Clinical Corner – Anti-Depressants and Suicide

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Introduction

Many people have asked me for advice about how to respond to questions from patients and the lay public about the recent press, and ultimately US Food and Drug Administration (FDA) warnings, about suicidality and antidepressants.

A Matter of Scale

The first issue that I would suggest addressing is the one of scale. Fluoxetine (Prozac) became available in 1987, and other selective serotonin reuptake inhibitors (SSRIs) became available shortly thereafter. In the 17 or so years that we are talking about here, there have been millions -- if not tens of millions -- of prescriptions resulting in numerous satisfied patients and practitioners. If SSRI-associated suicidality truly is a major problem, it is difficult to understand why it would only be coming to light now. The idea that these medications might cause some people to commit suicide was discussed in a few studies in the early 1990s, but these were dismissed as exceptional cases. It is not at all clear why this is becoming an issue again in 2004.

It must be emphasized how important the newer generation of antidepressants has been in improving the lives of many individuals. These medications, despite their current negative press, have been enormously effective in reducing the burden of depression. Their side-effect profile is relatively low (although certainly not zero) and they are considerably safer in overdose than their predecessors, making them considerably *less* risky for suicide.

The Risks

It is important to directly acknowledge the suicide risk caused by these medications. It is real and well understood, at least by experienced psycho-pharmacologists. There are 2 mechanisms that we know about that cause these medications to potentially precipitate suicidality. One is extremely rare, and the other is milder but more common. The rare one is the potential for SSRIs to precipitate an akathisia. This movement disorder, usually associated with antipsychotic medications, has been reported as a rare side effect of SSRIs. This intense restlessness can be so dysphoric (anxiety provoking) for patients that they might consider suicide rather than endure the restlessness. This is something that practitioners should warn patients about, and look for closely, as it is quite treatable with adjunctive medication.

The second mechanism involves the natural history of recovery from depression. Depression is a disorder with numerous symptoms, and when the disorder is treated effectively, the symptoms do not resolve all at the same time. Classically, the physical symptoms of depression (including lack of energy, difficulty concentrating, and sleeping and eating disturbances) resolve first and the subjective depressed mood resolves last. As a result, patients who are being treated for depression can have increased energy and increased functionality as they recover, while still struggling with subjectively depressed mood. This increases their suicide risk; they may have lacked the energy or the ability to attempt suicide prior to starting treatment, but as they begin to recover they regain ability and motivation before they have a subjective sense of improvement. As a result, patients are usually at greatest risk a week to 10 days after starting medication, and by 2-3 weeks later, that risk is resolved. Experienced clinicians understand this as a function of the disease, not the specific treatment, and are careful to watch for it and to instruct family and friends to also be aware of it. The problem may be exacerbated by the trend of primary care physicians treating depression. They usually see patients for 10- or 15-minute periods of time and very rarely more frequently than once a month

Why Is This an Issue Now?

Why did this happen? What started this whole process of questioning whether these drugs are safe, and as such what should be the thresholds for prescribing them? It appears that this all started in Great Britain, when the UK equivalent of the FDA began to look at data from clinical trials in children. The concern that the researchers expressed has been greatly misunderstood. They did not say that these drugs routinely caused suicide; what they said was that there seemed to be very little evidence that these drugs were particularly effective in children. When compared with placebo, the children taking medication did not seem to be doing all that much better. Thus, there appeared to be little benefit to the medication, and since there were a few more episodes of suicidal behavior (there were virtually no completed suicides on these clinical trials), the risks vs. benefits may not justify prescribing these medications for children.

There are a number of reasons why placebo-controlled trials of antidepressants for children often have trouble separating the responses of the drug group from the placebo group. Subjects participating in clinical drug trials get a lot of attention. They come in for frequent visits and talk about depression often. This talking about depression can get them thinking about depression and can be, in effect, de facto cognitive therapy. When you consider the fact that children are considerably more impressionable than adults, it may explain why medications that are in common clinical use in the treatment of depression in children may not look so great in a clinical study. If you have concerns about the efficacy of newer-generation antidepressants in the treatment of depression in children, talk to child psychiatrists who use them. The enthusiasm for these medications among the practitioners who pharmacologically treat depression in children is quite strong. If they didn't work that well, these are the people who would know.

Public Opinion

Recently, the press has been full of heart-wrenching stories of young people who have been started on antidepressants and shortly thereafter have committed suicide. No one doubts the veracity of these stories. All of us who are parents can begin to imagine the horror that the parents of these victims endure. In many -- if not most -- of these cases, we will probably never fully understand what happened. Perhaps some of them developed an akathisia, perhaps some of them did recover somewhat enough so that their negative thinking motivated them to act on the feeling that life was no longer worth living. What is happening now, however, is that the sensationalism of these reports is providing the public -- who had previously enthusiastically embraced these medications -- with a very short memory. If the outcome of this negative press is that it prevents people from seeking treatment for depression or, more specifically, encourages them to refuse medication for severe depression, this controversy itself may cause more suicides than the medications ever did. The risk of suicide goes down most dramatically when people get treatment and comply with it. It is a responsibility of all practicing psychopharmacologists to do whatever they can to reinforce this message. We are the ones with the experience with these medications. We have seen the successes, and we have seen the failures. We need to make absolutely clear that the former grossly outnumber the latter.