Antidepressants for Children, Teens Impugned by Study

By Gil Ross — January 29, 2016

A new study published in *BMJ* suggests that selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) may double the risk of suicidality and aggression among children and adolescents.

Clinical study reports for antidepressants duloxetine, fluoxetine, paroxetine, sertraline and venlafaxine were obtained from regulatory agencies in the UK and Europe. Summary trial reports for duloxetine and fluoxetine were taken from the drug company Eli Lilly’s website. (However, in the Eli Lilly summary trial reports, almost all deaths were noted, but suicidal attempts were missing.)

The meta-analysis (a study of other studies), entitled "Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports," was authored by a group of Danish researchers affiliated with the Nordic Cochrane Centre in Copenhagen. (Interestingly, the lead author, Tarang Sharma, is a PhD student, two other authors are medical students. The only faculty author is Peter C. Gøtzsche, professor at the University of Copenhagen.)

Their study only included double-blind placebo controlled trials that contained patient narratives or individual patient listings of associated harms. They analyzed 70 trials comprising 18,526 patients. They found that these trials had limitations in the study design and discrepancies in reporting, which may have led to serious under-reporting of harms. For example, some outcomes appeared only in individual patient listings in appendices, which they found for only 32 trials, and they did not have case report forms for any of the trials.

The values for suicidality among children and adolescents were close to three-fold elevated (2.79), and for aggression, over two-fold elevated (2.15). For adults, there were no significant differences between the groups taking the studies antidepressants and those not taking them. In the summary
trial reports on Eli Lilly's website, almost all deaths were noted, but all suicidal ideation events were missing, and the information on the remaining outcomes was incomplete.

The authors note that clinical study reports could not be obtained for all trials and all antidepressants, and individual listings of adverse outcomes for all patients were available for only 32 trials. Their main concern was that "The true risk for serious harms is still unknown [because] the low incidence of these rare events, and the poor design and reporting of the trials, makes it difficult to get accurate effect estimates."

This study documents that "serious under-estimation of the harms" in the studies of these antidepressants published by the drug companies, especially those published by Eli Lilly on duloxetine and fluoxetine.

The authors conclude that, "because of the shortcomings identified and having only partial access to appendices with no access to case report forms, the harms could not be estimated accurately. In adults there was no significant increase in outcomes, but in children and adolescents the risk of suicidality and aggression doubled. To elucidate the harms reliably, access to anonymised individual patient data is needed."

Based on the results, the authors recommend "minimal use of antidepressants in children, adolescents and young adults," but cautioned that there was not enough patient data available from clinical trials to assess the true risk of all associated serious harms.

It must be borne in mind that such retrospective analyses cannot show a cause-and-effect relationship, merely an association. While awaiting more key data, it seems logical to infer that the data being reported by the pharmaceutical companies on the effects of commonly used antidepressants in young people seems to have significantly understated the adverse effects, and should at least give caregivers for children and adolescents with depression pause and cause for concern.

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