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News

Analysis of large database

Antisuicidal Effect Of Psychotropics Remains Uncertain

'We have to ask if medication is the only way' to approach the prevention of suicide.

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Contributing Writer

BOCA RATON, FLA. — Psychotropic therapy did not appear to have a marked impact on suicide risk, examination of a large database indicated—in fact, no class of medication had much more or less effect than placebo, Dr. Arif Khan said at a meeting of the New Clinical Drug Evaluation Unit sponsored by the National Institute of Mental Health.

Overall, attempted and completed suicides among patients with diverse psychiatric conditions are substantially more frequent than had been expected, the analysis suggested.

"Given that suicide is such a complex behavior ... we have to ask if medication is the only way to [approach] it," said Dr. Khan of Northwest Clinical Research Center, Bellevue, Wash.

The conventional response to suicidality in psychiatry is pharmacotherapy. The assumption that this will be beneficial "is never challenged much," Dr. Khan said, and raises ethical questions about clinical trials, such as whether patients assigned to placebo may be exposed to increased mortality risk. Some observers, on the other hand, have suggested that psychotropics may themselves increase the risk of suicide.

In fact, the only biologic treatments for which there are many data on this score are ECT and lithium, which have been shown to reduce suicidality. More limited data support a similar effect for clozapine.

Dr. Khan reported an analysis of clinical trial data for drugs approved by the Food and Drug Administration between 1985 and 2000. This included suicide and attempted suicide rates for more than 71,604 patients treated with the atypical antipsychotics risperidone, olanzapine, and quetiapine; all the selective serotonin reuptake inhibitors; nefazodone, mirtazapine, and bupropion; the benzodiazepine alprazolam; and the anticonvulsant valproate.

One striking finding was the elevated rate of completed suicides for patients during these trials. Compared with the rate of 11/100,000 persons per year for the population at large, the rates of completed suicide were 752/100,000 persons per year for those in antipsychotic trials; 718 in antidepressant trials; 425 in trials of medication for social anxiety disorder; 136 for panic disorder; and 105 for obsessive-compulsive disorder.

This was particularly surprising in light of the attempt, in most clinical trials, to exclude patients who are actively suicidal, Dr. Khan said.

Figures on attempted suicide found similarly increased risk. The figures implied that 5% of patients who enroll in antipsychotic trials will attempt suicide in the following year; 3.7% of those in antidepressant trials will make an attempt; and 1.2% of those in trials of medication for anxiety disorders will attempt suicide.

Suicide rates were higher, in the trials taken as a whole, for patients who were assigned to placebo than to the investigational

drug (1,750/100,000 persons per year vs. 710/100,000 persons per year). But because participants were exposed to placebo for far less time than to the drugs (a mean of 33 days vs. 148 days), this could not be assumed to indicate an antisuicidal effect of medication, he said.

In the case of trials for depression and anxiety disorders, suicide rates were in fact higher among those who received the investigational drug than placebo, Dr. Khan said.

The high rates of suicide among patients studied might suggest an “iceberg effect” in the general population. The numbers that come to light under the close scrutiny of the clinical trial situation indicate the extent to which attempted and completed suicides are concealed or mislabeled in the community, Dr. Khan speculated.

Highlights of Six Specific DSM-V Research Agenda

1. Basic Nomenclature Issues of DSM-V

The most diffuse of the research agendas, this section consists of six independent subsections on issues of nomenclature:

▶ **How to define “mental disorder.”** DSM has never contained a detailed definition that is useful as a criterion for deciding what is, or is not, a mental disorder.

A useful definition should be developed.

▶ **Validity.** DSM-V should possibly include a rating of the quality of information and quantity of information available to support different diagnostic systems.

▶ **Dimensionality vs. categories.** Like the classification systems of many other branches of medicine, the DSM-IV system is categorical. A dimensional system would better represent variations in psychiatric symptomology, although it is premature to assume that DSM-V would be largely dimensional. However, research could provide valuable information about the usefulness of a dimensional system.

▶ **Reducing gaps between DSM-V and ICD-11.** APA's goal has always been to link DSM with the World Health Organization's International Statistical Classification of Diseases and Related Health Problems. However, differences still interfere with the compatibility of the two systems. Reconciliation is recommended; in the future, the decision may be made to create a single, unified, worldwide system for diagnosing mental disorders.

▶ **Cross-cultural use of DSM-V.** Diverse populations have diverse norms of functioning. To foster cross-cultural applicability of DSM constructs, norms, and guidelines, research should identify cultural variants in symptom definition and manifestation, and anthropologic approaches to different cultural models of mental illness.

▶ **Use of DSM-V in nonpsychiatric settings.** Primary care providers now also use the manual that was developed for use by psychiatrists. The study group identified a need to define diagnostic criteria in ways that can be applied outside the traditional psychiatric interview. Research is needed to develop tools for this, including lab tests and diagnosis, and psychological testing and diagnosis using standardized, computer-scored symptom-rating scales.

2. Neuroscience Research Agenda to Guide Development of a Pathophysiologically Based Classification System

The DSM classification system should evolve from symptomatic to etiologic, perhaps eventually becoming a multiaxial diagnostic system based on genotype, neurobiologic indicators, behavioral phenotype, environmental modifiers, and therapeutics. While this will probably not be reflected in DSM-V, neuroscience research over the next 10-20 years will have a profound impact on the existing diagnostic system.

3. Advances in Developmental Science

This agenda focuses on the deficiencies of the DSM-IV in relation to diagnosing children. Because the individual is a product of nested environments, from childhood to adulthood research should focus on discovering the links between childhood and adult disorders, and include epidemiologic, neuroscience, and genetic studies of children. Early childhood diagnosis at preschool age should also be the focus of research.

4. Personality Disorders and Relational Disorders

This agenda focuses on what many clinicians believe are the most unsatisfactory sections of the DSM-IV. It suggests creating a new dimensional model of diagnosing personality disorders instead of the current categorical classification system, which many feel fails to address the real-life complexity of these disorders.

Furthermore, the agenda suggests consideration of possibly introducing relational disorders with diagnostic criteria.

5. Mental Disorders and Disability

This agenda recommends separating the constructs of psychiatric symptoms and functional impairment in order to enable research into the factors that explain the varying degrees of disability that are observed across patients, given the same level of symptom severity.

Removing the impairment criteria from psychiatric diagnosing also will encourage early intervention for those at risk of future morbidity.

6. Culture and Psychiatric Diagnosis

DSM-IV criteria are meant to apply to all patients regardless of age, sex, or culture. However, different cultural backgrounds are tied to different expression of symptoms, and a generic set of criteria does not do justice to cultural diversity.

Research requires a truly integrative approach that investigates the expression of disorders, treatment response, and diagnostic criteria across the full population spectrum.