Neuroleptic drug use in psychiatric intensive therapy units: problems with complying with the consensus statement

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The pharmacological management of acute behavioural disturbance in psychosis is not straightforward. The real, or perceived, dose:effect relationship of the various neuroleptics in common use has an important influence on prescribing patterns leading, in certain situations, to very high doses of neuroleptic medication being prescribed. Data from a study of the use of neuroleptic medication in two psychiatric intensive therapy units illustrate the potential extent of the problem. Over half of the cases were not amenable to accurate dosage monitoring due to the use of depot neuroleptics, Clopixol Acuphase or polypharmacy. The majority received doses exceeding the limit suggested by the *British National Formulary*. Efforts to standardise the use of such drugs would help to optimise the clinical management of this challenging group of patients.

The use of high dose neuroleptic medication is an issue which has recently generated a great deal of publicity, and increasing concern over serious side-effects and sudden deaths has lead to the publication of a consensus statement on the subject by the Royal College of Psychiatrists (1993). Recent literature has referred to the doses of antipsychotic medication prescribed in relation to *British National Formulary* (*BNF*; British Medical Association & Royal Pharmaceutical Society of Great Britain, 1993) guidelines (e.g. Carvill, 1994), and the concept of neuroleptic 'equivalence' (Mullen *et al*, 1994). Of particular importance in this respect are the problems encountered in the pharmacological management of severe acute behavioural disturbance in association with psychosis. Many of these patients might be expected to receive doses approaching or exceeding these guidelines, particularly in the early stages of their admission, perhaps for reasons other than the treatment of psychotic phenomena *per se* (Kane, 1994). Knowledge of, and confidence in, prescribing for this group of patients is, however, inconsistent among general psychiatrists (Cunnane, 1994), prompting requests for specific, validated guidelines; a need which has yet to be fulfilled.

High-dose neuroleptics – which can be defined as those exceeding *BNF* guidelines – should only be used as a last resort (Hirsch & Barnes, 1994). It is accepted, however, that in clinical practice, particularly in intensive therapy units, this is likely to occur.

Conversion of prescribed doses into chlorpromazine equivalence would help to determine whether any recommendations have been exceeded. This, however, is far from straightforward. There is some consensus in relation to the oral preparations of many of the major tranquillisers; although even here there is disagreement over the relative potencies of, for example, haloperidol between the *BNF*, drug company literature (Foster, 1989), and generally held received clinical wisdom (Foster, 1989; Mullen *et al*, 1994). The latter, in particular, could be expected to lead to inaccuracies in prescribing resulting in over-medication. Guidelines for depot medication are scant; presumably since the pharmacokinetics of the depot preparation do not lend themselves easily to an estimation of daily dose deliverance. Similarly, doses of Clopixol Acuphase cannot satisfactorily be converted into chlorpromazine equivalence; its use in the management of acute psychosis, especially in association with disturbed behaviour, is becoming widespread (e.g. Richards & Wilkinson, 1994) despite the risks of administering a long half-life neuroleptic in an acute situation, especially to a neuroleptic naive individual (Thompson, 1994). Additionally, although the *BNF* specifies upper dose limits, which are often used for *ad hoc* comparisons with chlorpromazine, for some drugs it gives no limit for trifluoperazine and lists ranges rather than specific maximum doses for others.

This paper represents a preliminary report on a study comparing the use of psychotropic medication in two London psychiatric intensive care

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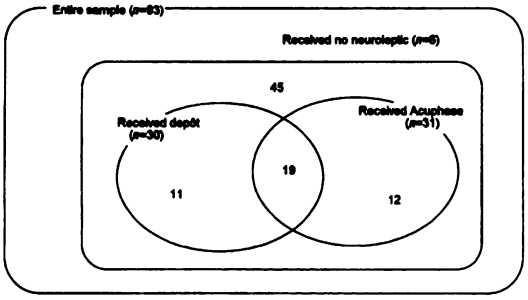

Fig. 1. Breakdown of neuroleptic medication received

units. These are wards which manage patients who are deemed inappropriate for an open psychiatric ward by virtue of their violent, overactive or severely suicidal behaviour. We present findings on the order of magnitude of doses used, the use of depot preparations, and the extent of polypharmacy.

The study

The case notes and prescription charts of all admissions to the two wards during the period of study (October 1991 to February 1992) were scrutinised. Data collected included patient characteristics, circumstances of admission, diagnosis and psychotropic medication – neuroleptics, membrane stabilisers and benzodiazepines – received during their admission. Route of drug administration, and whether it was given as a regular prescription or 'as required' (prn), were recorded.

Where possible, chlorpromazine equivalents were calculated by arriving at a consensus using information from a number of sources (*BNF*, 1993; Foster, 1989; Rowlands & MacNeill, 1990). For the purposes of estimation of overall (daily) dose received, depot preparations were assumed to remain present in the bloodstream for 14 days allowing for any accumulation of multiple doses within this period.

Findings

Of the total number of patients investigated (n=93), 87 (92%) received neuroleptic medication: 30 (35%) received depot medication and 31 (36%) Clopixol Acuphase, respectively, during their admission. A further 14 received trifluoperazine. Clozapine and risperidone were used with three patients.

Those patients receiving a single neuroleptic preparation accounted for 24.7% of the total sample. The majority, 69%, were prescribed two, or more, simultaneously with 3% receiving more than four (including depot) at some stage during their admission. Taking all neuroleptic medication, i.e. both regular prescription and 'as required' (prn) doses into account, the mean daily dose received, expressed in chlorpromazine equivalents, was 2108 mg. Of the 87 patients being prescribed neuroleptics, 33 (35.5%) received doses which did not exceed the limit suggested by the *BNF* (maximum dose: 1000 mg).

Comment

The patients investigated in this study all presented with behaviour or symptoms, or both, necessitating closer supervision and greater security than the general psychiatric wards could provide. Such patients represent a particular therapeutic challenge which, in this case, is exemplified by the high doses of medication, i.e. exceeding *BNF* maxima, received by the majority; and by the fact that polypharmacy is the rule, rather than the exception. These findings contrast with studies undertaken on general psychiatric wards (Carvill, 1994).

In over one-third of the sample – those receiving depot and/or Clopixol Acuphase – the potential for unwittingly exceeding *BNF* guidelines is high [Fig. 1]. Similar difficulties are likely to occur when patients receive two or more 'non depot' neuroleptic preparations. Variation of conversion factors – due to lack of consensus over relative potencies – might lead to an under- or overestimation of chlorpromazine equivalence. This potential source of error in prescribing would be compounded according to the degree of polypharmacy. When multiple prescribing and the use of 'atypical' antipsychotics are also taken into account, then over half (51%) do not lend themselves to accurate dosage monitoring. Hence the risks of over-medication, and of serious adverse effects, are significant.

The assumption that higher doses lead to greater antipsychotic effect has been questioned (Rifkin *et al*, 1994) whereas there is general agreement that the frequency and severity of many adverse effects is dose related and may jeopardise continuing clinical improvement (Tardiff, 1992).

Prescribing antipsychotic medication remains, therefore, an inexact science. Although dopamine blockade *in vitro* can be extrapolated to clinical improvement *in vivo* (Richelson, 1984), the exact correlation between the two has yet to be accurately defined. Individual patient characteristics influencing symptom resolution, and predisposition to adverse effects, will ensure that dosage regimes are likely to remain largely empirical. Converting doses to an equivalent dose of chlorpromazine as a measure of relative

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potency would introduce a measure of objectivity to prescribing, and hence optimise clinical management and reduce the risks inherent in over-medication. This conversion is relatively straightforward when a patient receives just one oral preparation but becomes more difficult with a more complex drug regime, particularly when depot neuroleptics are involved. It is apparent therefore that for this reason among others, polypharmacy should be avoided wherever possible.

Consistent and comprehensive guidelines based on sound clinical and pharmacological principles are required; while calls for education and continuing training on the safe and effective management of these patients remain valid and topical.

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