Stopping antidepressants

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SYNOPSIS

Depressive illness is now recognised as a major health problem. As many patients do not need indefinite treatment, clinicians need to be aware of the symptoms associated with the discontinuation of antidepressants. Gradually reducing the dose is the best approach. Abrupt cessation of antidepressants should be avoided unless medical urgency necessitates it. Particular care is required when changing from one antidepressant to another.

Index words: depression, withdrawal symptoms.

(Aust Prescr 2001;24:13–5)

Introduction

By 2020, major depression is projected to become second only to heart disease as the leading cause of morbidity.[1] The lifetime risk of depressive illness is 12–26% for women and 4–12% for men.[2] It is usually a chronic and recurrent illness (75–80% of treated patients have recurrences) that frequently requires long-term maintenance treatment. Depression is often both unrecognised and undertreated. The aim of treatment is a full remission and long-term recovery rather than short-term response.

When is the right time to stop treatment?

The decision to stop treatment should be made after an assessment of the patient's current mood state and other factors that may indicate the likelihood of a relapse or recurrence of depression. These factors include the number and severity of previous episodes, success of treatment of earlier episodes, the risk of suicide if another episode were to ensue and the disruption caused by depression to the lives of the patient and their family. Discussion of these factors with the patient (and a key family member, if possible) would be essential in coming to a decision about discontinuing therapy.[3]

How to stop treatment

If antidepressants are withdrawn, higher doses should be gradually tapered off, unless there are medical indications for an abrupt cessation. These indications could include pregnancy, severe adverse reactions or inability to take oral medications. Precise guidelines concerning the time needed to taper off the dose are lacking. A gradual reduction is recommended to prevent discontinuation effects and to allow adaptation at the receptor level. A rule of thumb is 6–8 weeks after 6–8 months treatment[3] or 3–6 months after maintenance therapy. Many patients, particularly those on lower doses, may be able to stop more quickly without adverse effects.

If the response to treatment has been unsatisfactory, a switch to a different antidepressant may be necessary. The prescriber should check the product information to see if the two drugs interact, but reducing the dose over a 1–2 week period may be adequate. Patients taking high doses of an antidepressant or who are on an antidepressant with a shorter half-life (e.g. paroxetine and venlafaxine) are more likely to develop discontinuation symptoms during short taper periods. Patients must be educated about the importance of supervised dose reduction when discontinuing antidepressants and about what symptoms they may experience. They can be reassured that these symptoms will remit with time.

Monitoring

Education is a critical aspect of treatment and enhances compliance with medication. The patient and their family should be informed that adverse effects are common, but are usually mild and resolve on continued treatment, and that the depression is likely to recur if treatment is stopped too soon.[4] Other educational messages that are associated with better compliance include advice to take the medication every day and to continue even when feeling better.

Patients must be warned that as depression is typically a recurring disorder, stopping medication is always a trial and may lead to symptoms reappearing. They also need to be instructed to contact their doctor as soon as any symptoms start to recur. The assistance of a key family member can play a crucial role in this respect. The doctor may need to continue to monitor patients periodically after medication has been stopped.

Problems associated with discontinuation

Discontinuation reactions may have physical or psychological symptoms, which appear after stopping or reducing the dose of medication. The symptoms may start within 1–10 days, but usually within three days of stopping treatment. These are distinct from the symptoms of depression, which can also recur within hours to days after cessation of treatment. However, recurrences are less likely than discontinuation reactions to occur in the first week after stopping treatment. Discontinuation reactions are more common in patients who have been treated for more than eight weeks and with higher dosages of antidepressants. Discontinuation symptoms must also be distinguished from an intercurrent illness. They are often overlooked in the acute hospital setting.

Table 1

Symptoms associated with withdrawal of tricyclic antidepressants[4,6]

Gastrointestinal	nausea, vomiting, abdominal cramps, diarrhoea
General somatic distress	lethargy, flu-like symptoms, headache
Sleep disturbance	insomnia, abnormal dreams including nightmares
Affective symptoms	anxiety, agitation, low mood
Less commonly	movement disorders, mania, hypomania, arrhythmias, tachycardia, ventricular ectopic beats

Discontinuation symptoms from abrupt cessation of tricyclic antidepressants (TCAs) (see Table 1) and monoamine oxidase inhibitors (MAOIs) have long been recognised, but features of addiction such as tolerance and addictive use are rare.[5] Gastrointestinal effects, flu-like symptoms, affective symptoms and sleep disturbance are the most common problems after stopping a TCA. Discontinuation effects are also common after withdrawal of MAOIs and include disorientation, confusion, myoclonus, ataxia, agitation, cognitive impairment, catatonia, paranoid delusions, aggressiveness, hallucinations, depression, suicidality, slowed speech and sleep disturbance.

The commonest cessation effects of SSRIs are dizziness, light-headedness, nausea, lethargy and headache (see Table 2). Distinguishing a discontinuation syndrome from a recurring depression can be difficult (see 'Medicinal mishaps: serotonin states' Aust Prescr 1998;21:63). The cessation effects of SSRIs are generally less frequent than those of the TCAs. Reports vary from 33% for clomipramine to 80% for amitriptyline, while the rate is 35% for paroxetine and much less (2–14%) for other SSRIs.[6] The commonest withdrawal symptoms are also different for each class of antidepressant. Two symptoms which are prominent after stopping an SSRI are balance and sensory abnormalities. These do not occur after a TCA is stopped.

There are few reports in the literature about the cessation of newer antidepressants. Stopping venlafaxine has resulted in symptoms of dizziness, light-headedness, irritability, dysphoria, insomnia and sweating.[6]

Effects when changing treatment

If a patient is not responding to an antidepressant, or relapses, a different drug may be necessary. The effects of discontinuing the first drug may not appear until after starting the new drug. It is important not to confuse the symptoms of discontinuation with the adverse effects of the new drug. If time permits, it is helpful if the patient has 3–4 days off medication before starting the new drug. This allows discontinuation symptoms to be identified and distinguished from new adverse events. Advice for changing from one antidepressant to another is published in Therapeutic Guidelines: Psychotropic.[7]

Table 2

Symptoms associated with withdrawal of selective serotonin reuptake inhibitors[6]

Gastrointestinal	nausea, vomiting, diarrhoea, loss of appetite, abdominal pain, abdominal distress
General somatic distress	lethargy, flu-like symptoms
Sleep disturbance	insomnia, abnormal dreams including nightmares and decreased need for sleep
Affective symptoms	irritability, anxiety symptoms, agitation
Problems with balance	dizziness, vertigo, light-headedness, ataxia
Sensory abnormalities	paraesthesia, numbness, blurred vision/diplopia, 'electric shock', visual lag

Management of discontinuation reactions

Problems occurring on cessation of an antidepressant may be minimised by preventative measures, supportive treatment and, if necessary, specific treatment. Preventative measures include emphasising the need for a supervised reduction of the dosage, advising the patient of the risk of discontinuation reactions and warning of possible symptoms that may occur. If possible, avoid high doses and abrupt cessation of medication.

Usually supportive treatment is sufficient. The patient should be reassured that symptoms are not life-threatening and that they will resolve spontaneously within 1–2 weeks. If symptoms are severe, resuming therapy may be necessary. The discontinuation syndrome will then typically resolve within 24 hours or so. A slower reduction of the dose may minimise cessation reactions the next time withdrawal is attempted.

Conclusion

Depressive illness is now recognised as a major health problem. Recent guidelines recommend long-term maintenance treatment for patients with recurrent depression. Higher doses and longer treatment periods may lead to the more frequent occurrence of discontinuation reactions in future. Approximately one in three patients do not respond to the first antidepressant they are prescribed and are switched to another. This changeover period is a risk time for discontinuation reactions as well as drug interactions.

Clinicians need to be aware of the symptoms associated with discontinuation of antidepressants and inform their patients what to expect. Abrupt cessation of antidepressants should be avoided unless medically necessary and gradually tapering off the dosage should be the norm.

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Self-test questions

The following statements are either true or false (answers on page 23)

5. When changing from one antidepressant to another it can be difficult to differentiate discontinuation symptoms from adverse effects of the new medication.
6. After a patient has recovered from depression, the antidepressant dose is usually tapered off.

ABNORMAL LABORATORY RESULTS

Creatinine clearance and the assessment of renal function

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SYNOPSIS

The selection of the most appropriate measurement of renal function depends on the clinical question being asked, the accuracy required and the inconvenience to the patient. Serum creatinine and calculated creatinine clearance yield a reasonable estimation of renal function with minimal cost and inconvenience. A urinary creatinine clearance is more accurate if the urine collection is complete. Isotopic measurement of glomerular filtration rate can be used when greater accuracy is required, when renal function is poor or muscle mass is significantly outside the normal range. Glomerular filtration rate should be corrected for body surface area and interpreted in the context of physiological effects such as pregnancy and blood pressure.

Index words: glomerular filtration, kidney.

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Introduction

Estimation of renal function is important in a number of clinical situations (Table 1), including assessing renal damage and monitoring the progression of renal disease. Renal function should also be calculated if a potentially toxic drug is mainly cleared by renal excretion. The dose of the drug may need to be adjusted if renal function is abnormal.

Renal function and glomerular filtration rate

The glomerulus is a high-pressure filtration system, composed of a specialised capillary network. It generates an ultrafiltrate that is free of blood and significant amounts of blood proteins. Renal damage or alterations in glomerular function affect the kidneys' ability to remove metabolic substances from the blood into the urine.

Glomerular filtration rate (GFR) is the rate (volume per unit of time) at which ultrafiltrate is formed by the glomerulus. Approximately 120 mL are formed per minute. The GFR is a direct measure of renal function. It is reduced before the onset of symptoms of renal failure and is related to the severity of the structural abnormalities in chronic renal disease. The GFR can

Table 1

Indications for renal function testing

Test	*Setting*	*Clinical indication*
Serum creatinine	Screening for renal disease	Hypertension Urine abnormalities Potential renal diseases (e.g. diabetes) Non-specific symptoms (e.g. tiredness)
	Monitoring renal function	Chronic renal disease Transplantation Drug toxicity
Calculated GFR/ creatinine clearance	Initial evaluation of renal disease	Glomerulonephritis Proteinuria Chronic renal failure Chemotherapy dosing
	Monitoring of renal disease	Glomerulonephritis Chronic renal failure
Isotopic GFR	Accurate GFR	Monitoring therapy in glomerulonephritis
	Low levels of GFR	Deciding when to start dialysis Chronic renal failure
	Altered muscle mass	Body builder Chemotherapy dose in wasted patient

GFR = Glomerular filtration rate