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Does Age Moderate the Relationship between Depressive Symptoms and Suicidal Ideation in Middle Aged and Older Patients with Schizophrenia and Subthreshold Depression?

John Kasckow, MD, PhD^{*,1,2}, Shahrokh Golshan, PhD³, and Sidney Zisook, MD³

¹VA Pittsburgh Health Care System MIRECC and Behavioral Health Service; 7180 Highland Dr., Pittsburgh, PA 15206

²Western Psychiatric Institute and Clinics, University of Pittsburgh Medical Center, 3811 O'Hara St. Pittsburgh, PA 15213

³VA San Diego Health Care System, San Diego, CA; Department of Psychiatry, University of California, San Diego, San Diego, CA

Abstract

Background—Suicidal deaths in middle aged and older individuals with schizophrenia is a public health concern. Depression and schizophrenia are major risk factors for suicide. However, it is unknown whether age moderates the relationship between depression and suicidal ideation in patients with schizophrenia and subthreshold depression.

Methods—In outpatients > 39 years old with schizophrenia and subthreshold depression (n = 213), suicidal ideation was assessed with the Intersept Scale for Suicidal Ideation and CGI-Suicide Severity scale. Using linear regression, we examined whether depression (based on Calgary Depression Rating Scale scores), age and 'age by depressive symptoms' predicted suicidal ideation.

Results—Depressive symptoms predicted suicidal ideation. Neither age nor 'depressive symptoms by age' predicted suicidal ideation.

Conclusions—In this population, age does not appear to moderate the relationship between depressive symptoms and suicidal behavior. Thus, assessing depressive symptoms as a risk factor is important at all ages in this population.

Keywords

schizophrenia; age; moderation; suicidal ideation; depression

Objectives

Suicide is a leading cause of premature death among people with schizophrenia and depressive symptoms are a risk factor. Cohen et al (1) studied patients with schizophrenia

*Corresponding author: John Kasckow, MD, PhD, VA Pittsburgh Health Care System, Behavioral Health, 7180 Highland Dr, Pittsburgh, PA 15206, Phone: (412) 954-4344, Fax: (412) 954-4305, kasckowjw@upmc.edu.

age > 54 and determined that a history of prior suicide attempts was associated with depressive symptoms. Although the risk of completed suicides in individuals with schizophrenia is highest in those less than age 40 (2), suicidal behavior in the middle aged and elderly patient with schizophrenia is still a public health concern. For instance, a psychological autopsy case series of individuals with schizophrenia who completed suicide indicated that one third of suicide victims were over age 45 (3); furthermore, 64% of the suicides occurred while patients experienced depressive symptoms.

In this study, we examined the relationship between depressive symptoms, age and suicidal ideation in middle aged and older individuals with schizophrenia and subthreshold depressive symptoms. We hypothesized that age moderates the relationship between depression and suicidal ideation. From a public health perspective, answering this question is important since it can help guide clinicians in determining suicide risk in middle aged and older patients with schizophrenia.

Methods

Participants were recruited for an NIMH sponsored trial to study the effectiveness of citalopram versus placebo in augmenting the treatment of patients with schizophrenia/schizoaffective disorder and subthreshold depressive symptoms. The study was previously described by Zisook et al (4). Subjects were outpatients at: 1.) University of California, San Diego/ Veterans Affairs San Diego Healthcare System and 2.) University of Cincinnati/ Cincinnati VA Medical Center. The Institutional Review Board at both sites approved the study.

Patients needed to have a diagnosis of schizophrenia or schizoaffective disorder as verified by the Structured Clinical Interview for DSM-IV Axis 1 disorders. Patients also needed to have at least 2/9 items required for major depression and a baseline 17 item Hamilton Depression score (5; HAM-D) ≥ 8 . In addition patients needed to be 1.) > 39 years of age, 2.) have adequate decisional capacity and 3.) have a caregiver. Patients were excluded if they had 1.) dementia, 2.) major depression or mania within the past 2 months or 3.) active substance abuse/dependence. The average HAM-D scores ($\pm$ standard deviation) was 13.6 $\pm$ 4.2. In addition, age, gender, marital status, living situation, educational level and race was documented.

Our primary outcome scale assessing depression was the Calgary Depression Rating Scale (CDRS; 4). For assessing suicidality, we administered the 12 item InterSePT scale for Suicide Thinking (ISS; 4) and the Clinical Global Impression-Severity of Suicide Scale (CGI-SS; 4).

Statistical Analysis

Continuous variables were assessed for normality of distribution within groups and for homogeneity of variance across groups. Descriptive statistics were obtained to characterize our sample. Our analysis used Pearson Correlation and Multiple Linear Regression methods with standard moderation analyses using multiple regression. SPSS version 19 was utilized. All analyses were two-tailed, where applicable, with $\alpha = .05$.

Results

The sample included 213 participants. The mean age $\pm$ standard deviation was 52.5 ± 7.0 years; the median age was 52 years, and the range was 40-75; 94% were age 40-64 and 6% were 65. Furthermore, 78% of the participants were men, 59% Caucasian, 33% African American, 1% Native American, 2% Asian American and 5% 'other' (for instance, multiracial). Fourteen percent were married/cohabitating and 40% had a diagnosis of schizoaffective disorder and 60% had a diagnosis of schizophrenia. The average CDRS score was 6.7 ± 3.2 ($n = 192$), the average ISS score ($n = 195$) was 1.09 ± 2.4 and the average CGI-SS score was $1.19 \pm .493$ ($n = 192$). The frequency of responses from the HAM-D is in Table 1.

We initially determined that there was a significant correlation between depressive symptom (CDRS scores) and measures of suicidal ideation (CGI-SS: $r = 0.366$; $n = 194$; $p < 0.001$; ISS: $r = .425$; $n = 197$; $p < 0.001$). There was no significant correlation between CDRS scores and age ($r = -.087$; $n = 209$; $p = 0.212$). We then tested whether each of the 2 measures for suicidal ideation could be predicted by a linear regression model involving age, depressive symptoms and the interaction term 'depressive symptoms by age'. Although in both cases, the models were significant, the interaction term of 'depressive symptoms by age' was not. Specifically, the models containing the interaction term yielded the following F values and significance levels (see also Table 2): for CGI-SS, $F(3, 188) = 9.85$ $p < .001$; for ISS, $F(3, 191) = 14.48$; $p < 0.001$. Without the interaction term, the values were: for CGI-SS, $F(2, 189) = 14.81$, $p < .001$; for ISS, $F(2, 192) = 21.61$; $p < 0.001$. Furthermore in each of the 2 factor models, CDRS scores significantly predicted suicidal ideation: for CGI-SS, $t = 5.41$, $p < .001$; for ISS, $t = 6.48$; $p < 0.001$. On the other hand, in each model, the t value for the age factor was not significant.

Discussion

In this sample of middle aged and older patients with schizophrenia and subthreshold depressive symptoms, we observed that depressive symptoms associated positively with levels of suicidal ideation. This is consistent with previous studies of Cohen et al (1) who determined that in patients with schizophrenia age > 54 , a history of prior suicide attempts was associated with depressive symptoms. Furthermore, when using regression analysis to determine whether depressive symptoms, age and a 'depressive symptoms by age' interaction term predicted suicidal behavior, we determined that age did not moderate the relationship between depressive symptoms and suicidal ideation. These findings have important clinical implications. It suggests that when clinicians evaluate middle aged and older patients with schizophrenia for suicidal risk, depressive symptoms should be considered as a risk factor equally at all ages.

Alexopoulos et al (6) examined similar questions in a group of older individuals (age range 61-93 years) with major depression but without schizophrenia. They found that age did not influence the distribution of scores assessing suicidal ideation. The authors also noted that the severity of depressive symptoms but not age, predicted the course of suicidal ideation both at initial evaluation and at endpoint follow up (mean 1.8 years). Likewise in our

sample, we also determined that depressive symptom severity was predictive of suicidal ideation and that age was not. Alexopoulos et al (6), however, did not test whether age moderated the relationship between depressive symptoms and suicidal ideation.

As reported by Zisook et al (4) about 90% of the participants in this study were taking stable doses of either second generation antipsychotics alone (71%) or in combination with first-generation antipsychotics (19%) for at least 1 month. Also, there were 3 participants taking lithium and 3 taking clozapine. Patients were not on any therapeutic doses of antidepressants at the time of assessment; however, some patients were on subtherapeutic doses of trazodone for insomnia or tricyclic antidepressants for pain. No one was on citalopram (4).

Our sample included 40% of individuals diagnosed with schizoaffective disorder and 60% with schizophrenia. Zisook et al (7) reported that patients with schizoaffective disorder are more likely to endorse more intense “guilty ideas of reference” and exhibit higher CDRS scores than those diagnosed with schizophrenia. In addition, the average severity of patients' CDRS scores was 6.7 ± 3.2 . We realize that some individuals may have had scores consistent with levels observable in individuals with major depression (8). However, individuals were excluded if they had ≥ 5 DSM IV symptoms of major depression (including either depressed mood or anhedonia) present most of the time for at least the past 2 weeks.

Our sample had a high proportion of men. This is important to consider since Martin-Reyes et al (9) compared CDRS scores in patients with schizophrenia with regards to gender and family history and found a significant difference between subgroups, i.e., significantly more severe depression in female patients from the groups with or without a family history relative to the subgroup of men without a family history.

There were several limitations to the study. As described by Links et al (10) there is modest evidence suggesting that suicidal ideation can serve as a surrogate endpoint for suicide in older individuals. Links (10) further stated that there is currently a paucity of studies examining this and indicated the need for more research in this area. Secondly, although approximately 200 subjects represent a relatively large group, a larger group would have allowed us to look at other clinically important subtypes (such as late-onset versus early-onset schizophrenia and paranoid versus nonparanoid patients). Furthermore, the sample was heterogeneous in that it included individuals with and without past histories of major depression, schizoaffective disorder and schizophrenia. In addition our sample possibly included subjects with residual or prodromal symptoms of depression, and even some with prominent negative symptoms. An important next step would be to extend these findings to the entire age range of patients with schizophrenia.

Conclusions

Depressive symptoms predicted suicidal ideation. Neither age nor ‘depressive symptoms by age’ predicted suicidal ideation. In this population, age does not appear to moderate the relationship between depressive symptoms and suicidal ideation. Thus, assessing depressive symptoms as a risk factor is important at all ages in this population.

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Table 1
Frequencies of responses on Hamilton Rating Scale for depression items (N= 213)

Symptom	Item Response 0 (%)	Item Response 1 (%)	Item Response 2 (%)	Item Response 3 (%)	Item Response 4 (%)
Depressed Mood	2.8	38.2	45.3	13.2	0.5
Work and Activities	28.8	39.2	23.5	8.0	0.5
Suicide	67.5	19.8	11.3	1.4	
Feelings of Guilt	30.2	24.5	32.5	11.3	
Initial Insomnia	36.8	15.1	48.1		
Middle Insomnia	60.8	16.0	23.1		
Delayed Insomnia	58.0	22.6	19.3		
Psychomotor Retardation	54.7	34.4	10.4	0.5	
Agitation	57.5	36.3	6.1		1.9
Anxiety (Psychological)	25.5	20.3	32.5	19.8	0.5
Anxiety (Somatic)	57.5	21.7	14.2	6.1	
Loss of appetite	61.8	22.6	13.7	1.9	
Somatic Symptoms (General)	30.7	54.2	14.6	0.5	
Loss of Libido	68.9	19.3	11.3	0.5	1.9
Hypochondriasis	66.0	17.9	13.2	0.9	
Weight Loss	64.2	28.8	6.6	0.5	
Loss of insight	53.8	39.6	6.6		

Score of 0 means symptom is absent; scores ranging from 1 to 4 indicates greater severity of symptoms.

Table 2
Key Statistical Findings

Model	Dependent Variable	Overall F value	P value
3 Factor Model Predictors: 1 CDRS, 2 Age 3 * CDRS by Age	Clinical Global Impressions – Suicidal Ideation	F(3, 188) = 9.85	< 0.001
	Intersept Scale for Suicidal Ideation	F(3, 191) = 14.48	< 0.001
** 2 Factor Model Predictors: 1 CDRS 2 Age	Clinical Global Impressions – Suicidal Ideation	F(2, 189) = 14.81	< 0.001
	Intersept Scale for Suicidal Ideation	F(2, 192) = 21.61	< 0.001

CDRS = Calgary Depression Rating Scale

* the t value for the interaction term in the 3 factor model was not significant

** in the 2 factor model, with Clinical Global Impression-Scale for Suicidal Ideation scores as the dependent variable, the t value for CDRS was significant: $t = 5.4$ ($p < 0.001$); with Intersept Scale for Suicidal Ideation scores as the dependent variable, the t value for CDRS was also significant: $t = 6.48$ (< 0.001).