CORRESPONDENCE

Antidepressant Withdrawal and Rebound Phenomena

A Systematic Review

by Dr. med. Jonathan Henssler, Prof. Dr. med. Dr. phil. Andreas Heinz, Lasse Brandt, and Prof. Dr. med. Tom Bschor in issue 20/2019

Tapering off Is by No Means Easy

The authors reject the term antidepressant dependence syndrome, arguing that sustained substance use does not exist in spite of confirmed unequivocally harmful sequelae (1). We remain unconvinced. Many affected patients continue to take antidepressants (and accept adverse effects, such as emotional distance, weight gain, increased risk of hemorrhage, sexual dysfunction) only to avoid the disagreeable effects of withdrawal (namely, withdrawal symptoms). User surveys have shown that tapering off antidepressant treatment usually takes several months and is by no means easy (2). Years of practical experience show us that attempts to discontinue the medication are often stopped. Discontinuing these medications will frequently produce rebound syndromes several months later, which are known regularly but falsely labeled as “renewed depressive moods.” The authors also use the term “relapses” for these syndromes although they mention the study by Andrews et al., which provides arguments in support of rebound syndromes. Furthermore, increasing evidence supports the suspicion of long-term medication harms with regard to the course of depressive moods, as was shown by the Zurich cohort study over a 30-year observation period (3). We suspect that the rebound phenomena are implicated in this too. All this necessitates short-term use only, or, if the drugs are used longer-term, slow tapering off—an approach that we favor with regard to other potentially addictive substances too.

In Reply:

In contrast to what the readers’ letter suggests (“The authors also mention “relapses,” although...”), in our review article we explain rebound phenomena in great detail, as the title itself suggests (1). These are overshooting counter-regulations in the context of the development of drug tolerance, which make the course of the illness worse after stopping the medication than it would have been without any medication at all. This has been shown for acetylsalicylic acid and antihypertensive drugs, for example (2).

In contrast to what our correspondents say, rebound phenomena are not among the dependence/addiction criteria in the ICD-10. The authors incorrectly interpret the dependence criterion “sustained substance use in

In our opinion, the third criterion that is required to diagnose simple medication dependence is more than met (withdrawal syndrome, development of tolerance and continued use despite the users’ awareness that the substance is negatively affecting their mental and physical health). Acknowledging this would guarantee affected patients the long overdue support and recognition the World Health Organization called for as long ago as 1998 (4). We could then find answers to practice-relevant questions like for instance how many weeks an antidepressant can be used without risks in view of its respective potential for dependence.

DOI: 10.3238/arztebl.2019.0677a

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spite of confirmed adverse effects.” This is not met simply if substance use is continued to avoid withdrawal symptoms, because that would mean that this criterion is tautological with “withdrawal symptoms”. Rather, what is meant is that because of the urge to use the substance, affected persons continue using it although they are aware of harmful consequences. Continued alcohol consumption in spite of cirrhosis of the liver might be one such example. Like other medications, antidepressants cause the development of tolerance and withdrawal symptoms as a result of neuroadaptive counter-regulation, as well as possible rebound phenomena when drug intake is stopped abruptly. They are therefore not drugs with the potential for dependence, but the described adverse effects have

to be taken very seriously, especially as the effectiveness of antidepressants is confirmed only for severe depression (3). Accordingly, the indication should be defined cautiously, and the drugs should be prescribed for a time limited period. Tapering off should be undertaken at a very slow pace.

DOI: 10.3238/arztebl.2019.0677b

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Conflict of interest statement

The authors of both contributions declare that no conflict of interest exists.

CLINICAL SNAPSHOT

Port Occlusion Due to Curcumin Infusion

A woman with metastasized endometrial sarcoma presented repeatedly with occlusion of the catheter port. The *Figure* shows the explanted catheter system with the port chamber opened; the latter is covered with an oily granulate. The outlet connection is clogged with a yellow substance, and the septum and polyurethane catheter display deep yellow discoloration. We established that the most likely reason was the regular infusion of curcumin that had been carried out in a private physician's office without informing the oncologist. There was no record, and the patient had no memory, of any other potentially staining substances being given via the port.

Curcumin is an unstable reactive compound with low oral bioavailability. It is administered in the form of an infusion in the context of alternative or integrative tumor treatments. The areas of application include—despite critical research findings on the action in humans—colorectal cancer, pancreatic cancer, and dermatological or neurological diseases. We were unable to find any relevant studies for endometrial sarcoma. Furthermore, curcumin may partially inhibit the effects of some chemotherapeutic drugs. In addition, severe or even fatal allergic reactions have been described. In the case described here, therefore, not only the administration via a port but also the indication for curcumin is questionable.

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Conflict of interest statement: Prof. Gebauer has received reimbursement of congress attendance fees and travel costs, lecture fees, and study support (third-party funding) from C. R. Bard. The remaining authors declare that no conflict of interest exists.

Translated from the original German by David Roseveare.

Cite this as: Kildal D, Feldhaus FW, Gebauer B: Port occlusion due to curcumin infusion. *Dtsch Arztebl Int* 2019; 116: 678. DOI: 10.3238/arztebl.2019.0678

Figure: Explanted catheter system with opened port chamber