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Stopping medicines – antidepressants

Antidepressants should typically be reserved for patients with moderate to severe depression (defined using the DSM-IV criteria).[1,2] Selective serotonin re-uptake inhibitors (SSRIs) are considered first-line in adults because of their more favourable adverse event profile.[1,2] [Note: specific advice regarding the use of antidepressants in children and adolescents has been issued by the CSM.][3]

Discontinuation symptoms have been reported with all the different classes of antidepressants, including tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), and the other antidepressants, such as mirtazepine and venlafaxine.

There may be several reasons for stopping an antidepressant:

- Inadequate response.

  It can take up to two weeks for an antidepressant to exert an effect and it should be continued with review every one to two weeks for at least four weeks (six weeks in the elderly) to assess the full effect. If the response is partial, the length of treatment may need to be extended (e.g. for another two weeks) or the dose increased. Treatment should be stopped if there is no improvement after this period and switching to another antidepressant should be considered. Depression can return in patients on continuing treatment.

- An adverse event (ADR).

  The development of a serious ADR, e.g. hyponatraemia or hypersensitivity, would necessitate stopping therapy. Hyponatraemia (usually in the elderly) should be considered in all patients who develop drowsiness, confusion or convulsions when taking antidepressants (particularly SSRIs). Other serious adverse events necessitating stopping might include suicidal ideation, or neuroleptic malignant syndrome. A patient may wish to change their therapy if an ADR that was initially tolerable becomes unacceptable long-term, e.g. sexual dysfunction.

- A change in health status.

  The patient may develop an intercurrent illness or require concomitant medication that may impact their treatment. Pregnancy may change the risk/benefit ratio associated with continuing treatment.

- Remission has been achieved for the desired period and/or the patient wishes to stop taking the medicine.

  Patients should be counselled about taking their medicine as prescribed and the need to continue treatment for six months following recovery (12 months in the elderly).[1,2,3] Patients with a significant risk of relapse or recurrent depression should receive maintenance therapy for two years.

The main problems with stopping are:

- Relapse or recurrence of depression. Careful follow-up is required especially in patients who have been on long-term maintenance therapy for recurrent depression.

- Discontinuation symptoms. Patients should be forewarned that these can occur when stopping, missing doses or, occasionally, reducing the dose, but they can also be reassured that addiction does not occur.

Discontinuation symptoms are usually mild, short-lasting, and manageable with reassurance and explanation, but they can be severe and interrupt normal functioning, especially if the medicine is stopped abruptly. (Severe symptoms should be reported on a yellow card to Yellow Card Centre Wales.) They are more common with higher doses and longer courses and with agents with a short half-life, such as paroxetine.

Symptoms of withdrawal syndromes include gastrointestinal upset, 'flu-like symptoms, anxiety, sleep disturbance, dizziness, paraesthesia, shock-like sensations, and sometimes, hypomania, and movement disorders.[3,4]

How to discontinue therapy

When stopping antidepressants, the doses should be tapered. (The exception is fluoxetine, which has a long half-life; a 20 mg fluoxetine dose can be stopped immediately). If stopping higher doses of fluoxetine,[5] or if stopping other antidepressants early in the course of treatment, doses may be gradually reduced over one or two weeks.[1,4] Otherwise, for patients who have been treated with antidepressants for at least eight weeks, the reducing schedule should extend over about four weeks (or longer for drugs with a short half-life, such as paroxetine or venlafaxine). Patients who have been taking maintenance therapy may need to have the dose gradually reduced over six months.

Symptoms can still occur with gradual withdrawal and the period of tapering can be extended if symptoms develop. In some cases the patient may want to consider whether a short intense tapering period is preferable or less disruptive than a longer, less severe withdrawal.[5]

Specific instructions relating to switching between different antidepressants should be consulted where appropriate. A drug-free interval may be required after withdrawal of certain drugs to avoid significant interactions and, in the case of agents with serotonergic activity, the potentially lethal serotonin syndrome. Symptoms of this include cognitive behavioural changes, autonomic dysfunction, and neuromuscular abnormalities. Particular caution is needed when transferring to or from any MAOI, and from fluoxetine to another antidepressant.

References:

1. National Institute for Health and Clinical Excellence (NICE). Depression. Treatment and management of depression in adults. NICE clinical guideline 90 (partial update of CG23). October 2009. www.nice.org.uk

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3. British National Formulary (BNF) 58. September 2009. http://bnf.org

4. Withdrawing patients from antidepressants. DTB 1999; 37: 49-51. www.dtb.org.uk

5. Antidepressants – swapping and stopping. In: Taylor D et al. Maudsley Prescribing Guidelines, 9 Ed. London: Informa Healthcare, 2007: 235-243.