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EDITORIAL

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Antidepressants and suicidality

The regulatory agencies of different European countries and the U. S. have published statements and warnings concerning a possibly increased risk of suicidality associated with the use of antidepressants in pediatric patients (Licinio and Wong 2005). Such warnings are helpful to avoid risks; however they also can hold risks in themselves. The scientific and also the broad public discussion about the possible suicide-inducing effect of antidepressants has created uncertainty in patients, parents of depressed children and primary care physicians whether the use of antidepressants in depressed patients is still justified. Because of the negative publicity in the last two years, it has to be expected that many pediatric and adult patients will no longer be treated with an antidepressant. What might be the balance between possible benefits and harms of the warnings?

Children and adolescents

The evidence base for the efficacy of most selective serotonin reuptake inhibitors (SSRI) and other antidepressants in children and adolescents is lacking or less broad and less convincing than for adults (Jureidini et al. 2004). Against this background, small risks also gain in importance. Therefore, the tendency of an increase in suicidal thoughts and self harm found in pooled analyses of short-term controlled trials with SSRI and other newer antidepressants in children and adolescents as compared to placebo (4 % versus 2 %) has to be taken seriously (Gunnell and Ashby 2004). Although no completed suicide was reported in these studies comprising 4400 patients, for most antidepressants the possible risks are not balanced by a clearly proven benefit. This demands a restricted use of these antidepressants and special care with close monitoring when treating pediatric patients. At present, the evidence base for efficacy is best for fluoxetine: in older trials and in a recent multicenter study positive results were shown for depressed pediatric patients. Fluoxetine is therefore considered to be the only antidepressant with a positive risk-benefit balance and is first choice when treating children and adolescents with antidepressants.

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Adults

The discussion of the use of antidepressants in pediatric patients has spread over to the treatment of depressed adults. Here the risk-benefit balance is clearly in favor of the antidepressants. On the one hand, there are fewer signals of a negative and more of a positive impact on suicidality than in pediatric patients (e. g., Gibbons et al. 2005; Bruce et al. 2004); on the other hand, their efficacy both concerning acute and long-term treatment of depression is clearly documented. Since suicidality is highest within the depressive episode, it has to be assumed that shortening depressive episodes and preventing relapses and recurrences by antidepressants is reducing the risk of completed and attempted suicides, although for methodological reasons it might be hard to prove. For adults, there is a considerable risk that undertreatment of depression has increased due to the negative publicity associated with antidepressants.

Do selective serotonin reuptake inhibitors (SSRIs) have a higher risk of increasing suicidality?

SSRIs, as mostly non-sedating antidepressants, have been associated with increases of suicidality in case reports and were initially in the focus of attention in the reanalyses of the pediatric studies with antidepressants. However more systematic and broader reanalyses of published and unpublished randomized controlled tri-

als led the "Psychopharmacologic Drug and Pediatric Advisory Committee" to conclude that the finding of an increased risk of suicidality in pediatric patients applied not only to SSRI but also to other drugs studied including sedating ones such as mirtazapine. The Committee recommends that any warning related to an increased risk of suicidality in pediatric patients should be applied to all antidepressant drugs (FDA Statement September 16, 2004).

The first days and weeks after starting antidepressant treatment could be in general a high risk period concerning suicidality independently of the drug used (Jick et al. 2004). Several factors could explain this:

- Many patients come into contact with medical services during disease stages when despair and suicidality are highest.
- Antidepressants might initially improve drive in some patients without a corresponding improvement of depressive mood and despair. This could facilitate the realization of suicidal plans.
- The lack of rapid improvement or initial adverse treatment effects might be negatively interpreted or integrated into depressive delusions, increasing the suffering and despair.

It has to be expected that these and other factors work not only in pharmacotherapy but can also initially increase the risk of suicidality in psychotherapy and other nonpharmacological treatments (Baca-Garcia et al. 2005; Möller-Leimkühler 2003; Diaz et al. 2003). To emphasize the importance of careful monitoring of the depressed patient when starting any antidepressant treatment is in line with old text book knowledge.

Since SSRIs have been the focus of attention of public discussion concerning possible increases in suicidality, it can be expected as a consequence that in a considerable number of patients the pharmacological treatment has been stopped or shifted to tricyclic antidepressants (TCA). The latter aspect is dangerous keeping in mind the low safety in overdose of TCA and the high number of patients using antidepressant overdose in suicide attempts (Brådvik and Berglund 2004).

All together the broad discussion of relations between antidepressants and suicidality has sharpened our view on the risk-benefit balance of antidepressant treatment in pediatric patients and on the necessity of a careful monitoring of pediatric and adult depressed patients especially in the days and weeks after starting treatment. What remains an open question is the risk-benefit ratio of changes in the care of depressed patients resulting from this discussion itself.

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