Faculty of the Psychiatry of Old Age

Atypical antipsychotics and BPSD

Prescribing update for Old Age Psychiatrists

A) Introduction

1. In March 2004 the Faculty for the Psychiatry of Old Age of the Royal College of Psychiatrists issued a joint guidance note (JGN) with the British Geriatrics Society, the Royal College of General Practitioners and the Alzheimer's Society[1]. The guidance note followed the Committee on Safety in Medicines (CSM) safety message on the use of atypical antipsychotics in patients with behavioural and Psychiatric symptoms of Dementia[2].

2. Since the CSM alert and the JGN however, there have been reports of inappropriate interpretations of this guidance including groups of patients having their medication withdrawn *en masse* without considering the individual circumstances of the patients and/or switching patients to other medications which are likely to have more harmful side effects[3].

3. There have been also been long-standing concerns about inappropriate use of antipsychotic medication in older people with dementia namely: drugs given at for the wrong reason (e.g. given for depression) or without any documented reason for the prescription, two or more antipsychotic prescribed at the same time, drugs given at too high a dose and for too long without reviewing the need or the dose[4].

4. This note seeks to clarify the issues and suggest good practice for old age psychiatrists in the United Kingdom. It must be read in conjunction with the CSM alert (CSMA) and Joint Guidance Note (JGN) mentioned above.

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[1] http://www.rcpsych.ac.uk/college/faculty/oap/professional/guidance_summary.htm and http://www.rcpsych.ac.uk/college/faculty/oap/professional/guidance_summary.htm#notes

[2] http://www.mca.gov.uk/ourwork/monitorsafequalmed/safetymessages/antipsystroke_9304.htm and http://www.mca.gov.uk/ourwork/monitorsafequalmed/safetymessages/atypicalantipsychotic_qa.htm

[3] Insau, P and Lawley, D. (2004) CSM guidance on antipsychotic use: **in** Care of the Elderly in Psychosis Supplement *Geriatric Medicine* July 2004 6-7

[4] For example see Oborne,C.A., Hooper,R., Chi Li Ka, et al (2002) An indicator of appropriate neuroleptic prescribing in nursing homes *Age and Ageing* 31:435 –439 and commentary by Waite, J. (2002) Keep taking the Medicine *Age and Ageing* 31:423 –425

B) The risks

1. The initial CSMA and JGN followed from analysis of manufacturer data which showed an increased risk of cerebrovascular adverse events (CVAEs) with risperidone and olanzapine.

2. CVAEs range from strokes to transient ischaemic attacks (TIAs). 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 or preferably from someone who has observed this episode. They should regard as potentially serious any unexplained dizziness, loss of balance or alterations of consciousness occurring while taking atypical antipsychotics.

3. The increased risk of CVAEs is not yet quantified , the CSM data suggested a threefold increased risk from 1.1% to 3.3% over, typically, a 12 week period of the studies analysed.

4. The people at highest risk of CVAEs from atypicals seem to be the oldest 'old' (i.e. over 80 years of age). People with other risk factors for strokes and TIAs such as obesity, diabetes, hypertension, smoking, diabetes, and cardiac arrhythmias would logically seem to be at more risk of CVAEs from atypical antipsychotic use but there is no trial evidence to back up this assumption. The Summary of Product Characteristics for risperidone and olanzapine adopt the precautionary principle and suggests prescribers should give due consideration to these risk factors.

5. The same CVAE risks could apply to another atypical antipsychotic, quetiapine. The risk of CVAEs for the older 'typical' antipsychotics is unknown but a recent study [5] suggested that in a general elderly population given atypical antipsychotics their risk of stroke was not greater compared to those given typical antipsychotics.

C) Behavioural and psychiatric symptoms of dementia (BPSD)

1. They are common in dementia and most patients at some point in their illness will manifest these behaviours. These behaviours are the result of a complex interaction between the illness, the environment, physical health, medication and interactions with others.

2. These behaviours are a major source of distress to patients and carers. They significantly impair quality of life for both.

3. These symptoms can often remit spontaneously, but they can also be persistent and severe.

[5] Herrmann, N, Mamdani, M. and Lanctot, K.(2004) Atypical antipsychotics and risk of cerebrovascular accidents *American Journal of psychiatry* June 161:1113-1115

D) Drug Management of BPSD

1. 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 practitioner needs to decide what symptoms needs to be tackled first by what approach.

2. Drug, behavioural and environmental approaches are not mutually exclusive. What initial management approach is appropriate depends on the symptom, its severity, frequency and impact of the symptom and the situation in which it occur.

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

4. Anti-dementia drugs do have a beneficial effect on some behavioural symptoms of dementia though the benefits have so far been shown in people with milder behavioural problems and it takes some a few weeks for their effect to be manifest[6 7 8].

5. Drugs may be an appropriate first response to BPSD symptoms in the following situations:
    a. Where drugs have a specific indication (e.g. depression or psychosis), whatever the severity and frequency of the symptom
    b. Where the problem symptom is severe and treatment is needed quickly e.g. 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' approach is good practice:
    - drug treatments should have a specific **t**arget symptom
    - the starting dose should be low and then **t**itrated upwards and
    - drug treatments should be **t**ime limited

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

[6] Tariot PN, Cummings JL, Katz IR, et al. (2001) A randomised double-blind placebo-controlled study of the efficacy and safety of donepezil in patients with AD in the nursing home setting. *Journal of the American Geriatrics Society* 2001;49:1590-9.
[7] McKeith I, DelSer T, Spano P, et al. Efficacy of rivastigmine in dementia with Lewy bodies: a randomised double-blind placebo-controlled study. *Lancet* 2000;356:2031-6.
[8] Feldman H, Gauthier S, Hecker J, et al.(2001) A 24-week randomised double-blind study of donepezil in moderate to severe AD. *Neurology* 2001;57:613-20.

7. Whatever the severity and urgency of the situation, it is vital that the doctor assesses the situation as fully as practically possible by speaking to the patient and informants and then decides the best balance or risks and benefits for the patient of every possible treatment.

8. If the patient has capacity to understand these risks and benefits of treatment approaches then consent to treatment should be sought. If the patient does not have capacity to consent to treatment then these risks and benefits should, where practical, be discussed and communicated to the General Practitioner, relatives and carers. Ultimately the doctor 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 kept in mind[9].

E) Antipsychotic drugs and treatment of specific symptoms

1. The atypical antipsychotics risperidone and olanzapine have the best evidence base for effectiveness compared to placebo for physical aggression, agitation and psychosis [10] [11] [12] [13] [14]

2. The effect of atypical antipsychotics in these situations is not entirely attributable to sedation [15]

3. Typical antipsychotics are effective with similar symptoms [16] [17] [18].but have a weaker evidence base

4. Similar types of side-effects can occur with all antipsychotics but the severity and frequency of each side effects is different in the two groups.

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[9] 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.

[10] Brodarty *et al* (2003) A randomised placebo-controlled trial of risperidone for the treatment of agitation, aggression and psychosis of dementia *Journal of Clinical Psychiatry* 64:134-143

[11] De Deyn *et al* (1999) A randomised trial of risperidone, placebo and haloperidol for behavioural symptoms of dementia *Neurology* 53:946-955

[12] Chan W, et al (2001) A double-blind placebo-controlled trial of risperidone for the treatment of psychosis and behavioural symptoms of dementia *International Journal of Geriatric Psychiatry* 16:1156-62

[13] Katz, *et al* (1999) Comparison of risperidone and placebo for psychosis and behavioural disturbances associated wit dementia *Journal of Clinical Psychiatry* 60:107-115

[14] Street J.S. *et al* (2000) Olanzapine treatment of psychotic and behavioural symptoms of patients with Alzheimer's disease in nursing care facilities: a double blind randomized control trail. The HGEU Study group. *Archives of General Psychiatry* 57: 968-76

[15] Howard, R (2003) Management of behavioural problems in patients with dementia *Progress in Neurology and Psychiatry* 7(5) September/October

[16] Lanctot *et al* (1998) Efficacy and safety of neuroleptics in behavioural disorders associated with dementia *Journal of Clinical Psychiatry* 59:550-561

[17] Sneider L.S. Et al (1990) a meta-analysis of controlled trails of neuroleptic treatment in dementia. Journal of the American Geriatric Society 38: 353-63

[18] Lonergan, E. *et al* (2001) Haloperidol for agitation in dementia (Cochrane Review) in: *The Cochrane Library* 4, Oxford, Update Software

[16] Neil W. et al (2003) Antipsychotic prescribing in older people *Age and Ageing* 32:475-463

- At effective doses typical antipsychotics tend to have more side effects which are more severe[19] . 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, disrupt blood glucose control, hyperlipidaemia and CVAEs. 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 the individual circumstances of the case.

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

F) Patients already on atypical antipsychotics

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

2. 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 [20] suggests that antipsychotics could be withdrawn successfully in people who have been relatively free of behavioural symptoms for at least three months. It is prudent to withdraw antipsychotic drug treatment cautiously and gradually unless there are specific and distressing side effects from medication.

3. However, not everyone on atypical antipsyhotics should have their drug stopped or changed. BPSD can persist in the long term and often resistant to treatment. Atypicals should be continued for
    a. people who still have continuing BPSD,
    b. where it is felt that severe adverse consequences may occur (or have occurred) if they are discontinued, and
    c. where no alternative treatment approaches are suitable.

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

[20] Ballard CG *et al* (2004), A 3 month randomised 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.