WeMeReC
Welsh Medicines Resource Centre
Canolfan Adnoddau Moddion Cymru

Online content

# Stopping medicines – antipsychotics

Antipsychotics are used for schizophrenia to relieve a variety of symptoms such as thought disorder, hallucinations, and delusions, and to prevent relapse.[1] Long-term therapy may be necessary to prevent chronic illness. These medicines are usually started by specialist mental health services or, where necessary, by experienced doctors in consultation with an appropriate service.[2]

Antipsychotic medicines also work as tranquillisers without impairing consciousness or causing paradoxical excitement and can be used in the short-term to alleviate severe anxiety and calm disturbed patients (those with schizophrenia as well as those with brain damage, mania, toxic delirium, or agitated depression).[1] Because of the risk of adverse effects (see below), these medicines are not recommended for dementia-related psychosis and/or behavioural disturbances. (The exception is risperidone,▼ which has a limited short-term indication for Alzheimer's dementia.)

Atypical antipsychotics are the most commonly prescribed antipsychotic agents in Wales, both in primary and secondary care.[3] They are generally better tolerated than the older agents, with less frequent extrapyramidal effects.[1] Chlorpromazine and haloperidol are the two most frequently prescribed "older" antipsychotics.[3]

## There may be several reasons for stopping an antipsychotic:

- Inadequate response.

  Treatment with antipsychotic medication should be an "explicit individual therapeutic trial".[2] Initiation should be with lower doses that are titrated upwards and a person's progress should be monitored and recorded regularly and systematically. A trial of medication at optimum dosage should be carried out for four to six weeks. If necessary, a switch to another agent may be considered. Combined therapy should not be prescribed, other than for short periods when switching medicines. Generally, suitable therapy will be continued long-term, e.g. for two years.

  Clozapine is reserved for people with schizophrenia whose illness has not responded adequately to two different antipsychotic agents (at adequate doses), including one second-generation antipsychotic.[2]

- Adverse effects.

Antipsychotic medicines are associated with a variety of adverse effects which may warrant switching to an alternative agent. These might include:

- Extrapyramidal effects.

  Parkinsonian symptoms – these may appear gradually. They can be treated with antimuscarinics but this may unmask or worsen tardive dyskinesia (see below).

  Dystonia and dyskinesia – these can appear after a few doses.

  Akathisia – often occurs after large initial doses (may resemble the original condition).
- Venous thromboembolism.
- Prolongation of the QT interval (see below for when treatment may need to be stopped).

- Hypotension.
- A lowered seizure threshold.
- Antimuscarinic effects (dry mouth, blurred vision, urinary retention, constipation, cutaneous flushing).
- Impaired glucose tolerance; an increase risk of diabetes.
- Weight gain.
- Sedation.
- Hyperprolactinaemia (leading to problems such as amenorrhoea, reduced fertility, galactorrhoea, sexual dysfunction and gynaecomastia).
- Photosensitivity (with chlorpromazine).

The elderly are at higher risk of postural hypotension, extrapyramidal effects, and antimuscarinic effects. These, and changes in temperature regulation, make older patients particularly susceptible to dangerous falls, hyperthermia, and hypothermia. They are also at increased risk of stroke and there is a small increased risk of death when used in elderly people with dementia.

Antipsychotics should not be used for mild to moderate psychosis in the elderly; any use in the elderly should be reviewed regularly.

Some serious effects warrant immediate discontinuation and careful monitoring.

- Tardive dyskinesia – occurs frequently, especially in the elderly; usually but not always with long-term or high-dose therapy; short-lived symptoms may occur after withdrawal of n antipsychotic. This may be irreversible, but withdrawal at the earliest signs may halt full development.
- Prolongation of the QT interval (to exceed 500 msec).[4]
- Neuroleptic malignant syndrome (hyperthermia, muscle rigidity, autonomic instability, and fluctuating consciousness) is very rare but life-threatening – stopping the antipsychotic is essential and urgent medical treatment is needed. Mortality without treatment is 20%. The condition may last for five to seven days after stopping the antipsychotic; longer if depot preparations were used.[4]
- Neutropenia or agranulocytosis (particularly with clozapine).[1]
- Myocytosis or cardiomyopathy (reported with clozapine).[1]

## The main problems with stopping are:

- Relapse, which is often delayed after cessation. Patients should be informed that there is a high risk of relapse if medication is stopped within one to two years.[2]
- Withdrawal reactions, such as cholinergic rebound (nausea, restlessness, anxiety, insomnia or withdrawal dyskinesias), when stopped abruptly.
- Long withdrawal periods for depot preparations; it can take a month or longer for adverse effects to subside. (When using depots, a small test dose may be required to check for adverse effects before starting treatment doses.)

## How to discontinue therapy

Always withdraw antipsychotics gradually after long-term use. Monitor for discontinuation effects and continue monitoring for relapse for two years. If switching to another agent, taper the dose slowly while the other agent is introduced (e.g. over three weeks). Record the rationale for continuing, changing, or stopping a medicine, and the effects of such changes.[3]

## References:


1. British National Formulary (BNF) 58. September 2009. http://bnf.org
2. National Institute for Health and Clinical Excellence (NICE). Schizophrenia. Core interventions in the treatment and management of schizophrenia in adults in primary and secondary care. NICE clinical guideline 82 (update of CG1). March 2009. www.nice.org.uk
3. CASPA (Comparative Analysis System for Prescribing Audit). Prescribing Services. http://howis.wales.nhs.uk
4. Clinical Knowledge Summaries. Schizophrenia. www.cks.nhs.uk.


## Further resource


Taylor D et al. Maudsley Prescribing Guidelines, 9 Ed. London: Informa Healthcare, 2007.