



Antidepressant tapering strips to help people come off medication more safely

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ABSTRACT

Antidepressants are commonly prescribed for many mental disorders, including psychosis. Withdrawal effects, resulting from inappropriately short duration of tapering or lack of flexibility in prescribing gradual reduction, are common. An observational study was conducted of the use of “tapering strips”, which allow gradual dosage reduction and minimise the potential for withdrawal effects. A tapering strip consists of antidepressant medication, packaged in a roll of small daily pouches, each with the same or slightly lower dose than the one before it. Strips come in series covering 28 days. Of 1194 users of tapering strips, 895 (75%) wished to discontinue their antidepressant medication. In these 895, median length of antidepressant use was 2–5 years (IQR: 1–2 years \geq 10 years). Nearly two-thirds (62%) had unsuccessfully attempted withdrawal before (median = 2 times before, IQR 1–3). Almost all of these (97%) had experienced some degree of withdrawal, with 49% experiencing severe withdrawal (7 on a scale of 1–7, IQR 6–7). The most common medications were paroxetine ($n = 423$, 47%) and venlafaxine ($n = 386$, 43%). Of the 895 wishing to discontinue, 636 (71%) succeeded in tapering their antidepressant medication completely, using a median of 2 tapering strips (IQR 1–3) over a median of 56 days (IQR = 28–84). Tapering strips represent a simple and effective method of achieving a gradual dosage reduction.

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Introduction

Antidepressant medications are widely used not only in disorders of anxiety and depression, but also in up to 37% of patients with psychotic disorder (Himelhoch et al., 2012) – despite limited evidence of effect (Galling et al., 2018).

McCormack and colleagues critically discuss recent meta-analytic evidence of effectiveness of antidepressants (McCormack & Korownyk, 2018), whereas Adlington introduces the worrying possibility that they are prescribed to “treat” social misery (Adlington, 2018). Here, we suggest an important unresolved consequence of these two issues: the growing number of people with chronic use of antidepressant medication (Moore et al., 2009) and the unknown proportion of those that continue to take medication because they experience difficulties coming off antidepressants.

There is evidence that a significant proportion of antidepressant users experiences difficulties coming off their antidepressant medication (Fava, Gatti, Belaise, Guidi, & Offidani, 2015; Tint, Haddad, & Anderson, 2008). Clinicians are often untrained to anticipate withdrawal difficulties and often advise

a too rapid rate of withdrawal. Significant withdrawal can cause considerable distress, which may precipitate a relapse of the mental syndrome, perhaps particularly in those with the most severe problems such as psychotic disorder. Also, there is growing evidence of the occurrence of supersensitivity and rebound, where the reappearance of the original condition – depression or psychosis – may not be just a relapse but a result of the biochemical changes in the brain resulting from taking the drug itself (Murray et al., 2016).

Although there are differences between medications in the degree to which a withdrawal syndrome may occur, all antidepressants may give rise to withdrawal (Baldwin, Cooper, Huusom, & Hindmarch, 2006). Surprisingly, despite evidence that a substantial proportion of patients have difficulties coming off antidepressant medication (Klein et al., 2017), there is no research on helping people to come off antidepressant medication targeting the withdrawal syndrome itself, for example in the form of personalised tapering technology allowing for slow titration of dosage to reduce the intensity of withdrawal symptoms.

In addition, there is little to guide practitioners in how to help patients, given that virtually all antidepressants come in a limited number of registered dosages that do not allow for flexible and personal tapering in the form of slower and more gradual dose reduction over time. Although some antidepressants can be cut or come in fluid form, these methods are cumbersome and imprecise (Eserian, Lombardo, Chagas, & Galduroz, 2018), and were not developed or tested for tapering.

Methods

In recent years, the not-for-profit organisation Cinderella Therapeutics in the Netherlands, in response to users of antidepressant medication trying to come off, oversaw the development of personal tapering strips for very gradual reduction of antidepressant medication in those suffering withdrawal or deemed at risk. A tapering strip consists of antidepressant medication, packaged in a roll or strip of small daily pouches. Each pouch is numbered and has the same or slightly lower dose than the one before it. Strips come in series covering 28 days and patients can use one or more strips to regulate the rate of dose reduction over time. Dose and day information printed on each pouch allow patients to precisely record and monitor the progress of their reduction (Groot, 2013). Here, we report on the experience of 1194 users of psychotropic tapering strips in the Netherlands, who responded to routine and anonymous quality assessment follow-up questionnaires which, at the request of Cinderella, were sent by the Rainbow Pharmacy to patients who had used tapering strips ($n = 1750$, response rate 68%). Participants who had previously tried to stop taking their antidepressants were asked to respond to the question '*Did you experience withdrawal symptoms?*' on a seven point scale with anchor points of 1 = 'not at all' and 7 = 'very much'. Patients were given information about the purpose of the questionnaire and were considered to provide consent by sending back a completed questionnaire.

Data were analysed by PCG and JvO. Under Dutch law, medical ethical approval is not required for analysis of anonymous routine quality assessment data.

Results

Of the 1194 users of tapering strips, 1121 had used the strips for tapering antidepressant medications, whereas 73 had used them for other medications. Of the 1121 who used the strips for reducing antidepressant medications, 895 (80%) indicated they had specifically wished to discontinue their antidepressant medication, 118 (11%) wanted to reduce the dose of their antidepressant medication, 18 (2%) used the strip for other reasons and 90 (8%) had missing values. Of the 1121, 692 (62%, 97 with missing data) had unsuccessfully attempted withdrawal before. Of these 692 almost all (97%) had experienced some degree of withdrawal (2–7 on the seven point scale), with 339 (49%) reporting the most extreme of the six levels of withdrawal (7 = 'very much'). In the 895 who had used the strips specifically to discontinue their antidepressant medication, median length of antidepressant use was 2–5 years (Interquartile range [IQR]: 1–2 years - >10 years). Two-thirds (66%) had unsuccessfully attempted

withdrawal before (median=2 times before, IQR 1–3), with 51% reporting the most extreme of the six levels of withdrawal (7 = ‘very much’). The most common medications were paroxetine ($n = 423$, 47%) and venlafaxine ($n = 386$, 43%). Of the 895 wishing to discontinue, 636 (71%) succeeded in stopping their antidepressant medication entirely, using a median of 2 tapering strips (IQR 1–3) over a median of 56 days (IQR = 28–84). A total of 67 (8%) said they were still trying to stop their medication using further tapering strips. They had used a median of 2.5 tapering strips (IQR 1–4) over a median of 70 days (IQR 28–112).

Of the 192 (21%) who had not succeeded in stopping their antidepressant medication and were not attempting further tapering, 39 (4%) indicated this was because of severe withdrawal symptoms and 53 (6%) because of re-emergence of symptoms associated with the mental disorder. The 192 had used a median of 3 tapering strips (IQR 2–4) over a median of 84 days (IQR 56–112).

Previous experience of withdrawal was less in the 192 who did not succeed in coming off their antidepressant medication, compared to those who did come off ($n = 636$) (standardised regression coefficient (beta) per point on a 1–7 scale: -0.11 , $p = 0.007$).

In the 636 who successfully stopped their antidepressant medication, number of days used to taper was positively associated with length of antidepressant medication use (4.3 more days of tapering per unit of previous use over five units, $p < 0.001$), and also with higher level of perceived failure of previous attempts to stop medication (2.8 days per unit perceived failure over 7 units).

In the 636 who discontinued their antidepressant medication, there was a significant random effect of medication in the model of number of tapering days ($F = 2.67$, $p = 0.007$). Compared to the reference category of paroxetine, all medications took less days to taper (from -78 days to -13 days), with the exception of mirtazapine (+21 days). However, none of the direct comparisons with paroxetine was statistically significant.

Discussion

In conclusion, this is the first study shedding light on the likelihood of being able to discontinue antidepressant medication in those who previously failed because of severe withdrawal symptoms. The results indicate that a very large proportion of these individuals can be successfully withdrawn from antidepressants using tapering strips.

These findings are relevant to people with psychosis, of whom between 40 and 50% are exposed to polypharmacy (Ballon & Stroup, 2013), resulting in pharmacokinetic and pharmacodynamic interactions that may result in a range of adverse events when trying to come off co-prescribed medications such as antidepressants. Estimates of patients with psychotic disorders using antidepressants range from 10 to 40% (Himmelhoch et al., 2012; Lam, Peters, Sladen-Dew, & Altman, 1998). In addition, there is a growing call for improved methods to safely taper antipsychotic medication, in order to discontinue medication or find the lowest possible dose, without provoking a relapse due to dopamine supersensitivity induced by chronic use of dopamine D2-receptor blockade (Murray et al., 2016). Thus, tapering methodology as described here could be helpful to safely explore dose adjustment strategies in people using antipsychotics too, regardless of being co-prescribed antidepressant medication, particularly for medications that do not allow flexible dose reduction regimes.

Disclosure statement

No potential conflict of interest was reported by the authors.

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