Drug-induced depression and suicidality

Various drugs have been associated with depressive complaints, depressive disorder, suicidality and suicide. These are rare and potentially fatal side-effects, whose precise mechanism remains unknown. The most comprehensively examined class of drugs in this respect is that of the selective serotonin-reuptake inhibitors (SSRIs). Meta-analyses of randomised trials have found an elevated risk of suicidality and suicide attempts among children, but not among adults. The risk may have been underestimated, however, by the exclusion of patients at high risk of suicide in randomised trials. Observational studies have yielded contradictory results, but this type of research is subject to bias due to the lack of randomisation.

The same considerations apply to the anti-epileptics, for which a meta-analysis of randomised trials found a two-fold increased risk of suicidality. A number of observational studies have yielded different results. Research evidence at the highest level for an elevated risk of suicidality is also available for efavirenz and atomoxetine. Adverse effects reporting centres have had numerous reports of psychiatric side-effects of drugs to alleviate withdrawal symptoms, especially varenicline. Meta-analyses of randomised trials, carried out by the agent’s manufacturer, found no elevated risk of depression, suicidality or suicide. The studies of varenicline also excluded patients with an elevated risk of suicide, however, so that they probably underestimated the risks.

Large cohort studies have found plausible evidence for an increased risk of suicidality from the use of benzodiazepines and isotretinoin, and some evidence on ACE-inhibitors has been found in case-control studies. Lower-level evidence for depressive complaints and suicidality, including reports to adverse effects reporting centres, has been published for a large number of other drugs, including 5α-reductase inhibitors, quinolones, corticosteroids, interferons, mefloquine, montelukast and oseltamivir. Although β-blockers and statins have also been associated with such side-effects, these suspicions have been refuted by evidence from a meta-analysis of randomised trials as well as by some evidence from a case-control study. One limitation of all types of research has been the coding and recording systems used for the side-effects, and the inconsistent terminology. In addition, there is a major influence of confounding, for instance regarding the use of psychopharmaceuticals by patients with psychiatric disorders and their relation with suicidality, where the disorder itself may have played a role in the development of the side-effect.

If doctors prescribe a drug which is suspected of being associated with an elevated risk of depressive complaints or suicidality, they need to take any psychiatric history of their patient into account. In all cases, the risk of a potentially fatal side-effect must be weighed against the expected favourable effects of the agent, especially if the latter are limited. It is important that doctors, pharmacists and patients report suspected side-effects as fully as possible, that is, including information on the possible temporal relationship, co-medication or other possible causes.

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*The literature refers to the Dutch text*