods of integrating these categorical and dimensional approaches (Rousanville et al 2002; Widiger and Coker, 2003). Consistent with this reasoning, Phillips et al (2007) demonstrated that dimensional measures of depressive symptoms were more powerful predictors of suicide risk than categorical diagnoses and that the risk of suicide increases linearly with increased severity of depression in patients with various psychiatric diagnoses.

In the current study we also found that dimensional measures of depression (number of symptoms, level of effect of depression on the subject, etc.) were more closely associated with suicide in persons with schizophrenia than the pattern or severity of psychotic symptoms. Almost all previous psychological autopsy studies (Cavanagh et al 2003) rely on dichotomous diagnostic categories and, thus, may have underestimated the importance of subsyndromal depression and anxiety that may be best measured on a continuum (Kreuger, 1999; Connor et al 2001). Improved prediction and management of suicidal behavior will require a fundamental change in the strategy for assessing risk: both screening and diagnostic assessments should include dimensional measures of psychopathology and other risk factors, an approach that had been included in an earlier generation of structured clinical interviews for psychiatric diagnoses (Endicott and Spitzer, 1999).

Community screening for depression and diagnostic assessment of persons in high-risk groups are important components of suicide prevention efforts (Gaynes et al 2004). Our results indicate that it is also important for clinicians to screen patients with schizophrenia for accompanying depressive symptoms. However, many screening schedules for depression (such as the PHQ2; Gilbody et al 2007) use 'skip-outs' so that if the subject does not report depression or anhedonia other depressive symptoms that may be predictive of suicide such as thoughts of death, may go undetected.

There are interventions that should be considered in patients with schizophrenia who present with depressive symptoms or other risk factors for suicide. The effectiveness of SSRIs in the treatment of depressive and suicidal symptoms in subjects with schizophrenia has been demonstrated (Zisook et al 1999, 2009, in press; Spina et al 1994) and the potential suicide-preventive effects of clozapine versus other antipsychotics reported in the Intersept study (Meltzer et al 2003) have been recognized by the FDA. However, in both China and in other countries the potential benefit of these other interventions for reducing the high rates of suicide among individuals with schizophrenia will remain unknown until clinicians and other care-givers proactively identify and manage depressive symptoms and other risk factors for suicide in these individuals. With the dramatic recent socio-economic changes in China along with the way mental health care is delivered, our findings point out that the recognition of depressive symptoms are important risk factors clinicians need to be aware of when screening for suicidal behavior. Our findings are consistent with risk factors for suicidal patients with schizophrenia which researchers have determined to be important predictors in industrialized Western nations (Hawton et al 2005). As China continues to rapidly industrialize and exhibit expansion with their mental health systems, clinicians will need to carefully observe these risk factors in patients with schizophrenia to help prevent suicidal behaviors.

Acknowledgments

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Table 1

Characteristics of suicide and accidental death decedents with schizophrenia from China

Characteristic	Accidental Control (N = 24)		Completed Suicide (N = 74)		Analysis	
	Mean	SD	Mean	SD	t (df)	Adjusted p[c]
Age (years)	46.8	16.6	44.4	14.6	0.68 (96)	0.767
Age of onset of symptoms	28.6	12.4	33.5	12.6	-1.65 (96)	0.282
Duration of illness from onset to death (years)	18.3	13.1	10.9	12.2	2.50 (96)	0.066
Mean number of negative life events in last year	2.56	1.54	3.47	2.23	-1.84 (96)	0.200
Mean effect of negative life event in last year	37.65	38.72	77.66	58.37	-3.14 (96)	0.024
Mean overall quality of life in prior month (0-100)	42.13	14.13	44.16	10.85	-0.74 (96)	0.702
	N	%	N	%	χ^2(df)	p
Female gender	9	37.5	22	29.7	0.50 (1)	0.672
Rural residence	16	66.7	50	68.0	0.01 (1)	0.999
Prior suicide attempts	0	0.0	28	37.8	12.71 (1)	0.021
Multiple episodes of depression	0	0.0	3	4.1	---	1.000 [a]
Had prior mental health treatment/admission	20	83.3	40	54.1	6.54 (1)	0.065
Had ever received treatment from psychiatrist	18	75.0	51	68.9	0.32 (1)	0.767
Used anti-psychotic in last month	11	45.8	41	55.4	0.67 (1)	0.695
Used antidepressant in last month	0	0.0	3	4.1	---	1.000[a]
Severity of illness in month before death						
None	0	0.0	1	1.4	---	0.854 [b]
Mild	1	4.2	4	5.4		
Moderate	5	20.8	23	31.1		
Severe	18	75.0	46	62.2		
Severe negative life event in 7 days prior to death	2	22.0	11	14.9	---	0.751 [a]
Family history of psychosis	3	12.5	10	13.5	---	1.000 [a]
Blood relative with history of depression	0	0.0	4	5.4	---	0.787 [a]

[a] Based on Fisher's Exact Test

[b] Freeman-Halton (1951) extension of the Fisher's Exact Test.

Note: Fisher's Exact Test used when expected frequency < 5.

[c] All p values were adjusted using the False Discovery Rate

Table 2

Symptoms at time of death of suicide and accidental death decedents with schizophrenia from China

Measure	Accidental Control (N = 24)		Completed Suicide (N = 74)		Analysis	
	n	%	n	%	χ² (df)	Adjusted p [b]
Delusions						
Delusions of references	12	50.0%	48	64.9%	1.69 (1)	0.434
Paranoid delusions	17	70.8%	48	64.9%	0.29 (1)	0.772
Grandiose delusions	9	37.5%	12	16.2%	4.88 (1)	0.106
Delusions of jealousy	4	16.7%	22	29.7%	1.59 (1)	0.425
Delusions of control	1	4.2%	12	16.2%	--	0.416 [a]
Delusions of thought broadcasting	0	0.0%	10	13.5%	--	0.280 [a]
Other types of delusions	4	16.7%	16	21.6%	--	0.845 [a]
Hallucinations						
Auditory	16	66.7%	57	77.0%	1.02 (1)	0.587
Commenting	10	41.7%	41	55.4%	1.37 (1)	0.474
Visual, olfactory or other	8	33.3%	29	39.2%	0.26 (1)	0.771
Disorganized speech	23	95.8%	53	71.6%	6.10 (1)	0.073
Bizarre behavior	21	87.5%	57	77.0%	--	0.696 [a]
Negative symptoms						
Flat affect	16	66.7%	42	56.8%	0.74 (1)	0.681
Alogia	6	25.0%	25	33.8%	0.65 (1)	0.682
Amotivation	13	54.2%	43	58.1%	0.12 (1)	0.864
Depressive symptoms						
Depressed mood	0	0.0%	20	27.0%	--	0.020 [a]
Anhedonia/Diminished interest	0	0.0%	13	17.6%	--	0.114 [a]
Appetite/Weight loss/gain	3	12.5%	13	17.6%	--	0.844 [a]
Insomnia/Hypersomnia	6	25.0%	22	29.7%	0.20 (1)	0.791
Psychomotor agitation/retardation	4	16.7%	22	29.7%	1.59 (1)	0.444
Fatigue	1	4.2%	15	20.3%	--	0.282 [a]

	Accidental Control (N = 24)		Completed Suicide (N = 74)		Analysis	
Measure	n	%	n	%	χ² (df)	Adjusted p[b]
Guilt/Worthlessness	0	0.0%	13	17.6%	---	0.123 [a]
Poor concentration/Indecisiveness	0	0.0%	11	14.9%	---	0.191 [a]
Thoughts of death	0	0.0%	26	35.1%	11.48 (1)	0.016
Meets DSM-IV criteria of major depressive disorder or minor depressive disorder	0	0.0%	20	27.0%	---	0.024 [a]
Hopelessness for 14 days prior to death	0	0.0%	14	18.9%	---	0.081 [a]
	Mean	SD	Mean	SD	t (df)	p
Mean severity of 8 depressive items (excluding thoughts of death item)	0.33	0.53	1.43	2.14	-4.10 (92)	0.042
Mean effect of depression on functioning (0-100)	1.62	4.84	17.79	25.48	-3.08 (96)	0.028
Severity of hopelessness (0-100)	0.00	0.00	12.14	23.64	-0.65(96)	0.745

[a]Based on Fisher's Exact Test.

Note: Fisher's Exact Test used when expected frequency < 5.

[b]All p values were adjusted using the False Discovery Rate