Chlorpromazine equivalents: a consensus of opinion for both clinical and research applications

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A consensus of available information is used to produce a working table of conversion for the most commonly used drugs to chlorpromazine equivalents. A user-friendly computer program has also been developed from this information. The use of the concept in the clinical setting and for research purposes is briefly discussed.

The use of high-dose neuroleptics has been debated in recent literature and reports of deaths occurring in patients given such high doses have received much publicity (Mehtonen *et al*, 1991). The Royal College of Psychiatrists responded to unease among its members on this subject by convening a consensus panel of experts to review the use of high-dose drugs (Thompson, 1994). Practice is changing towards using an effective antipsychotic dose of a neuroleptic with added benzodiazepines if required for tranquillisation. Awareness of effective antipsychotic dosages for different neuroleptics is therefore especially needed when changing from one neuroleptic to another.

Dopamine receptor binding studies have shown that the clinical potency of neuroleptic drugs correlates closely with affinity for dopamine D_2 receptors. These studies, together with clinical trial data, have led to the development of the concept of chlorpromazine equivalents which are meant to be a measure of the relative antipsychotic potency of neuroleptics. A recent survey of 67 psychiatrists with a range of experience has, however, revealed a wide variation in perceived potencies of specific drugs (Mullen *et al*, 1994).

The study

A variety of sources were consulted in order to reach a consensus view of chlorpromazine equivalents. These included standard textbooks, product data sheets and the medical information departments of pharmaceutical companies. Relevant articles from the medical literature were obtained from reference lists of publications and by searching the MEDLINE database from 1989–1995. 1989 was chosen as a starting point because this was the year of publication of the major papers by Rey and Schulz's teams which thoroughly reviewed the subject. No restrictive search parameters were imposed with regard to type of publication. If there was any discrepancy in the literature about chlorpromazine equivalence the most often quoted figure was used. A range is quoted for depot drugs because of the extreme lack of agreement in the literature. The results of our survey are illustrated in Table 1.

Comment

General agreement was found for most drugs with a few discrepancies for which several reasons are suggested. Firstly, equivalents are based primarily on dopaminergic blockade and not upon a drug receptor profile for cholinergic, serotonergic or histaminergic systems. This will have a bearing on the conversion of atypical antipsychotics into chlorpromazine equivalents. Secondly, it has been suggested that the relationship between dose and antipsychotic potency for some drugs (e.g. haloperidol) may not be linear, i.e. the relative antipsychotic potency of haloperidol significantly decreases as the dosage increases (Foster, 1989). Thirdly, confusion between antipsychotic activity and the sedative and anxiolytic effects of drugs would make drugs such as haloperidol seem less potent in comparison with chlorpromazine. This latter point was highlighted in Mullen *et al*'s survey of practising psychiatrists (1994).

While a consensus appears to have been reached for the equivalence between different depot antipsychotics we found discrepancies between the oral equivalent of depot antipsychotics. The manufacturers' literature suggests that 100 mg chlorpromazine orally per day

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Table 1. *BNF* advisory maximum daily doses and chlorpromazine dose equivalents

	***BNF* advisory maximum daily doses**	**Dose 'equivalent' to 100 mg oral chlorpromazine/day**
Oral neuroleptics		
Clozapine	900 mg	50 mg
Droperidol	120 mg	4 mg
Flupenthixol	18 mg	2 mg
Fluphenazine	20 mg	2 mg
Haloperidol	100 mg (occasionally 200 mg)	3 mg at <20 mg/d and 5 mg at >20 mg/d
Loxapine	250 mg	20 mg
Pericyazine	300 mg	24 mg
Perphenazine	24 mg	8 mg
Pimozide	20 mg	2 mg
Promazine	800 mg	100 mg
Prochlorperazine	100 mg	15 mg
Remoxipride	600 mg	75 mg
Sulpiride	2400 mg	200 mg
Thioridazine	800 mg	100 mg
Trifluoperazine	None	5 mg
Triluperidol	8 mg	2 mg
Depot neuroleptics		
Fluphenazine decanoate	100 mg 2 weekly	10–25 mg 2 weekly
Flupenthixol decanoate	400 mg weekly	16–40 mg 2 weekly
Zuclopenthixol decanoate	600 mg weekly	80–200 mg 2 weekly
Haloperidol decanoate	300 mg 4 weekly	40–100 mg 4 weekly
Pipothiazine palmitate	200 mg 4 weekly	20–50 mg 4 weekly
Fluspirilline	20 mg weekly	2 mg weekly

References: Foster (1989), Rey *et al* (1989), Schulz *et al* (1989), Bazire (1994), BMA & Royal Pharmaceutical Society (1994), Association of the British Pharmaceutical Industries (1994).

is equivalent to 40 mg flupenthixol decanoate intramuscularly (IM) every two weeks and 25 mg fluphenazine decanoate IM every two weeks. The data sheet for Haldol decanoate states that these doses of depot antipsychotics are equivalent to 100 mg haloperidol decanoate IM monthly but also states that this dose of haloperidol decanoate is equivalent to 500 mg oral chlorpromazine daily (a five-fold discrepancy). Therefore we have quoted what appears to be a consensus range for the chlorpromazine equivalents of depots. This example illustrates the vague nature of the concept of chlorpromazine equivalents. Although receptor occupancy is the basis for the concept, available data seems to derive from clinical and anecdotal sources rather than receptor occupancy studies for each individual drug. Beckmann & Laux (1990) pointed out that "when commonly recommended guidelines for the dosage of neuroleptic drugs are critically reviewed, unanswered questions outnumber accepted rules".

For this reason chlorpromazine equivalents are intended only as an approximate guide to clinical practice and caution is recommended in their use. Individual dosage instruction should be checked and doses should not be extrapolated beyond the maximum *British National Formulary* recommended doses without careful clinical consideration. It is recognised that there is great variability in patient response to antipsychotics, thus patients should be carefully monitored after any change in medication.

A WINDOWS® program has been developed from this data which will calculate chlorpromazine equivalents. Copies of this program are available as a result of an educational grant from Zeneca Pharmaceuticals. Requests for copies should be forwarded to the CNS team, Medical Research Department, Zeneca Pharmaceuticals, Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG.

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