Research report

Emergence, persistence, and resolution of suicidal ideation during treatment of depression in old age

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Abstract

Introduction: To determine the rate and clinical correlates of emergent, persistent, and resolved suicidal ideation during treatment of major depression in the elderly.
Methods: Based on the course of suicidal ideation before and during 12 weeks of antidepressant treatment, we classified 437 elderly patients (234 treated with paroxetine; 203 with nortriptyline) as either non-suicidal or as having “emergent”, “persistent”, or “resolved” suicidality. We compared the four groups on pretreatment demographic and clinical measures and with respect to depression, anxiety, and akathisia during treatment. Results: Rates of emergent, persistent, and resolved suicidality were 7.8%, 12.6%, and 15.6%, respectively. Patients with persistent suicidal ideation were more likely to have recurrent depression than non-suicidal patients or patients whose suicidality resolved with treatment. At the start of treatment, patients in all three suicidal groups had lower self-esteem than non-suicidal patients. During the course of treatment, emergent suicidality was more likely to have recurrent depression than non-suicidal patients or patients whose suicidality resolved with treatment. At the start of treatment, patients in all three suicidal groups had lower self-esteem than non-suicidal patients. During the course of treatment, emergent suicidality was not associated with akathisia, nor did rates of emergent suicidality differ between paroxetine- and nortriptyline-treated patients. While at baseline the levels of depression and anxiety and agitation were similar in the four groups, patients with resolved suicidality had a favorable treatment response, while patients with emergent and persistent suicidality were more likely to maintain higher depression scores and had higher levels of anxiety and agitation during treatment.
Discussion: Emergence of suicidal ideation is not common but is clinically significant during treatment of late-life depression and may signal more difficult-to-treat-depression.

Keywords: Elderly; Major depression; Suicidal ideation; Treatment

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1. Background

Older adults (age 60 and above) have the highest suicide rate among all age groups in most countries of the world (World Health Organization, 2005). Although depression is the most common diagnosis in elderly suicide attempters and completers (Conwell et al., 2000; Beautrais, 2002), to our knowledge no study has systematically examined emergence, persistence, and resolution of suicidality during treatment of late-life depression. Recent concerns about emergent suicidality during depression treatment in children and adolescent (US Food and Drug Administration, 2004) and its apparent association with akathisia or agitation induced by selective serotonin reuptake inhibitors (SSRIs) highlight the clinical importance of this issue. In late-life, the literature is inconclusive with respect to these issues and to the implication of prior course (e.g., single versus recurrent depression) for suicide risk.

Patients whose mood remains low when they regain energy may be at increased risk for suicide (Detre and Jarecki, 1971). Alternatively, increased anxiety and agitation in the face of non- or partially remitting depression may increase suicide risk (Akiskal et al., 2005). A few case series (Power and Cowen, 1992) and case reports (Rothschild and Locke, 1991) have suggested an association between suicidality and akathisia. However, other investigators did not find a relationship between treatment-emergent adverse events and suicidality (Tollefson et al., 1994). A review of the literature (Hansen, 2001, pp. 495) concluded that “akathisia cannot be unequivocally linked to suicidal behavior; however, it is certain that the condition of akathisia does cause considerable distress in an already vulnerable group of patients”. To our knowledge, no study other than case reports (Hansen and Wilkinson, 2001), has investigated a possible relationship between medication-induced anxiety/agitation and suicidality in the elderly.

According to psychological autopsy studies, anxiety disorders without comorbid mood disorders only modestly increase suicide risk in the elderly (Waem et al., 2002b). However, in one study insomnia and severe psychic anxiety predicted suicide in mid-life patients with major depressive disorder (Fawcett et al., 1990) and two recent reports found an association between mixed depression often marked by psychomotor agitation, and suicidal ideation and attempts (Akiskal et al., 2005; Balazs et al., 2006). The authors note that psychomotor agitation maybe related to an activation syndrome caused by antidepressants. In our previous study in elderly patients, decline in suicidal ideation was associated with remission of depression (Szanto et al., 2003). Thus, based on literature review, our previous findings, and clinical experience, we hypothesized that:

1) Emergence and persistence of suicidality during treatment would be associated with chronic/recurrent depression and higher baseline anxiety or agitation.
2) Patients with emergent or persistent suicidality would be more likely to have persisting low mood and higher levels of anxiety/agitation/akathisia compared to non-suicidal patients and to those whose suicidality resolved.
3) Patients treated with a SSRI would be more likely to become suicidal than patients receiving a tricylic. This association, if present, could be due to the onset of akathisia in the SSRI-treated group.

2. Methods

2.1. Study group

Data for this analysis were available for 473 participants in three federally-supported clinical trials of geriatric depression. We pooled data from the three studies because all dealt with the treatment of non-psychotic, non-bipolar major depressive episodes in old age and utilized similar assessment and treatment approaches administered in the same research setting. Patients were required to be 60 years or older, to have nonpsychotic unipolar major depression, determined by administration of either the Schedule for Affective Disorders and Schizophrenia (SADS) (Spitzer, 1978) or the SCID for DSM-IV (First et al., 1995); to score 15 or higher on the 17-item Hamilton Rating Scale for Depression (HRSD-17) (Hamilton, 1967), and 15 or higher on the Folstein Mini-Mental State Exam (MMSE) (Folstein et al., 1975). Patients with unstable medical conditions or medications that could cause depression were excluded. Written informed consent was obtained from each patient following procedures approved by our Institutional Review Board (see Fig. 1).

Because the course of suicidality during treatment cannot be reliably established if patients are not closely monitored and suicidal ideation is not formally assessed longitudinally, we excluded 36 patients who did not complete at least four assessments (baseline and three weekly assessments during treatment). Of these 36 patients, 10 withdrew consent and 26 were terminated. Reasons for termination were severe side effects; \( n = 13 \), need for electroconvulsive therapy; \( n = 2 \), psychosis; \( n = 1 \), non-compliance with protocol; \( n = 2 \), medical illness precluding further treatment; \( n = 5 \), and other reasons; \( n = 3 \). We compared the clinical characteristics and the presence of suicidality in those 36 patients with the 437 who remained in treatment for more than three...
weeks. Subjects with fewer than four assessments had higher levels of co-existing medical burden (scores on the Cumulative Illness Rating Scale for Geriatrics [CIRS-G] (Miller et al., 1992): 11.1 vs. 8.7, \( t = 3.71, df = 463, p < 0.0002 \)). Baseline severity of depression was similar in the two groups, while patients who left the study had lower MMSE scores (27.1 vs. 28.0, \( t = 2.02, df = 464, p < 0.05 \)) and were more likely to endorse ideation suicidal (21 out of 36, vs. 161 out of 437, \( \chi^2 = 6.49, df = 1, p < 0.02 \)).

3. Treatment

Patients were treated as in- and/or outpatients in three studies: Maintenance Therapies in Late-Life Depression-1 and-2 (Reynolds et al., 2006); (MTLD-1 and MTLD-2) or Nortriptyline versus Paroxetine (NT/PX) (Mulsant et al., 2001). Participants in MTLD-1 and MTLD-2 received open (non-blinded) acute treatment before being randomized to maintenance treatments. MTLD-1 patients received combined nortriptyline and Interpersonal Psychotherapy Treatment (IPT). MTLD-2 patients received combined paroxetine and IPT. NT/PX patients received randomized acute treatment with either paroxetine or nortriptyline under double-blind conditions. MTLD-1 and-2 patients had weekly medication visit checks and 45-minute IPT sessions. NT/PX patients had weekly medication visits. In all three studies patients could receive lorazepam as an adjunctive medication for anxiety or insomnia. In MTLD-1 and MTLD-2, if patients did not respond or only partially responded to treatment, a second antidepressant or lithium was administered as combined treatment. The data reported here are derived from the first 12 weeks of the open treatment in MTLD-1 and MTLD-2, and from the 12 weeks of randomized, double-blind treatment of NT/PX. In all, 203 patients were treated with nortriptyline and 234 with paroxetine.

4. Assessments

Assessments before the start of treatment included the 17-item Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1967), Interpersonal Support Evaluation List (Cohen et al., 1985) (ISEL), Cumulative Illness Rating Scale-Geriatric (Miller et al., 1992) (CIRS-G), and Folstein Mini-Mental State Exam (Folstein et al., 1975). The ISEL measures perceived emotional and practical support as well as self-esteem. All subjects were also rated weekly with the HRSD. In MTLD-2 and NT/PX, medication side effects were measured weekly using the UKU scale (Lingjaerde et al., 1987). Raters’ supervision, measurements of interrater reliability for the HRSD and the UKU, and reviews of diagnoses were carried out regularly. During the most recent assessment of interrater reliability, intraclass correlation coefficients were 0.93 for the HRSD total score, 0.97 for the HRSD suicide item, and 0.75 for the total UKU score. Interrater reliability of the HRSD suicide item was greater than 0.85 for the last 6 years.
The HRSD suicide item assesses suicidal behavior, suicidal thoughts, thoughts of death, and desire to live within the past 7 days. Suicidality was defined as a score of 2 or higher on this item (“patient reports or wishes he/she was dead, recurrent thought of death, or suicidal ideation or had a recent suicide attempt”). We chose this particular cut-point for the following reasons: first, based on data from 6891 psychiatric outpatients who were evaluated at the Center for Cognitive Therapy of the University of Pennsylvania, those who scored 2 or higher on the Hamilton Depression Rating Scale suicide item were 4.9 times (95% CI: 2.7–9.0) more likely to commit suicide than those who scored less than 2 during a 20-year prospective study (http://www.nimh.nih.gov/suicideresearch/adultsuicide.pdf). Second, we have shown in an earlier study (Szanto et al., 1996) that older depressed patients with either active or passive suicidal ideation had similar rates of life-time suicide attempts and similarly high levels of hopelessness, differing significantly from patients who denied suicidal ideation or thoughts of death.

We further classified patients as having persistent suicidality if they reported suicidality during the first two assessments and continued to endorse it at any point after 4 weeks of treatment. Patients who did not endorse suicidality at any of the first 2 assessments but reported it later at any point during treatment were classified as having emergent suicidality. Patients who endorsed suicidality during the first two assessments but did not report it after 4 weeks of treatment were considered to have resolved suicidality. Patients were judged to be non-suicidal if they never reported suicidality and never reported the feeling that life is empty or not worth living (i.e., they had a score of 0 on the HRSD suicide item at the inception of treatment and during each of the 12 weekly assessments). To ensure that we did not misclassify patients as non-suicidal, we used this criterion for non-suicidality (score of 0 on HRSD suicide item) for all 12-weeks of data. Thus, we excluded from further analysis 176 patients who were neither clearly suicidal nor non-suicidal; that is, patients who had an HRSD suicide item score of 1 at any time (“life is empty, not worth living”) but who never had a score of 2 or higher (recurrent thoughts of death, wishes he/she were dead, or suicidal ideation). We compared the demographic and baseline clinical characteristics of the 176 ambiguous cases with the 261 cases who were used for further analyses. There was no significant difference between these two groups regarding age, gender, educational level, baseline severity of depression, lifetime age of onset of first depressive episode, or levels of self-esteem (results are not shown, but available upon request).

As an additional check of the validity of our suicide group classification, we examined the Scale for Suicide Ideation (SSI) (Beck et al., 1979) scores in a subgroup (N=307) for whom SSI scores were available for the first two assessments (SSI scale was introduced later in the study). We used the highest summarized scores from the first two assessments for the first 5 (screening) items of the SSI (possible scores 0–10). Three SSI screening items assess the wish to live or the wish to die and two items assess the desire to attempt suicide. There is no clear cut-off point for the SSI; some studies have used an SSI score of 1 or higher to define suicidality (e.g., Bruce et al., 2004), while others used a score of 2 or higher (e.g., Brown et al., 2000). The classification by the HRSD suicide item was confirmed by the SSI. Of 69 non-suicidal patients where SSI data were available, 67 had a total score of 0 on the SSI first 5 items, only 2 had a score of 1 (97% agreement across scales). Within the persistent and resolved groups 65 of the 72 (86%) had a total SSI score of 1 or higher, and 28 of those had a score of 2 or higher, showing a significant level of suicidality. Of the 28 patients classified as emergent suicidality, 20 subjects had a baseline score of 0, six had a score of 1, and 2 had a score of 2 (thus using a cut-off score of two 7.9% was misclassified based on the SSI). Of the 138 ambiguous cases with concurrent SSI ratings, 119 (86%) had a score of 0 and 7 had a score of 2 or higher.

5. Assessment of combined symptoms of agitation/anxiety

We assessed agitation/anxiety using three items of the HRSD: item # 9 (agitation), item #10 (psychological anxiety), and item #11 (somatic anxiety) and noting at each assessment whether subjects score ≥ 2 on any single item. We used this categorical approach to investigate whether patients with emergent suicidal ideation were more likely than other patients to have these symptoms.

6. Assessment of akathisia

UKU data were available for a subgroup of MTLD-2 and NT/PX patients (n = 161). Using the UKU akathisia item (item #16, score 0–4), we investigated whether patients with emergent suicidal ideation were more likely to experience akathisia than other groups. A score of 1 on this item indicates: “Slight akathisia; however, the patient can keep still without effort”; a score of 2: “Moderate akathisia; however, the patient can, with an effort, remain sitting during the interview”; and a score of 3: “the patient has to rise to his feet several times during the interview because of akathisia”. Although the
UKU is intended to assess medication side effects, we also administered the UKU before treatment to insure that symptoms present before the inception of antidepressant pharmacotherapy (such as agitation) were not misattributed to treatment.

7. Statistical analysis

In comparing the demographic and clinical characteristics of the four groups, we used a one-way analysis of variance for continuous variables, followed by Tukey post-hoc contrasts for significant results. For categorical variables (e.g., presence of akathisia) we used chi-square tests. Mixed-effect models were used to examine depression (HRSD minus item # 3, suicide item) over the 12 weeks of treatment. The mixed-effect included group as a fixed effect, while subject and time were included as random effects. The fixed-effect parameter (group and group by time) of each suicidal group was examined and compared in models that demonstrated an overall significant effect. Satterthwaite degrees of freedom was used in the mixed effect model. A generalized logit model with repeated measures over time tested for differences in anxiety/agitation as indicated by a score of ≥2 on any of items 9, 10, or 11 of the HRSD.

8. Results

Of the 437 patients (the sample with at least four assessments), 123 patients (28%) reported suicidality during the first two assessments: of these, 55(12.6%) reported suicidality longer than the first 4 weeks ("persistent") while 68 (15.6%) did not report suicidality after 4 weeks in treatment ("resolved"). Thirty-four patients (7.8%) did not report suicidality during the first 2 assessments but did so later during acute treatment ("emergent"). Of these 34, 53% showed emergent suicidal ideation in the first month of treatment, 21% in the second month, and 26% in the third month of treatment. There were 104 patients who were non-suicidal throughout the 12-week treatment (i.e., consistently scored 0 on the HRSD suicide item). Thus, the rates of emergent suicidality in the sample of 437 were 7.8% (34/437), persistent suicidality 12.6% (55/437), and resolved suicidality 15.6% (68/437).

There were 4 patients who had attempted suicide the week before entering the study. No patient attempted or completed suicide during the 12 weeks of acute treatment. However, one patient attempted suicide during maintenance treatment, and one patient completed suicide after leaving the study and discontinuing treatment against medical advice.

Hypothesis 1. Association of suicidality with the presence of chronic/recurrent depressive illness, anxiety, and agitation before treatment (Table 1).

Patients with persistent suicidality had their first episode of depression on average 9 years earlier than non-suicidal patients or patients whose suicidality resolved and were more likely to have recurrent episodes than the resolved and non-suicidal groups. Patients in all three suicidal groups reported lower self-esteem (ISEL self-esteem score) than the non-suicidal patients, while

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Table 1
Sociodemographic and clinical characteristics of patients based on the presence/absence of suicidality (mean±SD)

<table>
<thead>
<tr>
<th></th>
<th>Non-suicidal (N=104)</th>
<th>Resolved suicidality (N=68)</th>
<th>Persistent suicidality (N=55)</th>
<th>Emergent suicidality (N=34)</th>
<th>F or χ²</th>
<th>Df</th>
<th>p</th>
<th>Post-hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73.1 (6.8)</td>
<td>73.3 (7.9)</td>
<td>70.3 (8.9)</td>
<td>73.4 (7.4)</td>
<td>2.05</td>
<td>257</td>
<td>.11</td>
<td></td>
</tr>
<tr>
<td>% Men</td>
<td>28</td>
<td>25</td>
<td>31</td>
<td>24</td>
<td>0.80</td>
<td>3</td>
<td>.85</td>
<td></td>
</tr>
<tr>
<td>% White</td>
<td>84</td>
<td>93</td>
<td>96</td>
<td>94</td>
<td>8.33</td>
<td>3</td>
<td>.04</td>
<td>NP</td>
</tr>
<tr>
<td>Education (years)</td>
<td>12.3 (2.7)</td>
<td>12.6 (3.3)</td>
<td>12.3 (2.6)</td>
<td>12.5 (2.5)</td>
<td>0.19</td>
<td>256</td>
<td>.90</td>
<td></td>
</tr>
<tr>
<td>CIRS-G²</td>
<td>8.9 (3.7)</td>
<td>8.4 (3.9)</td>
<td>8.6 (4.8)</td>
<td>8.8 (3.7)</td>
<td>0.22</td>
<td>254</td>
<td>.88</td>
<td></td>
</tr>
<tr>
<td>% Recurrent depression</td>
<td>65 (54)</td>
<td>82</td>
<td>74</td>
<td>11.12</td>
<td>3</td>
<td>.02</td>
<td>NP, RP</td>
<td></td>
</tr>
<tr>
<td>Age of onset (lifetime)</td>
<td>60.4 (16.2)</td>
<td>60.4 (20.0)</td>
<td>51.1 (19.2)</td>
<td>53.4 (19.1)</td>
<td>4.15</td>
<td>249</td>
<td>.007</td>
<td>NP, RP</td>
</tr>
<tr>
<td>% Age of onset before age 60</td>
<td>37.8 (35.3)</td>
<td>63.0</td>
<td>63.6</td>
<td>16.21</td>
<td>3</td>
<td>.001</td>
<td>NE, NP, PR, RE</td>
<td></td>
</tr>
<tr>
<td>Hamilton-16 at week 0</td>
<td>18.9 (3.9)</td>
<td>20.0 (4.5)</td>
<td>19.6 (4.1)</td>
<td>19.7 (4.4)</td>
<td>1.03</td>
<td>257</td>
<td>.38</td>
<td></td>
</tr>
<tr>
<td>MMSE³</td>
<td>27.8 (2.7)</td>
<td>27.4 (2.7)</td>
<td>28.8 (1.8)</td>
<td>28.8 (1.5)</td>
<td>5.37</td>
<td>253</td>
<td>.002</td>
<td>PR, RE</td>
</tr>
<tr>
<td>ISEL-Self-esteem⁴</td>
<td>6.3 (2.9)</td>
<td>4.7 (2.8)</td>
<td>4.5 (3.2)</td>
<td>4.6 (3.2)</td>
<td>5.68</td>
<td>216</td>
<td>.001</td>
<td>NP, NR, NE</td>
</tr>
<tr>
<td>Agitation/anxiety⁵</td>
<td>4.5 (1.6)</td>
<td>4.4 (1.7)</td>
<td>4.5 (1.5)</td>
<td>4.5 (1.9)</td>
<td>0.06</td>
<td>257</td>
<td>.98</td>
<td></td>
</tr>
</tbody>
</table>

1CIRS-G: Cumulative Illness Rating Scale-Geriatric.
2HRSD: Hamilton Rating Scale for Depression.
3MMSE: Folstein Mini-Mental State Exam.
4ISEL: Interpersonal Support Evaluation List, ISEL-Self-esteem: positive comparison when comparing oneself to others.
5Agitation/anxiety: Hamilton Rating Scale of Depression aggregate score of items: item # 9 (agitation), item #10 (psychological anxiety), and item #11 (somatic anxiety).
perceived availability of material aid, perceived availability of someone to talk to and to do things with did not differ among the four groups. Pretreatment levels of anxiety and agitation, co-existing medical burden, and severity of the current depressive episode did not differ among the groups. The UKU akathisia item scores also did not differ among the four groups at baseline.

**Hypothesis 2.** Association of emergent and persistent suicidality with persisting low mood and high levels of anxiety/agitation or akathisia during treatment.

9. Association of suicidal status with remission of depression

A mixed-effect model indicated a significant group and group by time interaction (16-item HRSD: group \(F=10.76, df=3.296, p<0.0001\); interaction \(F=7.94, df=3.241, p<0.0001\)). The fixed-effect parameters from the model showed that all 3 suicidal groups had higher levels of depressive symptoms over the 12 weeks of treatment than the reference (non-suicidal) group (resolved: \(t=2.45, df=299, p<0.02\); persistent: \(t=5.56, df=294, p<0.0001\); emergent: \(t=2.76, df=298, p<0.0007\)). There was a significant group by time interaction for the emergent group compared to the non-suicidal group (\(t=3.85, df=245, p<0.0002\)). Patients with emergent suicidality had levels of depression similar to those with persistent suicidality, while patients with resolved suicidality had lower levels of depression than those with persistent suicidality (\(t=-3.00, df=294, p<0.003\)). The results for the mixed effects were the same when we included only patients who received combined pharmacotherapy and IPT.

10. Association of suicidal status with agitation/anxiety

The repeated-measures logit model indicated a significant group difference between the non-suicidal and those with persistent suicidality (\(Z=3.26, p<.002\)), as well as between those with resolved and persistent suicidality (\(Z=2.41, p<.02\)). Non-suicidal patients and those whose suicidality resolved were less likely to score \(\geq 2\) on items measuring anxiety or agitation than patients with persistent suicidality. A significant group-by-time interaction was found between patients with persistent and emergent ideation (\(Z=2.05, p<.05\)); the latter demonstrated an increase in the percentage of patients scoring \(\geq 2\) on anxiety or agitation by week 12.

10.1. Akathisia

Of the 161 patients with UKU data, 97 had no akathisia (score =0), and 64 patients had akathisia scores of \(\geq 1\) at any time during treatment. Only seven patients had moderate akathisia (score =2) and only one had severe akathisia (score =3). There was no significant difference among the groups: 40% of the non-suicidal, 26% of the emergent, 43% of the persistent, and 44% of the resolved suicidality patients had a score of 1 or higher at any time on the UKU akathisia item (\(\chi^2_3=1.84, p=0.61\)).

11. Adjunctive medication use during the 12-week treatment (Table 2)

Patients who had persistent suicidal ideation were significantly more likely to receive lithium augmentation than non-suicidal patients or those whose suicidality resolved. Patients with emergent or persistent suicidal ideation were significantly more likely to receive antidepressant augmentation than those whose suicidality resolved. The use of lorazepam as anxiolytic/hypnotic was similar across the groups.

**Hypothesis 3.** Potential effect of nortriptyline versus paroxetine on emergence of ideation.

We limited our comparison of the effects of nortriptyline vs. paroxetine to the patients who were treated under randomized double-blind conditions (NT/PX study) because important clinical characteristics that may have influenced suicidality (e.g., rate of recurrence of illness) differed in the two open-treatment studies (MTLD-1 and MTLD-2); and because the NT/PX study did not allow augmentation with a second antidepressant. In 61 patients treated under double-blind randomized conditions, the proportions of patients with...
emergent suicidal ideation and thoughts of death did not differ between treatments (1 subject [3%] received paroxetine and none [0%] received nortriptyline) (Fisher exact \(p=0.27\)).

12. Discussion

In 437 elderly patients with major depression during 12 weeks of acute treatment, 7.8% showed emergence of suicidality, 12.6% persistence, and 15.6% resolution. While at the inception of treatment the suicidal and non-suicidal groups had similar severity of symptoms, during treatment patients with emergent and persistent suicidality had higher levels of depression and anxiety than non-suicidal patients or those whose suicidality resolved. Emergent suicidality was associated with low self-esteem, earlier lifetime onset, and non-or partial response to treatment (as indicated by high levels of depression and anxiety), but not with akathisia. Patients randomized to nortriptyline or paroxetine were equally likely to have emergent suicidality, however, this last result should be interpreted cautiously because of the small sample size.

To our knowledge, no study has examined emergent, persistent, and resolved suicidality in older adults during treatment of depression. The current study extends our previous finding that depressed elderly who endorse suicidal ideation or recurrent thoughts of death for the first time during the third and fourth week of treatment, non-response and giving up hope of ever getting better may be a causal factor. The strengths of this study include a large study group of elderly depressed patients referred from both mental health specialty clinics and primary care offices who were well characterized at baseline, received protocolized treatment over 12 weeks, and were assessed weekly using well-defined, reliable methods. The studies included frail and old subjects, those who were 70 and older, and patients with “double” depression (i.e., major depression superimposed on dysthyemia).

Although the classification of suicidality based on the single suicide item of the HRSD administered weekly over 12 weeks was confirmed by the SSI scores, it is a limitation of the study that we did not have SSI scores in the whole sample for each time point. Based on the HRSD suicide item, 176 patients who were neither clearly suicidal nor clearly non-suicidal were excluded. Using scales more specific to the assessment of suicidal ideation may have increased our ability to identify suicidal ideators and to reduce the number of “ambiguous” cases. Visual inspection of the HRSD scores over time showed that the “ambiguous” group fell in between the two groups with best treatment response (non-suicidal and resolved) and the two groups with worse response (persistent and emergent suicidality).

We reported previously in a subsample of the current study group that 15.5% of our study participants had a life-time history of suicide attempt. Because we did not have data in the whole study group on previous episodes of suicidality, we could not investigate the relation of life-time ideation and attempts to the course of current suicidality. Nonetheless, despite the limited information available, the use of repeated assessments and the association observed with distinct patterns of treatment outcomes provide evidence of the clinical utility and validity of our classification of suicidality.

The relatively low rates of suicidality in part could be due to the exclusion of psychotic and bipolar patients. Even though the burden of co-existing medical illness in study participants was moderately high, patients who dropped out from the study \(N=36\) were medically more burdened than those who remained in the study. Hence, results may not be generalizable to the most frail elderly, who may be at the highest risk for completed suicide (Waern et al., 2002a).

We noted that African Americans were more likely to be in the non-suicidal group than Caucasians. It is unclear whether this reflects a real difference in rates of suicidal ideation, corresponding to lower elderly African American suicide rates, or whether the measures used are not sensitive to assess suicidality in African Americans.

The rate of emergent suicidality (7.8%) was lower than the rate of emergent suicidality reported in a sample of medication-free depressed adolescent outpatients who received psychotherapy over a 12–16 week period.
(12.5%) (11/88) (Bridge et al., 2005). In this study, a self-report measure (Beck Depression Inventory) was more sensitive in identifying suicidal adolescents than clinical interviews. Thus, the majority of patients who had denied significant suicidal ideation during the clinical interview and were classified as emergent ideators by the research staff, also had endorsed suicidal ideation on the BDI at the start of treatment. To ensure that we were not mistakenly classifying patients as non-suicidal at baseline and then as having emergent suicidality, we required patients with emergent suicidality to have a score 0 on the HRSD suicide item for two consecutive weeks (at baseline and after 1 week of treatment). Still, despite using repeated assessments and a structured interview (the HRSD), we cannot eliminate the possibility that some patients in the “emergent” group in fact were not free of suicidality at the time of the first two assessments, but were not willing to disclose it to the unfamiliar treatment team, e.g., because of fear of being hospitalized.

The fundamental question is whether the course of suicidal ideation in late-life reflects illness characteristics and relates to treatment response variability; or is an adverse consequence of treatment. Because of the absence of a placebo group, we cannot make any causal inference linking treatment to emergence of suicidality. Clinicians followed a treatment protocol that took into consideration the results of the weekly structured assessments and the global clinical picture. The fact that patients with emergent and persistent suicidality were more likely to be prescribed a second antidepressant suggests that these patients were not responding to the first-line treatment. Further, as their persistently higher levels of depression and anxiety indicate, they were less likely to respond to second-line treatment as well. We did not find an association between akathisia and suicidal status. We should emphasize that akathisia was assessed only in a limited part of the sample. Further, we cannot refute the possibility that the low rate of akathisia in the sample was due to the successful psychopharmacological management of the patients or the exclusion of psychotic patients, probably those with the most severe agitation. Our observation that patients with emergent suicidality had persistently high levels of depression and anxiety despite augmentation pharmacotherapy supports the importance of partial or non-response to the emergence of suicidality, rather than akathisia.

It is also clinically important that patients with emergent suicidality had lower level of self-esteem at baseline than non-suicidal patients similarly to those who presented with suicidality at the start of treatment. Patients with persistent suicidality had an age of onset of depression on average 9 years earlier than the non-suicidal and the resolved groups, and the greatest percentage with depression onset below age 60 — suggesting that this may be a more persistently depressed/dysthymic group in general.

While patients whose suicidal ideation resolves rapidly have a favorable illness course, similar to non-suicidal patients, those with persistent ideation present a significant challenge to clinicians. A small group of older patients with emerging suicidality share the characteristics and treatment course of these challenging patients. Our data indicate that patients with emergent and persistent suicidality have had a more chronic illness course compared to non-suicidal patients and those whose suicidality resolved, marked by an earlier age of onset and by the higher percentage of patients having recurrent depressive episodes. Thus, emergence of suicidal ideation or thoughts of death, though relatively infrequent, is clinically important and often a signal of difficult-to-treat-depression.

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