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REVIEW

Stopping antidepressants

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Introduction

I was taught not to scratch if it's not itchy! It is not necessary to change a patient's treatment when his or her condition is stable. However, our complex world and the drive to precision treatment is forcing a rethink of these wise old words.

In the context of depression, it means scratching at the stable patient's treatment, and asking the question: "When is it safe to stop the antidepressant?" to which the answer is uncertain. There is a lack of external biomarkers, special investigations and research that can assist in determining the end-point of treatment. Therefore, the real question is: "How can the benefit of treatment be weighed up against the risk of not treating a person when contemplating treatment discontinuation?"

A multifactorial approach is needed to answer this question, and all of the available information considered in conjunction with the patient. Thereafter, a decision can be taken as to when and how to stop.

Table I lists the driving forces behind stopping medication[1]

Table I: The driving forces behind stopping medication

- Patient
- Doctor
- Cost of the medication
- Inconvenience of taking the medication

Patients view taking medication as a sign of ongoing illness, and fear that they will become dependent on it. The pervasive stigma attached to taking psychiatric medication is also an active driving force in the process. Patients tolerate side-effects if they know that there is an end-point to the treatment. Other people in a patient's life might find the side-effects or treatment to be unacceptable and place pressure on the patient to stop taking the medication.

Doctors evaluate and weigh up the benefit and risks of a patient's treatment. The cost of medication is a real issue in South Africa, and the inconvenience of taking medication needs to be less than the perceived benefit of taking it.

Risk factors that need to be considered prior to making a decision

Previous episodes of depression

Treatment can be stopped 6-9 months after the patient has been in remission in uncomplicated first-episode depression. The risk of relapse is highest in the first two months (20%) after stopping the medication, and then it reduces over the following year.[2-4]

How to proceed with regard to the second relapse is debatable. Some sources say that treatment should be stopped two years after the patient has been in remission, while others don't even mention how to manage the second relapse. Some of the other criteria can help to decide the treatment length in this instance.

Maintenance treatment is required for three or more episodes of depression, but information is scarce on how long the treatment should last. The risk of relapse increases by 16% with each episode of depression, and the protective effect of antidepressants decreases after the third relapse.[5] This implies that the risk of future relapses is high and therefore longer-term treatment is important, if not lifelong.

Phase of the illness

The safest time to consider stopping antidepressants is during the maintenance phase of treatment. The data are fairly consistent that this phase of treatment starts six months to one year after remission has been achieved. This stable treatment phase allows the patient and his or her family to be educated on how to identify a relapse and the discontinuation symptoms, as well as when to ask for help again.

Frequency and severity of past episodes

There was an 85% relapse rate in patients who needed inpatient treatment and or electroconvulsive thearpy.[6] Longer-term treatment is required for more than two episodes in five years, or three episodes in total. Psychosis and residual symptoms also increase the risk of future relapse.[2-4]

Older age

Patients aged 65 and older recover slower, and 60% are only in remission after two years of starting treatment, compared

to 35% in the first year of treatment.[7] Sixty per cent of patients experienced a relapse after medication was stopped after two years of treatment in a cohort study.[7] The disproportionately high impact of another depressive episode in late life also has to be considered, and although antidepressants take longer to work in old age, the number needed to treat is three in order to prevent a further relapse. Therefore, careful consideration should be given to stopping medication at all in this group.

The impact of a future depressive episode

Each person and the people in his or her network (work, family and religion) have limitations with regard to their tolerance of a relapse. The impact of further relapses has to be discussed in these broader terms, and if needed, the family needs to be involved in the decision-making process.

Treatment trials and augmentation

The longer it takes to achieve remission, the more antidepressant trials are needed. Augmentation with other drugs indicates a more severe form of depression, and therefore a higher risk of further relapse.

Co-morbid physical illness

Depression tends to be more severe when accompanied by chronic co-morbid illnesses, especially if there are major new limitations with respect to the patient, and if he or she is not used to being ill.

Current or ongoing social stressors

The ability to cope with stress is influenced by a person's entire life. Patients who experience major stressful events (moving, starting a new job, getting married or undertaking exams) have a higher risk of relapse due to the increased stress. Other variables are also introduced through stressors, and these can cloud the picture and hide early signs of relapse.

Earlier illness onset

Depression peaks in incidence in the 30s and 50s.[8] An earlier onset indicates a more severe form of the disorder. Younger people have underdeveloped coping mechanisms, and therefore are at higher risk of relapse and experiencing a potentially larger negative impact on their long-term emotional and social development secondary to depression.

How to stop and what factors to consider

Discontinuation of treatment is safer when it is carried out in a well-thought out process, and with a clear relapse plan in place.

Rate of stopping

Kaymaz et al[9] found that abruptly stopping medication in first-episode depression had no statistical difference on the relapse rate in a review, but that abrupt withdrawal led to higher rates of relapse in recurrent depression. In general, it is advisable to stop taking the medication gradually. A reduction in the dosage every two weeks and upwards tends to be well tolerated.

Dosage of antidepressant

High-dosage medication can be downtitrated slowly every 2-4 weeks, or even more slowly if this appears to be safer by the doctor or patient.

Length of usage

The longer a patient has been on medication, the slower the downward titration needs to be. Selective serotonin reuptake inhibitors (SSRIs) and sedating antidepressants (trazodone and mirtazapine) can suppress emotions, and a gradual reduction in the dosage allows patients to feel their emotions again, and helps them to discern between normal feelings and the early signs of relapse.

Discontinuation syndrome

Discontinuation syndrome occurs more frequently with short-acting antidepressants (paroxetine and venlafaxine). It consists of feelings of nausea, headaches, electrical shocks, feeling off balance, anxiety, depressive feelings and having a "woolly" brain. It does not appear within six weeks of starting the medication, and resolves in three weeks post stopping in most cases.

Restarting the medication quickly stops the syndrome. Patients who experience transient adverse effects when starting SSRIs are at risk of acquiring the syndrome. Slow and small changes to the dosage are the safest option, and if patients are warned, they are less likely to be apprehensive and to misinterpret the symptoms as a relapse. Patients can be switched to fluoxetine in severe cases.[10] Discontinuation symptoms are least likely to be experienced on fluoxetine owing to the long half-life of the active metabolite.

Sedating effects of a drug

Sedating medication needs to be stopped slowly because patients can experience too much emotion too quickly, and then feel overwhelmed.

Conclusion

The benefits of treatment need to be weighted up against the risks of not treating the patient, using a multifactorial approach. Medication for uncomplicated first-episode depression can be stopped 6-9 months after the patient has achieved remission. All other episodes of depression need to be carefully evaluated, and the risk factors clearly identified and discussed with the patient. In general, the best chance of successful discontinuation derives from a slow reduction in treatment over weeks to months, within the safety of regular follow-up.

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