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Research report

Anxiety symptoms are linked to new-onset suicidal ideation after six months of follow-up in outpatients with major depressive disorder

Ji Hyun Baek [a,d], Jung Yoon Heo [a], Maurizio Fava [c], David Mischoulon [c], Andrew Nierenberg [d], Jin Pyo Hong [a], Sungwon Roh [e], Hong Jin Jeon [a,b,c,*]

[a] Department of Psychiatry, Depression Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea
[b] Department of Health Sciences & Technology, Department of Clinical Research Design and Evaluation, and Department of Medical Device Management and Research, Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Seoul, South Korea
[c] Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
[d] Bipolar Clinic and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
[e] Seoul National Hospital, Seoul, South Korea

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ABSTRACT

Background: Suicide risk evaluation is one of the most challenging assessments of patients with major depressive disorder (MDD). Initial risk evaluation might be insufficient in predicting emergence of suicidal ideation during the maintenance period. We aimed to elucidate factors associated with emergence or persistence of suicidal ideation 6 months after initiation of outpatient treatment in patients with MDD.
Methods: A total of 300 participants with MDD defined by DSM-IV-TR criteria underwent face-to-face interview at baseline and follow-up phone interview at 6 months later. Severity of depression, suicidal ideation, and anxiety were evaluated.
Results: Among participants who did not report any suicidal idea at baseline, 10.9% reported suicidal ideation during the 6-month phone interview, while 28.4% of participants who reported suicidal ideation at baseline reported suicidal ideation during the phone interview. No significant difference in remission rate of depression was observed between the groups, but subjects without suicidal ideation at baseline had a higher rate of symptom improvement at the 6-month phone interview. After controlling for age, sex, baseline severity of suicide risk and depression and lifetime history of suicide attempts, emergence of suicidal ideation was significantly associated with anxiety level at baseline ($t=2.127$, $p=0.039$) and severity of depression symptoms at 6 month ($t=-3.028$, $p=0.004$); persistence of suicidal ideation was associated with severity of depression symptoms at 6 month ($t=-4.962$, $p<0.001$).
Limitation: Follow-up evaluation was done by phone interview.
Conclusion: Anxiety at baseline needs to be carefully evaluated in assessing suicide risk of patients with MDD.

1. Introductions

Despite recent advances in psychiatric treatment, suicide risk evaluation is still challenging for clinicians. For some patients, suicidal ideation remains as a residual symptom even after adequate treatment (Courtet et al., 2014; Szanto et al., 2003; Zisook et al., 2009). Others even experience newly emerging suicidal ideation after starting treatment (Szanto et al., 2007). The persistence or emergence of suicidal ideation during the course of treatment is not a rare phenomenon, and is associated with inadequate treatment responses (Courtet et al.,2014; Zisook et al.,2009) in the clinical setting.

Previous studies on emergence or persistence of suicidal ideation have mainly focused on the early course, typically 12 weeks after starting treatment with antidepressants (Gibbons et al., 2012; Seo et al., 2014; Stone et al., 2009; Zisook et al., 2011). Depression severity at baseline and younger age are suggested risk factors of the emergence of suicidal ideation during the early course of treatment. However, little is known about the emergence of suicidal ideation during the maintenance period in the real world outpatient setting.

We aimed to elucidate factors associated with emergence or persistence of suicidal ideation at 6 month after initiation of outpatient treatment in patients with MDD. Hypothesizing that suicidal ideation at baseline can affect the suicidal ideation at follow-

* Corresponding author at: Department of Psychiatry, Depression Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea. Fax: +82 2 3410 0050.
E-mail address: jeonhj@skku.edu (H.J. Jeon).

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up, we divided subjects into 2 groups i.e., with and without suicidal ideation at baseline. We explored baseline characteristics and factors that were associated with persistence (in the group with suicidal ideation at baseline) and emergence (in the group without suicidal ideation at baseline) of suicidal ideation 6 months after initiation of psychiatric treatment.

2. Materials and methods

2.1. Subjects

A total of 300 patients diagnosed with MDD according to the diagnostic criteria of the DSM-IV-TR were consecutively recruited from the outpatient clinic of the Department of Psychiatry and Depression Center of the Samsung Medical Center between May 2011 and April 2014. Those who had bipolar disorder, schizophrenia, other psychotic disorders, alcohol use disorders, organic mental disorders, mental retardation, neurologic illness including epilepsy, and serious medical illnesses were excluded.

Baseline evaluation was done at the time participants initially visited the clinic. Then we contacted the participants 6 months after starting psychiatric treatment by phone. We were unable to reach 72 of the subjects who had initially agreed to the phone interview (response rate 300/372 = 80.64%).

2.2. Baseline evaluation

Initial evaluation was the same as described in previous studies conducted at the depression center of the Samsung Medical Center (Baek et al., 2014). Initially, psychiatrists with more than 3 years' clinical experience evaluated the participants' psychiatric and medical histories, and confirmed their eligibility. A trained psychologist blinded to the psychiatrists' judgment separately explored the participants' psychiatric diagnoses and current mood states using the following measures: the Korean version of the Mini International Neuropsychiatric Interview's (MINI) (Sheehan et al., 1998), the Hamilton Depression Rating Scale (HAM-D) (Hamilton, 1967), the Beck's Anxiety Inventory (BAI) (Beck et al., 1988), Mood Disorder Questionnaire (MDQ) (Hirschfeld et al., 2000) and the Hypomania Symptom Checklist-32 (HCL-32) (Tomaszewski et al., 1992). In the Korean version of the MINI, Cohen's kappa values, ameasure of the inter-rater reliability, of the depression and suicide module were 0.71 (You et al., 2006). The MDQ and the HCL-32were used for evaluating potential bipolarity. All study procedures were approved by the Institutional Review Board of the Samsung Medical Center.

Once participants' diagnoses were confirmed, they all received standard psychiatric pharmacotherapy for MDD, i.e. standard antidepressant treatments including selective serotonin reuptake inhibitor (SSRI), serotonin norepinephrine reuptake inhibitor (SNRI), norepinephrine dopamine reuptake inhibitor (NDRI) and tricyclic antidepressant (TCA). Each participant's treatment regimen was chosen and modified depending on one's own clinical conditions by one's clinician.

2.3. Experience of suicidal ideation at baseline

Following a previous study (Perlis et al., 2007), the HAMD suicide item score, HAMD-3, which assesses suicidal ideation and behavior were used to define suicidality at baseline. Anyone who reported suicidal ideation by a HAMD-3 score of ≥ 1 was classified as a participant with suicidal ideation at baseline. Additionally, the MINI suicide module was used to evaluate participants' suicidality including recent experience of suicidal ideation and behavior and past suicide attempt history. The MINI suicidality score was estimated from the sum of the weighted score of the MINI suicide module questions. Both HAMD-3 score and the MINI suicidality score were valid measures to determine suicidality in previous studies (Desseilles et al., 2012; Roaldset et al., 2012).

2.4. Follow-up evaluation at 6 months after initiation of psychiatric treatment

At 6 months post-treatment initiation, a trained psychologist contacted participants and evaluated their mood symptoms using the Patient Health Questionnaire-9 (PHQ-9) (Kroenke et al., 2001). The PHQ-9 is a widely used validated measure to evaluate the presence and severity of depression and suicidality (Simon et al., 2013). It has also been used for phone interview in a previous study (Gega et al., 2012). The PHQ-9 has 9 questions on common symptoms of depression that the patient rates on a scale of 0–3 according to how often they experienced the symptoms in the previous 2 weeks. Standard cut-offs for PHQ-9 are 0–4, no depression; 5–9, mild depression; 10–14, moderate depression; 15–19 moderately severe depression; and 20–27, severe depression. Reported suicidal ideation by a PHQ-9 suicide item score of ≥ 1 was classified as persistence (in case of participants with suicidal ideation at baseline) andemergence (in case of participants without suicidal ideation at baseline) of suicidal ideation at follow-up. The PHQ-9 suicide item score also showed sound validity in determining suicidality in a previous study (Uebelacker et al., 2011). Remission at follow-up period was defined as PHQ-9 score ≤ 4.

2.5. Statistical analysis

Comparison of sociodemographic and clinical variables between those with and without suicidal ideation at baseline was performed with Chi-square or Fisher's exact test for categorical data, and the *t*-test for continuous variables with approximately normal distribution. To identify variables independently contributing to the emergence and persistence of suicidal ideation, a logistic regression analysis was performed with suicidal ideation at follow-up as the dependent variable. Emergence and persistence of suicidal ideation could have different characteristics, hence those with and without suicidal ideation at baseline were separately entered into the logistic regression model. Basic demographic variables including age and sex, baseline mood symptom severity and symptom severity at follow-up were entered as covariates. Probability (p) values of < 0.05 were considered statistically significant. All statistical analyses were done using Predictive Analytics Software (PASW) version 19.0 (SPSS Inc; Chicago, USA).

3. Results

Of all participants, a total of 110 (36.7%) subjects reported no suicidal ideation at baseline and 190 (63.3%) reported suicidal ideation at baseline. Table 1 shows baseline sociodemographic characteristics of participants. Participants with suicidal ideation at baseline tended to be younger, less married and more likely to live alone, as compared to those without suicidal ideation at baseline. No other statistical differences were detected between groups.

Table 2 describes baseline and follow-up symptom characteristics of participants. As expected, participants with suicidal ideation at baseline reported higher MINI suicide risk score and more frequent lifetime suicide attempt history, as compared to those without suicidal ideation at baseline. Those with suicidal ideation also reported greater HAM-D, BDI and BAI scores. Those with suicidal ideation reported greater HCL-32 scores than those without suicidal ideation, but no significant difference was