Atypical antipsychotics and behavioural and psychiatric symptoms of dementia

PRESCRIBING UPDATE FOR OLD AGE PSYCHIATRISTS

The Royal College of Psychiatrists Faculty for the Psychiatry of Old Age

In March 2004 the Faculty for the Psychiatry of Old Age of the Royal College of Psychiatrists issued a joint guidance note with the British Geriatrics Society, the Royal College of General Practitioners and the Alzheimer's Society (Working Group, 2004). The joint guidance note followed the Committee on Safety of Medicines (CSM) safety message on the use of atypical antipsychotics in patients with behavioural and psychiatric symptoms of dementia (BPSD) (Committee on Safety of Medicines, 2004).

However, since the CSM alert and the joint guidance note there have been reports of inappropriate interpretations of this guidance. For example, groups of patients having their medication withdrawn en masse without consideration for the individual circumstances of the patients, and/or switching patients to other medications which are likely to have more harmful side-effects.

There have also been long-standing concerns about the inappropriate use of antipsychotic medication in older people with dementia: for example drugs given for the wrong reason (e.g. for depression) or without any documented reason for the prescription; two or more antipsychotics prescribed at the same time; drugs given at too high a dose and for too long without reviewing the need or the dose (Oborne *et al*, 2002; Waite, 2002).

This note seeks to clarify the issues and suggests good practice for old age psychiatrists in the UK. It must be read in conjunction with the CSM alert and the joint guidance note mentioned above.

The risks

The initial CSM alert and the joint guidance note followed from analysis of manufacturer data which showed an increased risk of cerebrovascular adverse events with risperidone and olanzapine.

These cerebrovascular adverse events range from strokes to transient ischaemic attacks. Sometimes non-specific 'funny turns' are reported. These can mean a wide variety of subjective experiences. If this is reported, clinicians should take a history from the patient and preferably from someone who has observed this episode. Clinicians should regard as potentially serious any unexplained dizziness, loss of balance or alterations of consciousness occurring while taking atypical antipsychotics.

The increased risk of cerebrovascular adverse events is not yet quantified. The CSM data suggested a three-fold increased risk from 1.1% to 3.3% over, typically, a 12-week period in the studies analysed.

The people at highest risk of cerebrovascular adverse events from atypical antipsychotics seem to be the 'oldest' old (i.e. over 80 years of age). People with other risk factors for strokes and transient ischaemic attacks, such as obesity, diabetes, hypertension, smoking, and cardiac arrhythmias, would logically seem

to be at greater risk of cerebrovascular adverse events from atypical antipsychotic use; however, there is no trial evidence to support this assumption. The summary of product characteristics for risperidone and olanzapine adopts the precautionary principle and suggests prescribers should give due consideration to these risk factors.

The same risks could apply to another atypical antipsychotic, quetiapine. The risk of cerebrovascular adverse events for the older 'typical' antipsychotics is unknown but a recent study (Herrmann *et al*, 2004) suggested that in a general elderly population given atypical antipsychotics their risk of stroke was not greater compared with those given typical antipsychotics.

Behavioural and psychiatric symptoms of dementia

Behavioural and psychiatric symptoms of dementia are common in dementia and most patients at some point in their illness will manifest these behaviours. They are the result of a complex interplay between the illness, the environment, physical health, medication and interactions with others. Although these symptoms can often remit spontaneously, they can also be persistent and severe, causing considerable distress to patients and carers and significantly impairing quality of life.

Drug management of behavioural and psychiatric symptoms of dementia

The term BPSD covers a variety of behaviours and psychological symptoms. Each symptom needs to be treated specifically. More than one symptom can occur at the same time and the clinician needs to decide which symptoms need to be tackled first and by what approach.

Drug, behavioural and environmental approaches are not mutually exclusive. The appropriate initial management approach depends on the symptom, its severity, frequency and impact, and the situation in which it occurs.

In the UK there is no drug licensed specifically for BPSD, but there are some BPSD for which there are licensed indications (e.g. depression or psychosis). Drug treatments for many other BPSD symptoms are therefore 'off licence'.

Anti-dementia drugs do have a beneficial effect on some behavioural symptoms of dementia, although the benefits have so far been shown in people with milder behavioural problems, and it takes some drugs a few weeks to take effect (McKeith *et al*, 2000; Feldman *et al*, 2001; Tariot *et al*, 2001).

Drugs may be an appropriate first response to BPSD symptoms in the following situations:

- where drugs have a specific indication (e.g. depression or psychosis), whatever the severity and frequency of the symptom
- where the problem symptom is severe and treatment is needed quickly, for example if the target symptoms are severe (i.e. dangerous or distressing to the patient or others) and the behaviours have no clear situational trigger or occur in a setting where carers cannot cope with serious behaviour problems.

For drug treatments the '3T' (target, titration, time) approach is good practice:

- drug treatments should have a specific target symptom
- the starting dose should be low and then be titrated upwards
- drug treatments should be time limited.

For less severe BPSD and where management is not urgent then any combination of drug, environmental manipulation or behavioural treatments may be appropriate first-line approaches. However, practitioners should be aware that no single non-pharmacological intervention (e.g. multi-sensory stimulation, bright light therapy, aromatherapy etc.) has an evidence base that would justify its use as a direct alternative to antipsychotic medication.

Whatever the severity and urgency of the situation, it is vital that the clinician assesses the situation as fully and practically as possible by speaking to the patient and to informants. The clinician can then determine the best balance of risks and benefits for the patient of every possible treatment.

If the patient has the capacity to understand these risks and benefits of treatment approaches, then consent to treatment should be sought. If the patient does not have this capacity, then these risks and benefits should, where practical, be discussed and communicated to the general practitioner, relatives and carers. Ultimately the clinician has the responsibility for the decision to implement treatment. Relatives cannot consent on behalf of their incapacitated relatives. The relevant mental capacity legislation needs to be considered.[1]

Antipsychotic drugs and treatment of specific symptoms

The atypical antipsychotics risperidone and olanzapine have the best evidence base for effectiveness compared with placebo for physical aggression, agitation and psychosis (De Deyn *et al*, 1999; Katz *et al*, 1999; Street *et al*, 2000; Chan *et al*, 2001; Brodaty *et al*, 2003). The effect of atypical antipsychotics in these situations is not entirely attributable to sedation.

Typical antipsychotics are effective with similar symptoms (Schneider *et al*, 1990; Lanctot *et al*, 1998; Lonergan *et al*, 2001) but have a weaker evidence base. Similar types of side-effects can occur with all antipsychotics but the severity and frequency of each side-effect is different in the two groups.

At effective doses typical antipsychotics tend to have more side-effects which are more severe (Neil *et al*, 2003). Typical antipsychotic side-effects are more likely to include extrapyramidal side-effects, tardive dyskinesia, anticholinergic side-effects (with possible acceleration of cognitive decline) and drowsiness (in higher doses).

At their usual doses atypical antipsychotic side-effects are more likely to include weight gain, disruption of blood glucose control, hyperlipidaemia and cerebrovascular adverse events. At higher doses sedation and extrapyramidal side-effects can occur as well.

Both classes of drugs can cause paradoxical agitation. The choice between the two classes of drugs should be informed by these general side-effect profiles as well as any individual circumstances.

A decision to start atypical antipsychotic drugs should be adequately documented and all the factors considered in making this decision should be recorded. A clear date to review the need for these drugs should also be noted.

Patients already on atypical antipsychotics

The decision to continue an atypical antipsychotic is best taken by clinicians on a case-by-case basis and on the balance of potential risks and benefits in the same way that a decision is made for initiating drug treatment.

Long-term treatment with antipsychotics carries cumulative risks of cognitive decline, falls and other side-effects. The need for continuing treatment with antipsychotics should therefore always be reviewed. A recent study (Ballard *et al*, 2004) suggests that antipsychotics could be withdrawn successfully in people who have been relatively free from behavioural symptoms for at least 3 months. It is prudent to withdraw antipsychotic drug treatment cautiously and gradually unless there are specific and distressing side-effects from medication.

However, not everyone on atypical antipsychotics should have their drug stopped or changed. BPSD can persist in the long term and are often resistant to treatment. Atypical antipsychotics should be continued for:

- people who still have continuing BPSD
- where it is felt that severe adverse consequences may occur (or have occurred) if they are discontinued
- where no alternative treatment approaches are suitable.

The decision to continue these drugs should be documented and the factors considered in making this decision should be recorded, as discussed above.

[1] In England and Wales the relevant provisions of the Mental Incapacity Bill will need to be followed when the Act comes into force. In Scotland, the principles of the Adults with Incapacity (Scotland) Act 2000 should be followed. A clear statement should be made on a Section 47 form and associated treatment plan to the effect that the risks have been discussed as indicated in the Act and that treatment has been agreed.

References

Ballard, C. G., Thomas, A., Fossey, J., *et al* (2004) A 3-month randomized, placebo-controlled, neuroleptic discontinuation study in 100 people with dementia: the neuropsychiatric inventory median cut off is a predictor of clinical outcome. *Journal of Clinical Psychiatry*, **65**, 114–119.

Brodaty, H., Ames, D., Snowdon, J., *et al* (2003) A randomized placebo-controlled trial of risperidone for the treatment of agitation, aggression and psychosis of dementia. *Journal of Clinical Psychiatry,* **64**, 134–143.

Chan, W. C., Lam, L. C., Choy, C. N., *et al* (2001) A double-blind randomised comparison of risperidone and haloperidol in the treatment of behavioural and psychological symptoms in Chinese dementia patients. *International Journal of Geriatric Psychiatry*, **16**, 1156–1162.

Committee on Safety of Medicines (2004) Atypical antipsychotic drugs and stroke. http://www.mca.gov.uk/ourwork/monitorsafequalmed/safetymessages/antipsystroke_9304.htm; http://www.mca.gov.uk/ourwork/monitorsafequalmed/safetymessages/atypicalantipsychotic_qa.htm

De Deyn, P. P., Rabheru, K., Rasmussen, A., *et al* (1999) A randomized trial of risperidone, placebo and haloperidol for behavioural symptoms of dementia. *Neurology*, **53**, 946–955.

Feldman, H., Gauthier, S., Hecker, J., *et al* (2001) A 24-week, randomized, double-blind study of donepezil in moderate to severe Alzheimer's disease. *Neurology*, **57**, 613–620.

Herrmann, N., Mamdani, M. & Lanctot, K. L. (2004) Atypical antipsychotics and risk of cerebrovascular accidents. *American Journal of Psychiatry*, **161**, 1113–1115.

Katz, I. R., Jeste, D. V., Mintzer, J. E., *et al* (1999) Comparison of risperidone and placebo for psychosis and behavioural disturbances associated with dementia. *Journal of Clinical Psychiatry*, **60**, 107–115.

Lanctot, K. L., Best, T. S., Mittmann, N., *et al* (1998) Efficacy and safety of neuroleptics in behavioural disorders associated with dementia. *Journal of Clinical Psychiatry*, **59**, 550–561.

Lonergan, E., Luxenberg, J. & Colford, J. (2001) Haloperidol for agitation in dementia (Cochrane Review). *The Cochrane Library,* issue 4. Oxford, Update Software.

McKeith, I., DelSer, T., Spano, P., *et al* (2000) Efficacy of rivastigmine in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled study. *Lancet,* **356**, 2031–2036.

Neil, W., Curran, S. & Wattis, J. (2003) Antipsychotic prescribing in older people. *Age and Ageing*, **32**, 475–483.

Oborne, C. A., Hooper, R., Li, K. C., *et al* (2002) An indicator of appropriate neuroleptic prescribing in nursing homes. *Age and Ageing*, **31**, 435–439.

Schneider, L. S., Pollock, V. E. & Lyness, S. A. (1990) A metaanalysis of controlled trials of neuroleptic treatment in dementia. *Journal of the American Geriatric Society*, **38**, 553–563.

Street J. S., Clark, W. S., Gannon, K. S., *et al* (2000) Olanzapine treatment of psychotic and behavioural symptoms in patients with Alzheimer's disease in nursing care facilities: a double blind, randomized, placebo-controlled trial. The HGEU Study Group. *Archives of General Psychiatry*, **57**, 968–976.

Tariot, P. N., Cummings, J. L., Katz, I. R., *et al* (2001) A randomised, double-blind, placebo-controlled study of the efficacy and safety of donepezil in patients with Alzheimer's disease in the nursing home setting. *Journal of the American Geriatrics Society*, **49**, 1590–1599.

Waite, J. (2002) Keep taking the medicine. *Age and Ageing*, **31**, 423–425.

Working Group for the Faculty of the Psychiatry of Old Age of the Royal College of Psychiatrists, Royal College of General Practitioners, British Geriatric Society & Alzheimer's Society (2004) Summary – Guidance for the management of behavioural and psychiatric symptoms in dementia and the treatment of psychosis in people with history of stroke/TIA. http://www.rcpsych.ac.uk/college/faculty/oap/professional/guidance_summary.htm; http://www.rcpsych.ac.uk/college/faculty/oap/professional/guidance_summary.htm#notes