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Dependence on newer generation antidepressants

OPINIONS

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Withdrawal symptoms following use of antidepressants are more common, longer lasting and more severe than previously claimed. The treatment advice in Norway should be revised.

In 2019, the National Institute for Health and Care Excellence in England changed its recommendations for treating depression, and elucidated the scope, length and severity of withdrawal symptoms following treatment with antidepressants (selective serotonin reuptake inhibitors (SSRIs) and selective serotonin and norepinephrine reuptake inhibitors (SNRIs)). Norwegian guidelines (1), which have not been updated since 2009, should be amended accordingly.

> ***«Use of antidepressants continues to increase despite the uncertainty surrounding their clinical efficacy»***

Use of antidepressants continues to increase both internationally and in Norway, despite the uncertainty surrounding their clinical efficacy (2). However, in the scientific literature on the use of antidepressants, there is no

evidence to suggest a proven effect beyond six months (2, 3). Data from the United States show that more than 60 % of residents taking antidepressants have used them for more than two years (4).

Dependence and withdrawal effects

Antidepressants are addictive (5), and the effects can be seen following dose reduction, discontinuation and the change of medication (6). After six weeks of use, half of patients will experience withdrawal symptoms, during both rapid and gradual tapering (7), but these will be mild and short-lived for some. However, half rate their symptoms as long-lasting and/or severe (7). Reducing the dosage of antidepressants can lead to new onset of physical or psychological symptoms (8). Dysphoria, agitation, decreased concentration, sensory phenomena and gastrointestinal problems are all relatively common (8).

When long-term treatment with antidepressants stops, symptoms can return (rebound) at a greater intensity than before treatment, and patients can develop chronic, tardive conditions. This alters the natural, clinical course of the underlying condition (6). After discontinuation, patients can develop treatment-resistant, chronic affective states characterised by anxiety and depression (2, 8). A small number may develop persistent somatic symptoms (6).

> ***«When long-term treatment with antidepressants stops, symptoms can return (rebound) at a greater intensity than before treatment»***

A number of studies have concluded that antidepressants prevent the recurrence of depressive episodes (9, 10). The studies all have the same design and a study population made up of patients who have benefitted from the treatment. After a short tapering period, the patients were randomised to continued use of antidepressants or placebo. The placebo groups, however, experienced withdrawal symptoms that are also typical of depression relapses, such as sleep problems and agitation. This study design is therefore not particularly suitable for examining relapse prevention (2).

Cessation of antidepressants

Few scientific studies have been carried out on the discontinuation of antidepressants, and the evidence-based literature in the field is therefore limited. Patients have traditionally been advised to stop gradually over a period of four weeks, but this is far too quick for many (2). Very gradual tapering over months and years yields higher success rates (2, 11). Tapering should entail progressively smaller and smaller reductions in dosage (2). In an observational study, slowly reducing the dose to 0.5 % of the clinically applied dose yielded a success rate of 71 % in long-term users (12). In 2020, the Royal College of

Psychiatrists in England published a leaflet entitled *Stopping antidepressants*, which as the title suggests provides information on how to stop taking antidepressants (13). The information is also aimed at patients.

Despite gradual tapering and non-pharmacological supportive care, a proportion of patients will not succeed (2, 11), and this population should be offered other alternatives (6). Experience from international clinical research communities indicates that withdrawal symptoms following use of antidepressants can be treated with other groups of psychopharmacological medications. Unlike antidepressants and antipsychotics, benzodiazepines do not tend to permanently change the course of the underlying condition being treated (6). Fava et al. recommend clonazepam (11). Benzodiazepines can also be used to treat depression and a range of acute psychiatric and substance abuse disorders (11, 14).

> ***«Very gradual tapering over months and years yields higher success rates»***

Chouinard et al. recommend treatment with antiepileptic medications, particularly gabapentin or lamotrigine (8). Antiepileptic medications are given in parallel with a gradual reduction in antidepressants in the belief that such medications protect against the exacerbation of symptoms in cases of repeated discontinuation or long-term use of antidepressants (antikindling effects) (8).

New, revised guidelines

Withdrawal symptoms following use of antidepressants occur more often, and are more prolonged and more severe than previously claimed. The treatment advice offered in Norway should therefore be revised.

When starting antidepressants, the treating doctor should inform the patient about the possibility of addiction, the challenges in tapered discontinuation, and the possibility of chronic symptoms after discontinuation.

Up-to-date advice on stopping antidepressants should be given to patients who have used them for more than two years.

Some patients have made multiple unsuccessful attempts to stop. National competence networks and/or specialist departments should be established which can offer and develop treatment in Norway, based on models from other countries.

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