Antidepressants and Youth Suicide in New York City, 1999–2002

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ABSTRACT

Objective: To determine the proportion of youth suicides in New York City from 1999 to 2002 in which antidepressants were detected at autopsy. **Method:** This is a medical examiner surveillance study of suicides in New York City among those younger than 18 years of age. The outcome measure is serum toxicology for antidepressants. **Results:** From 1999 through 2002, there were 41 individuals younger than 18 years of age among residents of New York City who committed suicide. Thirty-six (87.8%) had a serum toxicological analysis and an injury death interval of 3 days or less. There was one (2.8%) suicide in which both buproprion and sertraline were detected at the time of autopsy. Antidepressants were not detected in any of the other youth suicides. **Conclusions:** The detection of antidepressants at autopsy was quite rare in youth suicides in New York City from 1999 to 2002. *J. Am. Acad. Child Adolesc. Psychiatry,* 2006;45(9):1054–1058.
Key Words: antidepressant, selective serotonin reuptake inhibitors, suicide.

There has been concern recently about a link between antidepressants and suicidal ideation and attempts. In 2003, the Medicines and Healthcare Products Regulatory Agency (MHRA) of the United Kingdom issued a warning that with the exception of fluoxetine, the benefits of antidepressant use in patients younger than 18 years of age do not outweigh the risks. This was based on reanalyses of placebo-controlled, randomized clinical trials (RCTs) for which a final report was issued in December 2004 (Committee on Safety of Medicines, 2004).

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The U.S. Food and Drug Administration (FDA) subsequently conducted meta-analyses of data from 25 RCTs of antidepressants for depression, anxiety, and attention-deficit/hyperactivity disorder in children and adolescents and presented those results to joint meetings of the Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee (Hammad, 2004). (*Note:* The February 2004 FDA Advisory meeting examined 24 RCTs, whereas the September 2004 meeting also included the data from the Treatment for Adolescents with Depression Study [March et al., 2004].) Only four of those RCTs demonstrated antidepressant efficacy on the primary outcome. Furthermore, in aggregate across the RCTs, there was a statistically significant twofold elevation in risk of suicide attempts or ideation among subjects on active medication relative to those on placebo. These findings are disquieting and suggest that the risk/benefit ratio involved in use of antidepressants among youths may be unacceptable. As a result, the FDA issued a black box warning regarding the need to monitor for worsening of clinical symptoms and suicide risk in children, adolescents, and adults taking antidepressants (U.S. Food and Drug Administration, 2004a).

The FDA warning was based on suicidal ideation and suicide attempts among subjects in the pediatric

antidepressant RCTs. There were no suicides in the more than 4,800 subjects who participated in the 25 RCTs that were examined. In contrast, in a population-based study, we examine in this article whether the association between antidepressants and suicidality extends beyond suicidal ideation and suicide attempts and applies to the most adverse outcome in the range of suicidal behavior, suicide deaths, as well. The objective of this article is to report the proportion of youth suicides in New York City who had antidepressants detected at autopsy from 1999 to 2002.

METHOD

Study Sample

This is a medical examiner surveillance study of people younger than 18 years of age who committed suicide in New York City. The Office of New York City Chief Medical Examiner investigates all deaths believed to be suicides, homicides, or accidents and instances of death unattended by a physician. The circumstances and environment of the fatality including evidence gathered at the investigation of the death scene (e.g., notes), statements from family and friends, the decedent's psychiatric and other medical history, and toxicological data all are used to determine the manner of death and specifically to distinguish between a suicide and an accident.

Our research group manually reviewed the medical files of each suicide that was certified by the Chief Medical Examiner of New York City from 1990 through 2002 with funding from the National Institute of Drug Abuse (R01DA06534, Principal Investigator: Kenneth Tardiff, M.D.). Elsewhere, we reported the results of toxicologic analyses of a variety of psychotropic drugs in suicides (Marzuk et al., 1995) and antidepressants in youth suicide from 1993 to 1998 (Leon et al., 2004). In this report, we included suicides that occurred from 1999 to 2002 among New York City residents younger than age 18 years. Inclusion criteria required that victims had undergone systematic toxicological analysis for antidepressant drugs. Furthermore, we recorded the injury–death interval for all cases. Based on the elimination half-life of the various antidepressants (Baselt, 2002), which ranges from hours to several days, we did not include toxicological results for those who survived more than 3 days. We used this strategy to reduce the chance of false-negative results. However, in this study, 36 of the 38 (94.7%) youth suicides with toxicology available died within 26 hours of their self-inflicted injury. Although antidepressants were not detected in the one suicide who lived longer than 72 hours, it is uncertain whether that individual had taken an antidepressant before the suicidal injury.

Toxicology

Antidepressants and their principal metabolites were screened at the Office of the Chief Medical Examiner of New York City by gas chromatography using a nitrogen phosphorous detector. The quantitation limit is 0.1 mg/L. All positive findings were confirmed by gas chromatography-mass spectrometry.

Study Variables

Demographic characteristics, serum toxicology, and method of suicide were examined. There was concern that some suicides would be misclassified as accidents and the resulting estimate of the presence of antidepressants would be biased. Therefore, toxicology was also examined for all accidental deaths in those younger than age 18 years of age.

Data Analyses

The analyses that were used involve descriptive statistics. The proportion of suicides and accidents with antidepressants detected at autopsy is presented.

RESULTS

Suicides

Among New York City residents younger than age 18 years, there were 41 suicides from 1999 through 2002. Based on the New York City population ages 10–17 years of 838,276 in 2000 (New York State Department of Health, 2000), this amounts to an annual rate of 1.22/100,000 compared to the U.S. rate for that age group of 3.11/100,000 (National Center for Injury Prevention and Control, 2005). Twenty-eight (69.8%) of the suicides were males (Table 1). There were more Hispanic Americans (n = 14, 34%) and African Americans (n = 12; 29%) than whites (n = 8; 19.5%), and this reflects the ethnic breakdown for that age group in New York City. Decedents ranged in age from 10 to 17 years (mean = 15.4, median = 16.0, SD = 1.9). Three of the suicides were younger than 13 years of age.The most common methods of suicide were hanging (n = 17; 41.5%), jump from heights (n = 8; 19.5%), and firearms (n = 5; 12.2%).

Results of toxicological analyses were available for 38 (92.7%) of the 41 suicides. Thirty-six (87.8%) of the suicides had both toxicology and injury-death intervals of 3 days or less, and our examination of the presence of antidepressants was limited to those subjects. Both buproprion and sertraline were detected in one (2.8%) of the suicides, a 16-year-old homeless African American male who died of an intentional drug overdose. Antidepressants were not detected in any other suicides.

Accidents

The Office of the Chief Medical Examiner of New York City certified 269 residents of New York City younger than age 18 years who died in accidents from 1999 through 2002. On average, those dying of accidents

TABLE 1
Description of Suicides Younger Than 18 Years of Age in New York City: 1999–2002

Characteristics	No.	%
Gender		
Male	28	68.3
Female	13	31.7
Race/ethnicity		
White	8	19.5
African American	12	29.3
Hispanic American	14	34.1
Other	7	17.1
Borough of death		
Manhattan	7	17.1
The Bronx	13	31.7
Brooklyn	9	22
Queens	10	24.4
Staten Island	2	4.9
Year of death		
1999	9	22
2000	9	22
2001	11	26.8
2002	12	29.3
Suicide method		
Hanging	17	41.5
Jumping	8	19.5
Firearm	5	12.2
Train	4	9.8
Drug overdose	3	7.3
Drowning	2	4.9
Other	2	4.9

(mean = 9.0 years, median = 9.0, SD = 5.7) were younger than the suicides. One hundred seventy-six (65.4%) were males. Nearly 52% of these youths were younger than 10 years of age. One hundred twelve (42%) were African American, 27 (28.6%) were Hispanic, and 55 (20.4%) were white. Pedestrian fatalities were the most common cause (n = 70; 26%). Toxicology was tested in 241 (90.3%) of the accidental deaths and 213 (79.8%) had both toxicology results available and injury–death intervals of 3 days or less. Imipramine was detected in two (0.9%) of the accidental deaths. Antidepressants were not detected in any of the other accidental deaths.

DISCUSSION

This medical examiner surveillance study examined serum toxicology for antidepressants among individuals who committed suicide and were younger than 18 years of age in New York City. Only one of those suicides had antidepressants detected at the time of autopsy. Antidepressants were detected in none of the other suicides.

This finding concurs with those of our earlier study, which found that antidepressants were detected in 4 of 54 (7.4%) youth suicides in New York City from 1993 to 1998 (Leon et al., 2004). On the surface, these results may appear to be inconsistent with the results of the FDA meta-analyses of 25 pediatric antidepressant RCTs on which the antidepressant black box warning is based. The analyses presented here, however, do not have direct bearing on the question of whether there is an association between antidepressants and non lethal suicidal ideation or suicide attempts. Instead, we found that antidepressants appeared to play little if any role in suicides among children and adolescents in New York City from 1999 to 2002. Similarly, none of the 4,800 study participants in the pediatric studies committed suicide during the course of the RCTs. Instead, the black box warning label is based on an increase in suicidal ideation and suicide attempts among those assigned to antidepressants relative to placebo. It is also worth noting that six of those studies excluded subjects with history of suicide attempts and most excluded volunteers with active suicidality.

A study of suicides in Sweden from 1992 to 2000 found that antidepressants were detected in 7 of 52 (13.4%) suicides younger than 15 years of age and in 13 of 324 (4.0%) suicides 15 to 19 years of age (Isacsson et al., 2005). Other types of studies, primarily in adults, have examined the association between antidepressants and suicidality. First, a report on a series of cases described an association between fluoxetine and suicidality (Teicher et al., 1990). Yet, subsequent observational studies have not shown an elevated risk of suicidality in those taking selective serotonin reuptake inhibitors (Ham, 2003; Isacsson et al., 1996; Leon et al., 1999; Martinez et al., 2005; Warshaw and Keller, 1996). Kessler et al. (2005) found no change in rate of suicide ideation and attempts during the past decade, a time when antidepressant use increased in the United States. Several ecological studies have found an inverse relationship between antidepressant sales and suicide rates (Carlsten et al., 2001; Gibbons et al.,2005; Grunebaum et al., 2004; Olfson et al., 2003), but they were unable to determine whether each suicide had been treated with antidepressants. In our study, we used medical examiner

certification of each suicide and toxicological analyses to determine antidepressant exposure among the suicides.

One RCT specifically recruited suicidal adults and demonstrated a protective effect of paroxetine (Verkes et al., 1998), yet we are unaware of any such studies in children or adolescents. Randomization would provide a balance of demographic and clinical characteristics between those who receive investigational and comparator treatments; however, randomized treatment assignment with suicidal individuals introduces ethical quandaries. Assignment would require careful choice of comparison interventions and aggressive monitoring of suicidality with comprehensive rescue provisions detailed in the protocol. In fact, this strategy was successfully implemented in an RCT for suicidal patients with schizophrenia (Meltzer et al., 2003).

Limitations

There are several considerations relevant to the interpretation of results of this study. First, we excluded 5 of the 41 suicides because toxicology was unavailable or the injury–death interval exceeded 72 hours. We could not determine the presence or absence of antidepressants for those cases. Our analyses did, however, consider the possibility that we under estimated antidepressant toxicology resulting from misclassification of suicides as accidents. Antidepressants were detected in only 2 of 213 youth victims of fatal accidents. If there were misclassification of suicides as accidents, then suicides without antidepressants in toxicology would be more likely misclassified as accidents because the medical examiner's office uses all information at its disposal to make a determination of the cause of death. Therefore, if any misclassification were present, then the overall proportion of suicides-with positive antidepressant toxicology shown here would likely be an overestimate, further strengthening the inference being drawn here. Second, we recognize that the detection level used in our study is such that we could miss cases that had low antidepressant blood concentration levels, below that of the screening threshold set by the Office of New York City Chief Medical Examiner. Third, we do not have information about psychotherapeutic interventions or unfilled prescriptions among the suicides. Finally, our findings may be interpreted as evidence that the suicides that did not have antidepressants detected at autopsy could have been prevented by antidepressant treatment. However, our post mortem study did not examine the protective effect of antidepressants among youths in New York City. Unfortunately, there are no precise estimates of the number of youths who are treated with antidepressants in New York City. Some studies (Gibbons et al., 2005; Grunebaum et al., 2004; Olfson et al., 2003) have examined prescription sales data, which are proprietary and unavailable to us. Those published data, however, do not correspond to the ages, calendar years, or geographic area that we studied and therefore do not provide estimates of antidepressant exposure in youths in New York City.

Clinical Implications

This study found antidepressants in only 1 of 36 youth suicides in New York City from 1999 to 2002. Although these results provide no evidence of a strong link between antidepressants and suicide, they do not rule out the possibility of suicidal thoughts or non lethal suicide attempts among youths taking antidepressants. Despite no demonstrable link at a population-based level, we suggest that clinicians and parents continue to carefully monitor the clinical status of youths who are prescribed antidepressants (U.S. Food and Drug Administration, 2004b).

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The Importance of Acknowledging Clinical Uncertainty in the Diagnosis of Epilepsy and Non-Epileptic Events R. Beach, R. Reading

Background: Failure to recognise diagnostic uncertainty between the epilepsies and non-epileptic events may be a factor in high rates of misdiagnosis. *Aims:* To explore the results of acknowledging diagnostic uncertainty in a cohort of children presenting with paroxysmal events. *Methods:* Children (29 days–16th birthday) with new presentations of paroxysmal disorders were ascertained through outpatients, admissions, and accident and emergency over a two-year period in a district hospital with a catchment population of 500,000. Cases were classified by diagnosis at entry and 6–30 months later. A random selection of cases was independently assessed. *Results:* A total of 684 cases were ascertained. Attacks were initially classified as febrile seizures (n = 212), acute symptomatic epileptic seizures (n = 5), epilepsies (n = 83), unclassified (possible epilepsy) (n = 90), isolated epileptic seizures (n = 51), and non-epileptic events (n = 243). Case review enabled reclassification of 61 of those initially unclassified—31 to an epilepsy and 27 to non-epileptic events. In 29 the final diagnosis was never clarified. These were 23 cases with confusing or absent histories and six with short lived seizure clusters. Prognosis for these 29 cases was good; 75% had been discharged. None were on long term medication. The diagnosis in the 131 cases confirmed as epilepsy was stable. Independent review of a random sample showed full concordance with one neurologist and 20% uncertainty with another. *Conclusion:* In addition to definite epilepsy or non-epileptic events it is helpful to recognise a group of cases where the diagnosis is uncertain—unclassified paroxysmal events. Reassessment of these cases enables accurate diagnosis and may prevent a hasty and incorrect diagnosis of epilepsy. **Archives of Disease in Childhood** 2005;90:1219–1222.