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R. M. LAWRENCE, K. SCOTT, A. DUGGAL, C. DARWIN, E. BROOKS AND G. CHRISTODOULOU

Medico-legal implications of drug treatment in dementia: prescribing out of licence

AIMS AND METHOD

There is increasing evidence-based knowledge in the drug treatment of psychotic and behavioural symptoms in dementia, but drugs do not possess a formal licence for these indications. Drug companies, health authorities, NHS trusts and medical defence unions were asked for their advice on the medico-legal implications for the prescribing clinician.

RESULTS

Drug companies, health authorities, medical defence unions and NHS trusts are aware of out-of-licence prescribing and leave ultimate accountability with the clinician. A suggested best practice is that of obtaining the patient's consent.

CLINICAL IMPLICATIONS

Out-of-licence prescribing for psychotic and behavioural symptoms in dementia is widespread. This patient group may be unable to grant consent. The accountability of individual clinicians should be supported by more adequate medico-legal frameworks.

Poorly informed prescribing in the elderly is increasingly recognised (Hesse *et al*, 1993; Aparasu *et al*, 1998; Fremont, 1999; Gambassi *et al*, 1999). Its regulation in nursing homes first was addressed in the USA by the introduction of the Omnibus Budget Reconciliation Act (OBRA) 1987 (Institute of Medicine, 1986; Morford, 1988), which stipulated that the prescription of specific psychotropic drugs in nursing homes must be controlled according to the clinical indications of certain listed conditions (Elon & Pawlson, 1992). No UK equivalent exists but there has been recent interest in the role of the pharmacist in the medication reviews in nursing homes (Furniss *et al*, 2000). Results from this recent study confirmed the inappropriate prescription of medication according to OBRA criteria in 54% cases, in line with the results of a comparable earlier USA study (Beers *et al*, 1992).

Guidelines for prescribing in the very elderly are unlikely to reflect knowledge informed by sufficient research because drug treatments are normally patented on the basis of a cohort population younger than 70 years of age, which is significantly younger, on average, than the patients under the care of psychogeriatricians (Fremont, 1999).

There is substantial evidence that neuroleptics are of benefit in the treatment of psychotic and behavioural symptoms in dementia (Schneider, 1999). Atypical antipsychotics have recognised advantages over conventional antipsychotics, owing to a more favourable side-effect profile, which is especially relevant in an elderly population (Herrmann, 2001). Risperidone has been studied most extensively to date, but evidence on olanzapine and quetiapine appears promising. Alternative treatments that are effective and relatively well tolerated include the antidepressants trazodone and citalopram and the anticonvulsants carbamazepine and valproate (Tariot, 1999). Other useful drugs, supported by anecdotal evidence, include benzodiazepines, beta-blockers and buspirone and hormonal treatments. There is also recent interest in cholinergic enhancers for directly improving psychotic and behavioural symptoms in dementia (Levy *et al*, 1999).

No drug treatment, however, is specifically licensed for use in the functional and behavioural symptoms of dementia. Furthermore, drug companies are not permitted to endorse their use for indications other than those on the Summary of Product Characteristics (SPC). In practice, the guiding principles of prescribing for non-cognitive manifestations of dementia (i.e. affective, psychotic symptoms and behavioural disturbance) are extrapolated from those applying to the treatment of functional illness in younger patients. This gap in information leaves clinicians engaged in the care of the elderly with mental illness less than equipped to justify their practice.

Method

The pharmaceutical advisors from companies producing commonly used psychotropic drugs (chlorpromazine,

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promazine, thioridazine, haloperidol, droperidol, trifluoperazine, sulpiride, flupenthixol, clopixol, risperidone, olanzapine, quetiapine, fluoxetine, sertraline, paroxetine, citalopram, trazodone, valproate, carbamazepine, lithium carbonate, diazepam and lorazepam) were contacted in writing and asked to comment on the indications of their product and their position with regard to out-of-licence prescribing. Similarly, three Local Authorities' Commissioning Managers for Prescribing and Community Pharmacy (Merton, Sutton & Wandsworth Health Authority, Lambeth, Southwark & Lewisham Health Authority and West Sussex Health Authority), four NHS trusts (South West London & St George's Mental Health NHS Trust, South London & Maudsley Mental Health NHS Trust, Epsom Healthcare NHS Trust and Worthing Priority Care NHS Trust) and two medical defence unions (Medical Protection Society (MPS) and Medical Defence Union (MDU)) were asked to comment on their position on out-of-licence prescribing.

Results

Reply from drug manufacturers

All drug manufacturers replied and this is a summary of their comments:

(a) All drug companies confirmed that their products were not licensed for dementia.

(b) In the case of paroxetine, citalopram, trazodone, sulpiride, flupenthixol, clopixol, quetiapine, valproate and lithium carbonate it was confirmed further that there is no plan to extend the licence. Chlorpromazine was confirmed as licensed in conditions that may occur in dementia but are not specific to dementia. The out-of-patent product and licence extension could not be supported on commercial grounds.

(c) All drug companies stated that the final prescribing decision is a matter for the clinician, based on the availability of other therapeutic options and a careful assessment of the potential risks and benefits.

Reply from the health authorities

Comments were returned by two of the three health authorities contacted. The main points in their replies are summarised as follows:

(a) In an official capacity, health authorities cannot support prescribing outside the licence indication.

(b) Health authorities are aware of the existence of prescribing outside licence.

(c) Prescribing is ultimately considered as a matter for the individual clinician's best judgement and each case should be treated individually.

(d) Clinicians are legally supported by the Bolam Rule, which states that if a representative body of opinion would have acted in a like manner then that would be acceptable.

(e) If general practitioners have any concerns, they should seek advice from the medical defence unions, whereas hospital doctors have to conform additionally to the rules of their employing trust.

Reply from NHS trusts

Comments were returned by three of the four NHS trusts contacted:

(a) NHS trusts are aware of out-of- licence prescribing.

(b) Out-of-licence prescribing negates the liability of the manufacturer, should harm occur.

(c) Trusts would 'presumably' support clinicians if their actions could be demonstrated to be adequately supported by the literature and considered reasonable by their peers.

(d) Informed consent from the patient should be sought when prescribing unlicensed medication.

(e) The Drug and Therapeutic Committees of NHS trusts should audit themselves, reviewing the use of medication across the trust and 'indicating acceptable medications in a normal and acceptable practice'.

Reply from the MDU and the MPS

The MDU and MPS confirmed that:

(a) In law, no medicine can be marketed for human use in the UK without a product licence granted by the licensing authority. Licensing arrangements only affect manufacturers, are determined by the Medicines Act 1968 and are implemented through the Medicines Control Agency.

(b) Doctors therefore are still free to prescribe unlicensed drugs or use drugs for unlicensed indications.

(c) Non-adherence to the provision set out in the data sheet can be justified if the licence indications do not reflect current knowledge.

(d) The prescriber is vulnerable to claims against him/her for negligence and liability.

(e) In prescribing unlicensed drugs, the doctor should obtain consent and tell the patient about the status of the drug.

Discussion

Our survey highlights the ethical and legal difficulties facing the old age psychiatrist when prescribing in this area. With the exception of cognition enhancers, all drugs used in the neuropsychiatric management of dementia are unlicensed for the specific purpose for which they are used. In the light of increasing research suggesting the efficacy of psychotropic drugs, especially atypical antipsychotics, we suggest that clinicians have little option but to prescribe out of licence. Indeed, in the UK clinicians are free to do so and are not bound by the licensing restrictions placed on the drug manufacturers by the Medicines Act 1968. However, clinicians are ultimately liable for the consequences of their prescribing, as was clear from our results, but we would argue without adequate frameworks for defence.

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The replies from both NHS trusts and medical defence unions state that the existing defence for the clinician is the Bolam Rule (*Bolam v. Friern Hospital Management Committee*, 1957), scientific evidence and written informed consent from the patient (General Medical Council, 2001). We suggest that all these components of defence are problematic as follows. First, although there is some evidence for psychotropic drugs in dementia, knowledge is still lacking, especially in the areas of the very elderly and those with concurrent medical illness, both of which affect a large proportion of our patients. We believe that the lack of knowledge, guidelines or true consensus in the profession potentially undermines an individual's defence. Second, obtaining consent is all too often impracticable in patients with dementia, especially written consent. Discussion about alternatives, such as assent or vicarious approval by a carer, are unlikely to satisfy legal or moral requirements. This area of clinical and medico-legal vulnerability is not exclusive to the old age psychiatrist, yet the latter is undoubtedly challenged by the seriously complex issue of having to reconcile treatment and the patients' chronic mental incapacity.

In the interest of elderly care and of the discipline, old age psychiatrists may wish to contribute to the growth of the missing research-based evidence and seek to determine more clearly the acceptable terms of medico-legal accountability in support of unlicensed practice. In particular, we suggest that frailer cohorts older than 70 years of age should be considered for local and national audits of efficacy and safety of psychotrophic treatments administered in dementia, and of combinations of these drugs with other commonly encountered medical conditions in the elderly. Drug companies should also widen the age range of their subjects in carrying out Phase II and III trials and devote specifically adapted titrations and efficacy/safety controls to the very elderly. We suggest that this would generate further research interest, inform our practice and contribute to the improved standards of care invoked by the recently published *National Service Framework for Older People* (Department of Health, 2001). Furthermore, although the suggestion of obtaining informed consent is generally unfeasible, adopting well-founded guidelines for prescribing would go a long way towards strengthening the defence of our practice as we await appropriate extension of product licences by the drug manufacturers.

Declaration of interest

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***Robert M. Lawrence** Consultant Psychogeriatrician and Honorary Senior Lecturer, **Katherine Scott** Senior Registrar, **Anita Duggal** Senior Registrar, **Cressida Darwin** Research Psychologist, **Elizabeth Brooks** Research Psychologist, **Georgina Christodoulou** Researcher, St George's Hospital Medical School, CranmerTerrace, London SW17 0RE

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