Occurrence and Course of Suicidality During Short-term Treatment of Late-Life Depression

Katalin Szanto, MD; Benoit H. Mulsant, MD; Patricia Houck, MSH; Mary Amanda Dew, PhD; Charles F. Reynolds III, MD

Background: Elderly persons (≥65 years) have the highest rate of suicide; still, little is known about the occurrence, course, and responsivity of suicidal ideation during treatment of depression in late life and how suicidality affects treatment response.

Methods: This study was undertaken to determine (1) how suicidal ideation changes during short-term depression treatment and (2) whether treatment response differs among 3 groups of patients based on their levels of suicidality at baseline and during treatment (those with a recent suicide attempt or current suicidal ideation [high-risk group; n=46], those with recurrent thoughts of death [moderate-risk group; n=143], or those with no suicide attempt, suicidal ideation, or thoughts of death [low-risk group; n=206]). This is a secondary analysis of pooled data from 3 treatment studies of late-life major depression. Participants were 395 elderly persons with a current major depressive episode, treated as inpatients or outpatients under protocolized conditions with paroxetine hydrochloride or nortriptyline hydrochloride, with or without interpersonal psychotherapy. Changes in suicidal ideation over time, rate of responses, and time to response in each group were compared.

Results: Suicidal ideation decreased rapidly early in the course of treatment, with more gradual change thereafter. At the beginning of treatment, 77.5% of the patients reported suicidal ideation, thoughts of death, or feelings that life is empty. After 12 weeks of treatment, suicidal ideation had resolved in all treated patients; 4.6% still reported thoughts of death. However, 6-week (P=.001) and 12-week (P=.02) rates of response were significantly lower in high-risk patients than in low- and moderate-risk patients. High- and moderate-risk patients needed a significantly (P<.001) longer time to respond than low-risk patients (median time to response, 6 and 5 vs 3 weeks).

Conclusions: While suicidal ideation resolves rapidly, the resolution of thoughts about death is more gradual. Suicidal elderly persons with depression require special attention during depression treatment because they have a lower response rate and need a longer time to respond.

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Suicidal ideation may be an important determinant of treatment outcome in patients with depression. Patients who feel hopeless, believe they would be better off dead, or think about killing themselves may have low or ambivalent motivation regarding treatment. Treatment compliance may be further compromised because many suicidal patients have difficulties relating to others (eg, deficits in building secure attachments). Thus, establishing and maintaining treatment alliance may be more difficult for these patients. In elderly persons (≥65 years), suicidal ideation, suicide attempts, and completed suicide occur most frequently in the context of major depression. Studies have shown the strong association between suicidal ideation and depressive disorders in diverse populations of elderly persons, including the general population, inpatients with acute medical illnesses, and patients in a dementia clinic.

In a group of elderly persons followed up naturalistically, the severity of depression was the most important determinant of contemporaneous suicidal ideation. Thus, adequate treatment of depression could be one of the most effective ways to reduce suicidal ideation and to prevent suicide. However, suicidality seems to be a trait (predisposing vulnerability) and a state (related to a depressive episode). Treating depression may be necessary, but not sufficient, to help suicidal patients become well. There is a paucity of empirical data on the course of suicidality in older patients with depression. It is assumed that suicidal ideation—as one of the symptoms of depression—resolves when de-
Examination; MTLD, maintenance therapies in late-life depression.

Tranylcypromine and reduce impulsivity and aggression13 suggests that antidepressants that increase serotonin neu-
tropathies with suicide ideators. Based on this finding, in the
other one in reducing suicidal ideation and behavior are
also lacking. There is no clear evidence whether certain
classes of antidepressants have differential efficacy. A re-
lation among impulsivity, aggression, suicidal behavior,
and serotonin disturbances has been established.12 This
suggests that antidepressants that increase serotonin neu-
rotransmission and reduce impulsivity and aggression13
(eg, the selective serotonin reuptake inhibitors [SSRIs])
may have a special role in the treatment of suicidal pa-
ients. Older suicidal people often contemplate suicide for
months, are less impulsive,14,15 and are less likely to have
a history of aggressive behavior than younger suicidal pa-
tients. Thus, SSRIs may not have an advantage in older sui-
cidal patients. To our knowledge, no published study has
contrasted the effect of SSRIs and other antidepressants
on the resolution of suicidal ideation in elderly patients.

To investigate these questions, we pooled data from 3
treatment studies of late-life major depression and ana-
lyzed the occurrence and course of suicidality in the par-
ticipants. In an earlier study,16 it was shown that older pa-
tients with depression who communicate a desire to die,
but state they would not kill themselves, share many simi-
larities with suicide ideators. Based on this finding, in the
present study, we classified patients into 3 groups based
on the highest level of suicidality reported 1 week before
and during treatment: high-risk group (recent attempt or
current suicidal ideation), moderate-risk group ( recur-
rent thoughts of death), and low-risk group (none of the
above). We compared the clinical characteristics, the drop-
out rates, and the time and rates of response of these 3
groups. We assessed the course of suicidal ideation dur-
ing 12 weeks. Finally, we assessed in a randomized sub-
group whether paroxetine hydrochloride or nortripty-
line hydrochloride had a differential effect on outcome in
the 3 groups.

Table 1. Description of the 3 Treatment Studies

<table>
<thead>
<tr>
<th>Variable</th>
<th>MTLD</th>
<th>Nortriptyline Hydrochloride–Paroxetine Hydrochloride Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruitment period</td>
<td>09/87-02/96</td>
<td>02/95-10/99</td>
</tr>
</tbody>
</table>
| No. of subjects who con-
tributed to the present analy-
sis                          | 169                   | 110                                                        |
| Inclusion criteria         | Nonpsychotic recurrent MDE | Nonpsychotic recurrent or single MDE                      |
| Age, y                    | ≥59                   | ≥69                                                       |
| Minimum score HRS D        | 15                    | 15                                                        |
| MMSE                      | 26                    | 20                                                        |
| Protocolized treatment*   | Open treatment with nortriptyline (plasma level, 80-120 ng/mL) and weekly IPT | Open treatment with paroxetine (dosage, 10-40 mg/d) and weekly IPT |
|                           |                       | Nortriptyline (plasma level, 50-120 ng/mL) or paroxetine (dosage, 20-40 mg/d) under double-blind randomized conditions |

Abbreviations: HRSD, Hamilton Depression Rating Scale; IPT, interpersonal psychotherapy; MDE, major depressive episode; MMSE, Mini-Mental State Examination; MTLD, maintenance therapies in late-life depression.

*All protocols allowed lorazepam as a rescue medication. No augmentation was used during the first 12 weeks of treatment.

This secondary analysis is based on data from 3 federally funded treatment studies of late-life major depression. Because the shortest study (of nortriptyline-paroxetine) was 12 weeks long, the data from the first 12 weeks of treatment were pooled as described elsewhere.17

METHODS

SUBJECTS

Table 1 summarizes the main characteristics of the 3 studies. The subjects were inpatients and outpatients with a mean (SD) age of 72.0 (7.4) years (age range, 59-95 years). They were recruited into 3 treatment studies of major depression: (1) maintenance therapies in late-life depression (MTLD)-1 was a study of maintenance therapies in persons with recurrent major depression, (2) MTLD-2 was a second study of maintenance therapies in persons with major depression, and (3) the nortriptyline-paroxetine study was a double-blind randomized comparison of nortriptyline and paroxetine. All patients met the criteria for a major depressive episode either based on Research Diagnostic Criteria, as established by a structured interview with the Schedule for Affective Disorders and Schizophrenia–Lifetime version18 (MTLD-1), or according to the DSM-IV, as established by the Structured Clinical Interview for DSM-IV19 (MTLD-2 and the nortriptyline-paroxetine study).20

All recruited patients from the 3 studies were included. Because 17 patients participated in 2 of the 3 studies, we included only data from the most recent trial, allowing for the most accurate characterization of these patients. Of the 395 participants included in these intervention studies, 21 had a history of alcohol abuse or dependence. Patients with current alcohol or other drug abuse were excluded from the trials. An unstable medical condition was also an exclusion criterion. However, most patients in all of the studies had several chronic medical problems, as shown by their mean (SD) Cumulative Illness Rating Scale for Geriatrics score of 8.6 (3.8) (range, 1-21).

TREATMENT

The pharmacologic treatment provided by the 3 studies is described in Table 1. During the short-term treatment phase of MTLD-1 and MTLD-2, doctoral- or master’s-level psychologists or social workers conducted weekly 45-minute interper-
sonal psychotherapy (IPT) sessions. The therapeutic foci were current interpersonal relationships in areas of role transition, role dispute, abnormal grief, and interpersonal deficits.21

Assessments

The 3 studies were conducted by the same study personnel at the same university-based research center. All subjects (or their authorized representative) provided written informed consent after the goals and procedures of the study were explained to them. Comparable assessment and treatment procedures were followed for the 3 studies. Subjects were assessed at baseline with the Hamilton Depression Rating Scale (HRSD),22 the Mini-Mental State Examination,23 and the Cumulative Illness Rating Scale for Geriatrics.24 In these 3 studies, all subjects were also rated weekly with the HRSD. Raters' training, measurements of interrater reliability for the HRSD, and reviews of diagnoses were performed regularly. Interrater reliability for the total HRSD score was excellent, as demonstrated by intraclass correlation coefficients of 0.78 to 0.95. In each of the 3 studies, the HRSD suicide item was asked in a standardized manner and the interrater reliability for this item was good: of 15 cases scored independently by 11 raters, there was only 1 case for which the scores differed by more than 1 point. In the MTLTD-1 and the MTLTD-2, HRSD ratings were obtained before the therapy sessions by an independent assessor.

Analysis

For this analysis, we used the HRSD suicide item (item 3; score, 0-4) to classify patients according to their highest score (ie, their highest level of suicidality) at any time during the 12 weeks of treatment. The serial use of suicide assessment increases the accuracy of identifying suicidal ideation. Suicidal ideation can occur at any point during a depressive episode, either persistently or intermittently, and patients may not reveal suicidal thoughts at the beginning of treatment to an unfamiliar clinician. The HRSD suicide item assesses suicidal behavior, suicidal thoughts, thoughts of death, and desire to live within the past 7 days. At any time during the 12 weeks of the study, patients with a score of 4 (ie, presenting after a suicide attempt) or 3 (ie, presenting with active suicidal thoughts) were classified as being at high risk for suicide; patients with a score of 2 (ie, reporting recurrent thoughts of death) were classified as being at moderate risk; and patients with a score of 1 (ie, denying suicidal ideation or thoughts of death, but reporting on direct questioning that life is empty or not worth living) or 0 (ie, denying all of the above) at all weeks were classified as being at low risk for suicide. Comparison of baseline demographic and clinical measures in the 3 groups was performed using χ² tests for categorical data and a 1-way analysis of variance for continuous measures. When there was a significant overall effect, post hoc comparisons were made with the Tukey pairwise test. The presence of suicidal ideation or thoughts of death (HRSD suicide item score ≥2) during the 12 weeks of treatment was analyzed with a repeated-measures logistic regression analysis in the whole sample.

Full treatment response was defined as achieving an HRSD total score of 10 or less, and partial response as a total HRSD score of 11 to 14. Response was classified on an intent-to-treat basis with last observation carried forward. Time to response (defined as the number of weeks required to reach a total score of 10 or less) was compared in the 3 groups with Kaplan-Meier survival analyses, and differences were tested using the Wilcoxon χ² test. A Cox proportional hazards regression analysis tested the effects of suicide group on time to response while controlling for variables that were related to suicidality, such as age, sex, age of lifetime onset of depression, recurrent vs single episode of depression, severity of depression (as indicated by the baseline HRSD score minus the suicide item score), and inpatient status. To compare the likelihood of response to nortriptyline or paroxetine in the 3 suicide risk groups, an analysis of response proportions using SAS statistical software (CATMOD; SAS Institute Inc, Cary, NC) with drug group, suicide risk group, and drug × suicide risk group interaction was performed. A significant drug × suicide risk group interaction would indicate that the treatment has a differential effect on response in the suicide risk groups. Finally, treatment response was reexamined in the 2 samples of subjects treated with combined antidepressant medication and IPT to assess the effect of IPT. Because patients were not randomized to IPT, and because of differences in the design of the studies, we could not perform a direct comparison of IPT with no IPT.

Results

Occurrence of Suicidality and Thoughts of Death

Of the 395 patients, 46 were classified as high risk (4 had a suicide attempt within 7 days before the beginning of treatment and 42 had suicidal ideation at least at one point during the 12 weeks of treatment), 143 reported thoughts of death, 141 reported that life is not worth living, and 65 did not report any of these. At baseline, 4 patients had a recent suicide attempt, 34 reported suicidal ideation, 120 had thoughts of death, 148 believed that life was empty, and 89 did not have any of these thoughts. Thus, 31 patients did not report either suicidal ideation or thoughts of death at baseline, but did so later during treatment: 8 reported suicidal ideation, and 23 reported thoughts of death. The emergence of suicidal ideation or thoughts of death was similar in patients treated with nortriptyline (17 [7.8%] of 219 patients) or paroxetine (14 [8.0%] of 176 patients).

The characteristics of the subjects classified according to their highest degree of suicidality are presented in Table 1. While the severity of depression (ie, HRSD total score minus suicide item score) was similar across the 3 groups, patients with an earlier lifetime age of onset or with recurrent episodes of depression were more likely to report suicidal ideation or thoughts of death than patients with a later onset or single episodes. Male sex increased the likelihood of suicidal ideation, but not thoughts about death.

Resolution of Ideation

Thoughts about death and suicide improved markedly in the whole group regardless of treatment assignment (repeated measures of logistic regression, z = −9.32, P < .001) (Figure 1).

At the beginning of treatment, 77.5% of the patients reported suicidal ideation, thoughts of death, or feelings that life is empty. By week 12, only 18.4% of the 239 patients for whom an HRSD score was available reported any of these thoughts; the remainder had a score of 0 on the HRSD suicide item (Figure 1). In the whole group, suicidal ideation decreased rapidly early in the course of treatment and then showed a more gradual change (Figure 1). Half of the patients (23 of 46 patients) who reported suicidal ideation or had a suicide attempt at the beginning of treatment later reported thoughts of death, which then per-
sisted in a small subgroup (n=8). At week 12, none of the patients who remained in treatment reported suicidal ideation, but 11 (4.6%) of 239 still reported thoughts of death. Of these 11 patients with persisting thoughts of death, 5 were treatment responders, 5 were partial responders, and 1 was a nonresponder. No patient attempted or completed suicide during short-term treatment. However, one patient attempted suicide twice during maintenance treatment and one patient completed suicide after leaving the study and discontinuing treatment against medical advice; both patients had suicidal ideation during the current episode.

TREATMENT DROPOUTS

Of the 395 patients who started treatment, 81 discontinued treatment before week 12 for various reasons (withdrawal of consent, intercurrent medical problems, medication adverse effects, emergence of psychotic symptoms, or hypomanic episode). We analyzed rates of treatment discontinuation in relation to suicide risk group. There were no statistical differences in the proportion of patients in the high, moderate, and low suicide risk groups who discontinued treatment for various reasons during the 12 weeks (13 [28.3%] of 46, 29 [20.3%] of 143, and 39 [18.9%] of 206 patients, respectively; \( \chi^2 = 2.02, P = .37 \)) and who withdrew consent and discontinued treatment against medical advice (5 [10.9%] of 46, 8 [5.6%] of 143, and 11 [5.3%] of 206 patients, respectively; \( \chi^2 = 1.93, P = .38 \)). Similarly, the median time to drop out did not differ significantly in the 3 groups (high-risk vs moderate- and low-risk groups, 3 vs 4 weeks; \( \chi^2 = 2.97, P = .23 \)).

TREATMENT RESPONSE

Low-risk patients were significantly more likely to be full responders by week 6 or 12 than moderate- or high-risk patients (Table 3). A post hoc comparison revealed that high-risk (\( P < .001 \)) and moderate-risk (\( P = .01 \)) patients had significantly lower rates of treatment response than low-risk patients at week 6, while at week 12, only high-risk patients had significantly (\( P = .005 \)) lower response rates than low-risk patients.

Results were similar when response rates were compared based on the HRSD total score minus the suicide item score (with response defined similarly as a total score \( \leq 10 \)): 176 (85.4%) of the 206 low-risk patients were responders, 110 (76.9%) of the 143 moderate-risk patients were responders, and 31 (67.4%) of the 46 high-risk patients were responders (\( \chi^2 = 30, P = .01 \)).

The time to response was longer in the high- and moderate-risk groups than in the low-risk group (\( \chi^2 = 25.49, P < .001 \) (Figure 2A)). Median times to response were 6 and 5 weeks in the high- and moderate-risk patients, respectively, compared with 3 weeks in the low-risk patients. When patients treated with nortriptyline or paroxetine were considered separately, times to response remained significantly longer in the high- and moderate-risk groups compared with the low-risk group (for patients treated with nortriptyline, Wilcoxon \( \chi^2 = 13.44, P = .001 \); and for patients treated with paroxetine, Wilcoxon \( \chi^2 = 8.11, P = .02 \) (Figure 2B and C, respectively). In a Cox proportional hazards multivariate regression model, increased time to response was significantly associated with higher suicide risk (\( \chi^2 = 10.24, P = .001 \)).

Table 3. Demographic and Baseline Clinical Characteristics of the 395 Patients Classified According to Their Suicide Risk

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>High (n = 46)</th>
<th>Moderate (n = 143)</th>
<th>Low (n = 206)</th>
<th>Statistic</th>
<th>( P ) Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>71.3 (8.2)</td>
<td>70.1 (7.7)</td>
<td>72.8 (6.9)</td>
<td>( F_{2,392} = 5.57 )</td>
<td>.005</td>
</tr>
<tr>
<td>Female sex‡</td>
<td>26 (56.5)</td>
<td>112 (78.3)</td>
<td>150 (72.6)</td>
<td>( \chi^2 = 8.35 )</td>
<td>.02</td>
</tr>
<tr>
<td>White race‡</td>
<td>44 (90.7)</td>
<td>134 (93.7)</td>
<td>181 (87.9)</td>
<td>( \chi^2 = 4.91 )</td>
<td>.09</td>
</tr>
<tr>
<td>Education, y</td>
<td>12 (2.5)</td>
<td>12 (2.5)</td>
<td>12 (2.5)</td>
<td>( F_{2,392} = 0.60 )</td>
<td>.55</td>
</tr>
<tr>
<td>MMSE score</td>
<td>283 (2.6)</td>
<td>282 (2.3)</td>
<td>277 (2.6)</td>
<td>( F_{2,392} = 1.86 )</td>
<td>.16</td>
</tr>
<tr>
<td>Cumulative Illness Rating</td>
<td>8.8 (4.5)</td>
<td>8.3 (3.8)</td>
<td>8.8 (3.7)</td>
<td>( F_{2,392} = 1.02 )</td>
<td>.36</td>
</tr>
<tr>
<td>Scale for Geriatrics score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifetime age of onset of depression, y</td>
<td>54.0 (21.8)</td>
<td>53.1 (17.9)</td>
<td>59.3 (17.5)</td>
<td>( F_{2,392} = 5.59 )</td>
<td>.005</td>
</tr>
<tr>
<td>Duration of the index episode, median (range), wk‡</td>
<td>24 (4-430)</td>
<td>21 (2-1482)</td>
<td>26 (2-1300)</td>
<td>( \chi^2 = 1.54 )</td>
<td>.46</td>
</tr>
<tr>
<td>Recurrent episode‡</td>
<td>35 (76.1)</td>
<td>109 (76.2)</td>
<td>128 (62.1)</td>
<td>( \chi^2 = 9.08 )</td>
<td>.02</td>
</tr>
<tr>
<td>Inpatient status‡</td>
<td>20 (43.5)</td>
<td>31 (21.7)</td>
<td>50 (24.3)</td>
<td>( \chi^2 = 9.07 )</td>
<td>.02</td>
</tr>
<tr>
<td>IPT‡</td>
<td>29 (63.0)</td>
<td>111 (77.6)</td>
<td>145 (70.4)</td>
<td>( \chi^2 = 4.35 )</td>
<td>.11</td>
</tr>
<tr>
<td>HRSD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score (17 items)</td>
<td>23.6 (3.5)</td>
<td>22.6 (4.3)</td>
<td>20.8 (3.7)</td>
<td>( F_{2,392} = 14.10 )</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total score minus suicide item score</td>
<td>19.1 (3.7)</td>
<td>19.4 (4.5)</td>
<td>19.1 (4.5)</td>
<td>( F_{2,392} = 0.26 )</td>
<td>.77</td>
</tr>
<tr>
<td>Score for the psychic and somatic anxiety items</td>
<td>3.6 (1.3)</td>
<td>3.7 (1.5)</td>
<td>3.7 (1.4)</td>
<td>( F_{2,392} = 0.18 )</td>
<td>.64</td>
</tr>
</tbody>
</table>

Abbreviations: HRSD, Hamilton Depression Rating Scale; IPT, interpersonal psychotherapy; MMSE, Mini-Mental State Examination.

†Tukey post hoc comparisons: the low-risk group differs significantly from the moderate-risk group for age, age of onset, and recurrent episodes and from the moderate- and high-risk groups for HRSD total score; and the high-risk group differs significantly from the low- and moderate-risk groups for sex.

‡Data are given as number (percentage) of patients.

§Kruskal-Wallis test of ranks.

| At baseline or any time during the 12-week treatment period.

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P = .001) and higher severity of depression (HRSD total score minus suicide item score, \( \chi^2 = 62.04, P < .001 \)). It was marginally associated with younger age of onset (\( \chi^2 = 3.72, P = .05 \)), but not with age (\( \chi^2 = 0.36, P = .55 \)), sex (\( \chi^2 = 1.83, P = .18 \)), recurrence status (\( \chi^2 = 0.13, P = .72 \)), or inpatient status (\( \chi^2 = 0.21, P = .65 \)). Because medical burden and treatment assignment may also have influenced treatment outcome, we controlled for these variables in a separate model, but they were not associated with time to response, and the other covariates were unchanged.

### POTENTIAL IMPACT OF IPT

When we examined only those patients who received combined treatment with medication and IPT, response rates and median time to response were similar to those of the whole sample.

### RESPONSE TO NORTRIPTYLINE OR PAROXETINE

We limited the comparison of the efficacy of nortriptyline and paroxetine to the patients who were treated un-
However, in an earlier study, it was shown that older elderly persons with depression are at high risk for suicide. In a large group of elderly persons, we found that view of life changes greatly during treatment of depression. At the beginning of treatment, only 22.5% of 395 elderly patients with depression denied suicidal ideation, thinking about death, or feeling that life is empty. After 12 weeks of treatment, this number increased to 81.6%. Elderly persons with early onset and recurrent episodes were more likely to report suicidal ideation than patients with late onset and single episodes. Suicidal elderly persons required a longer time to respond to treatment and had a lower rate of response than nonsuicidal elderly persons.

This report is based on a secondary analysis of a large group of elderly patients with depression who were well characterized at baseline, received protocolized treatment for 12 weeks, and were assessed weekly using well-defined methods. Using data from subjects who participated in 3 different studies and were treated with 2 different antidepressants increases the generalizability of the findings. However, our results may not be applicable to patients with psychotic symptoms or nonmajor depression, and we did not collect data on important suicide risk factors, such as hopelessness and social support. Also, we cannot assess the impact of current comorbid alcohol or other drug abuse or dependence because patients with these conditions were excluded from the 3 studies. Yet, the relationship we observed between earlier age of onset and level of suicidality may be because of a higher rate of (undetected) psychiatric comorbidities in patients with an earlier age of onset. Furthermore, our classification of high, moderate, and low suicide risk was based solely on the single suicide item of the HRSD. Using specific scales, such as the Scale for Suicide Ideation, may have increased our ability to identify suicidal ideators. Also, one could argue that all elderly persons with depression are at high risk for suicide. However, in an earlier study, it was shown that older patients with depression who are actively thinking about or planning to shorten their lives and patients who have thoughts about death and/or want to die differ from patients who think that life is empty or deny suicidal ideation or thoughts of death. Thus, in the present analyses of treatment response, we considered 3 groups with different risks based on their highest level of reported suicidality at baseline and during treatment: a high-risk group of patients with suicidal ideation or a recent suicide attempt, a moderate-risk group with thoughts about death, and a low-risk group with no such symptoms. Our observation of differential treatment response rates in relation to degree of suicide risk confirms the validity of this classification. The response rates in the high and moderate suicide risk groups were significantly lower compared with the rate in the low-risk group. However, in the low-risk group, patients who reported feeling that life is empty (119 of 141 or 84.4%) and those who denied any such feeling (56 of 65 or 86.2%) had similar 12-week response rates.

All of the patients who received IPT were treated openly, while the patients who did not receive IPT were treated under randomized double-blind conditions. Thus, we were not able to investigate the specific effect of combined IPT and antidepressants. Life events, especially losses that are frequent in late life, are independent risk factors for completed suicide. Psychotherapy may help patients who do not have confidence that they will get...
better to remain in treatment. Thus, it is conceivable that IPT in combination with antidepressants may provide additional benefits to older suicidal patients.

Comparing the effect of nortriptyline with that of paroxetine in suicidal patients, there was no difference in response rates and no evidence that patients treated with one antidepressant or the other were more likely to experience emergence of suicidal ideation or thoughts of death. Thus, our data do not support that suicidal patients respond better to SSRIs than to other classes of antidepressants or that SSRIs are associated with emergence of suicidality. Still, many clinicians prefer to use SSRIs in older suicidal patients because of their safety in instances of overdose and their more favorable adverse effect profile in elderly patients.

Our main finding is that high- and moderate-risk patients (ie, patients who report suicidal ideation or thoughts of death) were significantly less likely to be full responders after 6 or 12 weeks of treatment than low-risk patients, and those who responded required a longer time to do so (median, 6 and 5 vs 3 weeks). This finding seems to be robust because the observed differences were significant when data were analyzed using different statistical techniques and when controlling for potential confounders, such as age, age of onset, sex, recurrent vs single episode, inpatient status, and baseline severity of depression. Our findings are congruent with the results of a naturalistic follow-up study in which older patients with depression who had a history of a suicide attempt were less likely to remit than nonattempters. They also confirm the earlier findings from an analysis restricted to the patients in the MTLD-1 study. In this previous analysis, older patients with depression who had suicidal ideation were harder to treat than nonideators: ideators were more likely than nonideators to have received augmentation pharmacotherapy, and they were more likely to relapse during continuation treatment. However, when suicidal ideators were treated with augmentation therapy for up to 28 weeks, ideators had similar remission rates as nonideators. Taken together, these findings indicate that suicidal elderly persons require increased and persistent therapeutic attention.

Although there is a strong clinical belief that the risk of suicide increases as patients start to improve and regain the “initiative and energy that suicide requires,” the so-called roll-back phenomenon, we do not know of any published data directly supporting this belief. Our results actually suggest that suicidal ideation resolves rapidly in most patients who remain in treatment. Although the absence of data on suicidal ideation following dropping out of treatment limits inference, because the overall 12-week dropout rates and the median times to dropping out were not different in the 3 risk groups, it is unlikely that the sudden decrease in suicidal ideation is an artifact due to suicidal patients selectively leaving the study. Other studies have shown that suicidal ideation, insomnia, lack of appetite, and excessive guilt improved early, in contrast to a slower improvement in energy. Looking more closely at the course of suicidal ideation, half of the patients who had reported suicidal ideation at the beginning of treatment later reported thoughts of death, which then persisted in a small subgroup. Therefore, subtle signs of suicidality, such as thoughts of death, seem to respond to treatment more gradually. Waern et al emphasize that not only suicidal ideation but also life weariness and death wishes should be addressed in follow-up assessments. They warn that clinicians “neglect to discuss the topic at follow-up, assuming that suicidal feelings have dissipated as soon as other symptoms of depression begin to regress. However, residual symptoms may be a risk factor for suicide.”

In conclusion, the present data are encouraging for clinicians, elderly patients with depression, and patients’ families. View of life markedly changes in a positive direction during successful treatment of late-life depression. Still, persistence is needed to prevent suicides in older patients with depression; high-risk patients experience a slower and less robust response. Thus, they remain at a greater risk for a longer period. Furthermore, as an earlier study has shown, older suicidal patients are more likely to require augmentation pharmacotherapy and to relapse when treatment becomes less intensive. Therefore, treating depression in suicidal elderly persons may not be sufficient to prevent suicide. To design suicide-specific treatments, future studies have to identify the reasons for the lower and delayed treatment response in older suicidal patients. These studies will need to gather more data on potential mediators, including persistent hopelessness, comorbid anxiety or personality characteristics, and social support.

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