Suicidal Behavior Differs Among Early and Late Adolescents Treated With Antidepressant Agents

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KEY WORDS

suicide, adolescents, depression

ABBREVIATION

ICD-9-CM—*International Classification of Diseases, Ninth Revision, Clinical Modification*

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WHAT'S KNOWN ON THIS SUBJECT: Adolescent suicidal behavior is a major public health problem. Late adolescents (aged 15–18 years) have higher rates of suicide and suicidal behavior than early adolescents (aged 10–14 years), which possibly reflects differences in developmental stage, psychopathology, or methods used.

WHAT THIS STUDY ADDS: In 250 episodes of suicidal behavior from a cohort of adolescents prescribed antidepressants, 85.2% involved medication ingestion and half had previous attempts. Suicidal behavior among early and late adolescents differed in methods used, presence of psychotic disorders, and abuse history.

abstract

OBJECTIVE: To identify circumstances and characteristics of suicidal behavior among early (aged 10–14 years) and late (aged 15–18 years) adolescents from a cohort of youth who were prescribed antidepressant medication.

METHODS: In-depth reviews of all available medical records were performed for 250 randomly chosen confirmed episodes of suicidal behavior identified as part of a large retrospective cohort study of antidepressant users and suicidal behavior. Study data were obtained from Tennessee Medicaid records and death certificates from January 1, 1995, to December 31, 2006. Medical records and autopsy reports for cases identified from electronic data were adjudicated by 2 investigators blinded to exposure status and classified by using a validated scale.

RESULTS: Of the 250 cases reviewed, 65.6% were female and 26.4% were aged 10 to 14 years. Medication ingestion was the most frequent method of suicidal behavior for both early and late adolescents; however, early adolescents were significantly more likely to use hanging as a method of suicide. Nearly one-half of the adolescents had previously attempted suicide. Early adolescents were significantly more likely to have a history of sexual abuse and significantly less likely to have a history of substance abuse. Early adolescents were also significantly more likely than older adolescents to have a history of a psychotic disorder and to report hallucinations before the suicide attempt.

CONCLUSION: Suicidal behavior among early and late adolescents prescribed antidepressant medication differed in terms of methods used, previous psychiatric history, and proximal symptoms. *Pediatrics* 2011; 128:447–454

Suicide is the third leading cause of death among adolescents in the United States, and suicidal behavior represents one of the greatest public health issues for this population.^{1,2} In a biannual nationally representative survey of youths attending high school, 6% to 9% of 9th- to 12th-graders reported attempting suicide in the year before the survey and 2% to 3% reported seeking medical attention for suicidal behavior.³ Late adolescents (usually defined as youth aged 15–18 years) have higher rates of suicide and suicidal behavior than early adolescents (youth aged 10–14 years).⁴ The disparity in rates has been attributed to an increased prevalence of psychopathology, particularly substance abuse, and increased suicidal intent among late adolescents.^{5–7}

Adolescents treated with antidepressant agents are an important risk group for suicidal behavior because of the association between depression and suicide and recent concerns that some antidepressant agents may actually increase suicide risk for young people.^{8,9} Despite this widespread interest, little is known about the circumstances and characteristics of suicidal behavior by adolescents who are prescribed these agents. Information about the characteristics of suicidal behavior is crucial for clinicians who care for adolescents taking antidepressant agents and public health scientists interested in identifying risk factors for suicidal behavior. Understanding how suicidal behavior changes during adolescence given the rapid physical, cognitive, and social transformations occurring during this developmental phase is critical to further addressing this important public health problem.

The present study used Medicaid claims data augmented with in-depth chart review of all available medical records to identify, confirm, and

characterize medically treated suicidal behavior among early and late adolescents with prescriptions for antidepressant agents. The specific aims of the study were to (1) identify circumstances and characteristics of suicidal behavior among adolescents prescribed antidepressant medication and (2) compare these characteristics for youth in early and late adolescence.

METHODS

Sources of Data

The study was performed as part of an ongoing retrospective cohort study of antidepressant agents and suicidal behavior severe enough to require medical treatment in children and adolescents, which included 80 183 users of antidepressant agents. Study data were obtained from TennCare (Tennessee's Medicaid program), state hospital discharge records, state vital records files, and medical records from January 1, 1995, to December 31, 2006.

Cohort Assembly

In the larger study, TennCare pharmacy files were used to identify children and adolescents, ages 6 to 18 years, who had prescriptions filled for antidepressant agents during the study period. These agents included selective serotonin reuptake inhibitors (fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, and escitalopram), serotonin-norepinephrine reuptake inhibitors (venlafaxine and duloxetine), atypical antidepressant agents (mirtazapine, bupropion, trazodone, and nefazodone), cyclic antidepressant agents (imipramine, amitriptyline, clomipramine, desipramine, nortriptyline, protriptyline, doxepin, trimipramine, amoxapine, and maprotiline), and monoamine oxidase inhibitors (phenelzine, tranylcypromine, and isocarboxazid). Subjects were followed up from the first date of filling an antidepressant until (1) the last day

of the study, (2) their 19th birthday, (3) the date of death, (4) loss of TennCare enrollment for >7 days, (5) failure to fill an antidepressant prescription for 180 consecutive days, or (6) the day before the date of a medical claim for a life-threatening illness.

Identification of Potential Suicidal Behavior

TennCare claims (outpatient encounters, emergency department visits, and hospitalizations) and linked death certificates were searched to identify possible suicidal behavior occurring during follow-up using diagnostic codes that have been previously validated in population-based studies of suicide epidemiology.^{10,11} Potential suicidal behavior was identified by using *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) (claims) codes and *International Classification of Diseases, 10th Revision* codes (death certificates) for suicide and self-inflicted injury (E950–E959), injury undetermined whether accidentally or purposely inflicted, including injuries incurred by laceration or firearms (E980–E989 and E922), poisonings (960–979; E850–E858; E860–E869), fall from height (E881, E882, and E884), suffocation (E913), asphyxiation and strangulation (994.7), and motor vehicle accidents (E810, E815, and E816). For emergency department visits and hospitalizations, ICD-9-CM codes for significant intracranial injury (851–853 and 348.4), open wound of chest, back, or other site (875, 876, and 879), and internal injuries of the thorax, abdomen, or pelvis (860–869) were also identified.

Medical Record Confirmation of Suicidal Behavior

Medical records from encounters, including the selected ICD-9-CM codes, were requested from the facility where the subject received care, including re-

cords from emergency medical services, emergency department visits, hospitalizations (medical and psychiatric), and autopsies (for deaths). Trained nurses, unaware of medication exposure status, then used a standardized medical records abstraction form to review demographic characteristics of potential episodes of suicidal behavior to ensure that the appropriate subject was identified. Nurses were instructed to copy selected sections of the medical records, including the face sheet, discharge summary (for hospitalizations), history and physical, nursing notes, consultation notes from mental health providers, and disposition/discharge instructions. The nurses removed all identifying information from the copies before they were forwarded. The medical records were then reviewed to determine if the injury was self-inflicted and if intent to die was explicitly stated or could be inferred from the clinical documentation. Two physicians (Drs Callahan and Cooper) independently reviewed all potential cases. Using the Columbia Suicidality Classification Scale, self-injurious events were categorized as follows: completed suicide; attempted suicide; preparatory actions toward suicidal behavior; self-injurious behavior, intent unknown; self-injurious behavior, no suicidal intent; and suicidal ideation only.¹² Initially, both physicians reviewed 100 probable cases and found a 98% agreement in case status; thereafter, a 10% random sample was abstracted by the second reviewer, with 98% agreement.

Study Variables

For this study, a random sample of 250 confirmed cases of suicidal behavior (ie, completed or attempted suicide) from 3148 cases reviewed for the larger study were selected for in-depth review. One investigator (Dr Hysinger) performed all the in-depth reviews,

with a 10% sample reabstracted by a second author to confirm accuracy (Dr Callahan). Interrater reliability was 97%. Information recorded in the in-depth review was drawn from previous descriptions of psychological autopsies, including methods used, circumstances preceding the event, precipitating factors, psychiatric symptoms, family and personal psychiatric history, actions taken after the event, and treatment required.^{13–15} The method of self-injury was characterized, including names and amounts of medications for ingestions. Circumstances preceding the suicidal behavior—such as interpersonal problems (fights/arguments with nonromantic relations), failures in school, romantic relationship problems (arguments, termination of a relationship, or threat of termination of a relationship with a significant other), job problems, financial problems, parental divorce, death of a loved one, and other stressful events—were identified.^{16,17} Psychiatric symptoms associated with suicidal behavior (depressed mood, irritability, hopelessness, anxiety, rage, hallucination, manic/hypomanic symptoms, command hallucinations, and panic) within 2 weeks before the event or during evaluation were recorded.^{18–20} Family history of mental illness and completed/attempted suicide and abuse were included.^{17,21–23} We also characterized actions taken after the event (communication of event, witnesses of event, attempts to prevent discovery, and seeking medical care), as well as information about medical treatment and disposition.

Statistical Analysis

To assess differences in the characteristics of suicidal behavior among early versus late adolescents, we compared events for subjects aged 10 to 14 years (early adolescents) with those aged 15 to 18 years (late adolescents) at the time of the event. The age range was

chosen on the basis of previous literature and clinical judgment of the differences in development for younger versus older adolescents.⁵ χ^2 tests were used to assess differences in sociodemographic characteristics, psychiatric symptoms, family history, and event characteristics, and Fisher's exact test was used when appropriate using R Foundation for Statistical Computing 2.12.²⁴

Permission to use the study data were obtained from the Tennessee Department of Health and the TennCare Bureau. The study was reviewed and approved by the Vanderbilt University institutional review board.

RESULTS

Nearly two-thirds of the 250 adolescents with confirmed suicidal behavior were female, with 56.1% of early adolescents and 69.0% of late adolescents being female (Table 1). By far, the most common method of suicidal behavior was ingestion, used by 85.2% of the adolescents. When ingestion was not the method used, early and late adolescents differed in the means of suicidal behavior. Hanging was ~5 times more common among early adolescents than late adolescents (10.6% vs 2.2%; $P = .01$). Suicidal behavior was severe enough to require hospitalization in 81.2% of the subjects. There were no significant differences in medical or psychiatric hospitalization for early and late adolescents. Just <1% of the confirmed cases resulted in death, with no significant difference in the proportion of completed suicide for early versus late adolescents.

Approximately one-half of the adolescents had a history of a previous suicide attempt (Fig 1A); 15% had ≥ 2 suicide attempts. Early adolescents were nearly twice as likely to report a previous history of sexual abuse (29% vs 16%; $P < .05$). Late adolescents were much more likely to report cannabis,

TABLE 1 Characteristics of Confirmed Suicidal Behavior Grouped According to Early and Late Adolescents Treated With Antidepressant Medications

	Total (<i>N</i> = 250), %	Early Adolescents (10–14 y) (<i>n</i> = 66), %	Late Adolescents (15–18 y) (<i>n</i> = 184), %	<i>P</i> ^a
Gender				
Female	65.6	56.1	69.0	.06
Male	34.4	43.9	31.0	
Race				
White	80.0	74.2	82.1	.24
Black	18.8	25.8	16.3	.13
Other	1.2	0	1.6	.57
Method of self-harm				
Ingestion	85.2	81.8	86.4	.48
Cutting/stabbing	9.6	7.6	10.3	.68
Hanging	4.4	10.6	2.2	.01
Firearms	0.4	0	0.5	.99
Other	0.4	0	0.5	.99
Treatment required				
Medical hospitalization, any	37.2	39.4	36.4	.77
Psychiatric hospitalization, any	72.0	81.8	68.5	.06
Completed suicide	0.8	1.5	0.5	.46

^a Comparison by χ^2 and Fisher exact tests as appropriate.

alcohol, or other illicit drug abuse than early adolescents ($P \leq .01$). Compared with late adolescents, early adoles-

cents were more likely to have a history of a psychotic disorder (8% vs 2%; $P < .05$) (Fig 1B). The 2 groups did not

differ in terms of the proportion with a history of depression, bipolar disorder, oppositional defiant disorder, anxiety, or conduct disorder.

Interpersonal conflict, usually with a parent or family member, was the documented precipitant in the majority of occurrences of suicidal behavior and was significantly more common among early than late adolescents (85% vs 64%; $P \leq .01$) (Fig 1C). School problems were the next most frequently documented precipitant for early and late adolescents. Romantic relationships were significantly more likely to be documented as a precipitant for late adolescents than for early adolescents (26% vs 9%; $P \leq .01$). The groups did not significantly differ with respect to the proportion reporting school problems, legal problems,

FIGURE 1

Characteristics of early and late adolescents with confirmed suicide attempts in a cohort of patients prescribed antidepressant agents. A, Historical risk factors for suicidal behavior; B, current or past psychiatric disorders; C, precipitants or stressors; D, key symptoms before event. ^a $P < .05$; ^b $P \leq .01$.

death of a loved one, or parental divorce.

Depressed mood was more commonly reported among early adolescents than late adolescents (99% vs 90%; $P < .05$) (Fig 1D). Irritability, a closely related symptom to depressed mood, was also reported for more than one-half of early and late adolescents (61% vs 53%; P not significant). Taken together, 99% of early adolescents and 95% of late adolescents with suicidal behavior had documentation of depressed and/or irritable mood (data not shown; P not significant). Early adolescents were also more likely to report hallucinations (27% vs 10%; $P \leq .01$). Among early adolescents, 21% reported auditory hallucinations, 15% reported command hallucinations, and 14% reported visual hallucinations, all more commonly than late adolescents (all $P < .05$). The 2 groups were similar in terms of the proportion reporting hopelessness, anxiety, rage, or manic symptoms, including insomnia, mood lability, risk taking, impulsivity, increased energy, and grandiosity.

Because ingestions were the most common method of suicidal behavior, we further characterized the substances ingested among confirmed cases. Forty percent of ingestion-related suicidal behavior by both early and late adolescents involved ingestion of ≥ 2 substances. Medications were used in 95% of ingestions, including psychotropic medications, over-the-counter medications, and antibiotics. Early adolescents were significantly more likely than late adolescents to take antipsychotic agents as a suicidal behavior (24.1% vs 9.4%; $P = .01$) and significantly less likely to ingest nonsteroidal antiinflammatory drugs (0% vs 13.8%; $P = .003$) (Table 2). Early adolescents were significantly more likely than late adolescents to ingest nonmedicinal chemicals as a means of suicidal behavior (11.1% vs 2.5%; $P = .02$). The most common nonmedicinal

TABLE 2 Substances Ingested During Confirmed Episodes of Suicidal Behavior Among Early and Late Adolescents Who Were Treated With Antidepressant Medications

	Total (<i>N</i> = 213), %	Early Adolescents (<i>n</i> = 54), %	Late Adolescents (<i>n</i> = 159), %	<i>P</i> ^a
Selective serotonin reuptake inhibitor	31.9	33.3	31.4	NS
Tricyclic antidepressant agent	14.1	13.0	14.5	NS
Antipsychotic agent	13.1	24.1	9.4	.01
Benzodiazepine	13.1	9.3	14.5	NS
Antihistamine	12.2	16.7	10.6	NS
Acetaminophen	11.7	9.3	12.6	NS
Nonsteroidal anti-inflammatory drug	10.3	0.0	13.8	.003
Mood stabilizer	9.9	7.4	10.6	NS
Psychostimulants	5.6	5.6	5.7	NS
Antibiotics	4.7	5.6	4.4	NS
Trazodone	4.7	1.9	5.7	NS
Other medications	33.3	29.8	34.7	NS
Nonmedicinal chemicals	4.7	11.1	2.5	.02

Sum of columns exceeds 100% because of multisubstance ingestions.

^a Comparison using χ^2 and Fisher's exact tests as appropriate.

chemicals ingested were mouthwash, peroxide, bleach, gasoline, and nail polish remover.

DISCUSSION

In this group of 250 confirmed episodes of suicidal behavior randomly selected from cases identified in a cohort of adolescents treated with antidepressant agents, >85% of the cases involved ingestion of medications. Approximately one-half of the confirmed cases had previous suicide attempts. Early adolescents differed from late adolescents in terms of the methods used, presence of psychotic disorders, history of sexual abuse, and presence of hallucinations. In addition, the 2 groups differed in terms of the agents ingested during episodes of suicidal behavior. This study is one of the first to describe differences in suicidal behavior between early and late adolescents. These differences warrant further study in larger and more heterogeneous adolescent populations but suggest potential targets for suicide screening and prevention that have important implications for health care providers and public health scientists.

Many adolescent suicide attempts occur impulsively in the setting of a crisis with little or no warning.²⁵ However, suicidal behavior may also be a seri-

ous manifestation of adolescent depression. It is likely that some of the differences between early and late adolescent suicidal behavior described in this study reflect the developmental differences between the 2 groups. Adolescence is a dynamic period characterized by rapid physical, social, and cognitive growth.²⁶ Adolescent development is also characterized by increasing independence and shifting in the relative importance of relationships with parents, other family members, and peers.²⁶ Cognitively, adolescence is characterized by the progression from concrete ("here and now") thinking to abstract thinking and the ability to consider alternatives and consequences to proposed actions.²⁷ These changes may provide insight into the differences observed between early and late adolescent suicidal behavior in this study. For example, early adolescents were more likely than late adolescents to use hanging as a means of suicide. As concrete thinkers, early adolescents may be less likely to recognize a larger array of options for means of suicide and may not appreciate the physical and emotional consequences of violent methods to themselves and others. It is also possible that access to means of suicidal behavior is more limited for

early adolescents relative to late adolescents.

Historical risk factors for adolescent suicidal behavior are likely to be particularly important for clinicians and public health officials. Consistent with other studies showing that suicidal behavior is an important risk factor for later suicide attempts,^{1,2,5} about one-half of the medical records of early and late adolescent suicidal behavior in this study included documentation of previous suicidal behavior. In addition, nearly 1 in 4 subjects in this study reported either physical or sexual abuse, which is 20 times the reported national average.²⁸ This finding is consistent with previous research demonstrating a strong correlation between child and adolescent abuse and suicidal behavior.^{16,21,29–31} Abuse during childhood and adolescence has also been associated with poor development in areas of cognition, emotion, and social networks, which may vary with developmental stage. This maladaptation may lead to poor academic performance, fewer coping strategies, increased aggressive and uncontrolled behavior, low self-esteem, social isolation, and inappropriate peer relationships, which are all known risk factors for suicidal behavior.^{32–34} The range of psychiatric symptoms, including reported hallucinations in early adolescents, may reflect the trauma of previous abuse.

Changes in family and social relationships related to adolescent development are likely to explain some of the differences in precipitating events observed before suicidal behavior. Interpersonal conflict, particularly with parents, was the most common precipitant reported for all adolescents and was more common in early adolescents.^{35,36} Relationships with parents during early adolescence may be particularly tumultuous as the adolescents seek to develop identity and au-

tonomy and there is growing importance of the influence of peers. The increasing significance of romantic relationships throughout adolescence parallels our study's finding of a higher occurrence of conflict with a romantic partner as a precipitant of suicidal behavior in late adolescents than in early adolescents.^{37,38}

In this study of youth who were prescribed antidepressant medications, depressed and/or irritable mood was almost universally documented as a precedent symptom of suicidal behavior for both early and late adolescents. Hopelessness, anxiety, rage, and hallucinations, although documented less frequently, were still relatively common symptoms preceding suicidal behavior. The presence of hallucinations was more frequently documented as a symptom in early than late adolescent suicidal events. A growing body of literature suggests that hallucinations and other symptoms of psychosis are common in psychiatric illnesses during adolescence and that symptoms are predictive, but not pathognomonic, of future psychotic illness.³⁹ Although additional research is needed, the report of hallucinations, particularly among early adolescents, may have important short- and long-term implications for youth and warrant additional investigation by clinicians.

Our study has important limitations. The study population consisted of adolescents enrolled in TennCare and may not be generalizable to other adolescents. However, during the study period, TennCare covered ~30% of Tennessee children, which represents an important population at-risk for medical and mental health disorders.⁴⁰ Nationwide, ~20% of children are enrolled in Medicaid programs. The study cohort consisted of patients who filled prescriptions for antidepressant agents, which may limit its generalizability to the larger population of ado-

lescents. However, given the increasing use of antidepressant agents in all children,^{41,42} understanding the characteristics of suicidal behavior among antidepressant users is important. We only included adolescents with medically treated suicide attempts; thus, adolescents with suicidal behavior who did not enter the health care system were not included. Some of the differences between early and late adolescents in characteristics and potential risk factors for suicidal behavior represent small actual numbers and should be interpreted with caution. Finally, the majority of patients seeking care for suicidal behavior were evaluated in acute care settings where the treating clinicians are less likely to have a relationship with the patient and may not have access to previous medical records. The strengths of the study include the relatively large sample size and the structured chart review and adjudication of suicidal behavior.

CONCLUSIONS

Recognizing suicidal behavior is a critical step to preventing suicide and improving adolescent public health. This study suggests that although there are many commonalities in early and late adolescent suicidal behavior, there are also potentially important differences. These differences may be reflective of adolescent growth and development, highlighting the need to better understand how potential risks, precipitants, and characteristics of suicidal behavior may change during adolescent development.

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INTERVIEWING FOR MEDICAL SCHOOL: *Do you remember your interviews for medical school? Some, I will never forget. My favorite interview lasted almost an hour and we spent the entire time debating the relative merits of the British versus American political systems. Now, as an interviewer for the college of medicine, I like to discuss current events and tend to avoid the classic “why do you want to go into medicine” question, as too often the response seems practiced. Soon however, the medical school interview as we currently know it may disappear. As reported in The New York Times (Health: July 10, 2011), eight medical schools in the U.S., including the newest, and 13 medical schools in Canada use the multiple mini interview or M.M.I. to help guide the selection process. In one school’s M.M.I., applicants rotate through nine rooms. Taped to the door of each room is a slip of paper describing an ethical dilemma. Applicants have two minutes to review the information presented before entering the room to discuss the situation. The “interview” or discussion only lasts eight minutes before the applicant moves on to the next door and ethical challenge. The goal of the M.M.I. is to better assess applicant communication and social skills. School officials are quick to state that there are no wrong answers. Instead, the schools want to learn how the applicant thinks on his or her feet and interacts with the interviewer, particularly when the interviewer disagrees. Applicants who are too opinionated, jump to conclusions, or fail to listen are rated poorly. Proponents of the M.M.I. state that the system is designed to identify applicants with good social and communication skills, attributes that are essential to today’s modern team based approach to health care. The M.M.I. system was developed after research showed that most interviewers form an opinion of an applicant early and infrequently change that opinion. Moreover, situational interviews expose character flaws better than personal interviews. Rotating through multiple stations with multiple interviewers removes bias. The M.M.I. has been shown to correlate well with future tests of decision making, cultural sensitivity, and patient communication skills. While some students who have gone through the M.M.I. applaud the emphasis on problem solving and communication, others have not been as enthusiastic about the experience. Still, if we are seeking to ensure that our graduating medical students have superb communication skills, screening for that at the time of entry seems a reasonable idea—even if it means I can no longer spend 30 minutes discussing the current events of the day with an applicant.*

Noted by WVR, MD