Cost comparison of zuclopenthixol acetate and haloperidol

Clive E. Hyde, Colina Harrower-Wilson and Paul E. Ash

This prospective, sequential study compared the costs of using haloperidol or zuclopenthixol acetate for rapid tranquillisation. In the first phase, all 16 patients admitted to our psychiatric intensive care unit requiring rapid tranquillisation received haloperidol; in the second phase, all 26 such patients received zuclopenthixol acetate. Mean overall costs per patient were substantially lower in the zuclopenthixol acetate group than the haloperidol group, mainly because special nursing was used much less in the zuclopenthixol acetate group. All nursing staff preferred to use zuclopenthixol acetate rather than haloperidol. Zuclopenthixol acetate could potentially reduce the need for special nursing and produce valuable cost savings.

Our previous study (Hyde & Harrower-Wilson, 1995) investigated the total costs of operating our psychiatric intensive care unit (PICU). We found that most of the costs were fixed (e.g. staff salaries and overheads). Of the variable costs, which are of particular interest to management as they are amenable to manipulation, most were associated with patient violence (special nursing, extra staff required to manage violent incidents requiring rapid tranquillisation, and the costs of treating injuries sustained during a suicide attempt). Drug costs were very low, comprising only 0.5% of total costs.

The importance of violence as a contributor to hospital costs is consistent with a US study (Karson *et al*, 1991) which found that violent in-patients with schizophrenia cost 43% more to care for than their non-violent counterparts.

Zuclopenthixol acetate, an intermediate-acting neuroleptic effective for up to three days, was associated with a reduction of more than 50% in violent incidents after its introduction for the treatment of acutely disturbed patients in a psychiatric unit in Sweden (Omérov *et al*, 1995). This indicates that use of zuclopenthixol acetate could yield useful cost savings by reducing patient violence, as well as non-economic benefits such as a reduction in stress to staff and patients. The present study was conducted to compare patient management costs using zuclopenthixol acetate or a conventional neuroleptic (haloperidol), and to investigate staff preferences between the two drugs.

The study

The study included all patients admitted to the PICU of the Department of Psychiatry at the Withington Hospital, Manchester, between December 1994 and January 1996, with a diagnosis of schizophrenia, mania, manic depression (mixed/rapid cycling), substance misuse or other acute psychosis, and who required rapid tranquillisation for acute disturbance during their stay or immediately prior to admission.

Patients on a closed psychiatric ward interact with staff and each other, and may influence one another's behaviour. This makes it impossible to use the conventional randomised study design, since patients in one medication group may affect the behaviour of patients in the other. For example, a patient who is satisfactorily managed and calm on one study medication may be provoked into violence by aggression from another patient taking the comparison medication. To avoid this potential confounding factor, we adopted a sequential design. During the first part of the study (1 December 1994 to 5 July 1995) all study patients received haloperidol when rapid tranquillisation was necessary. From 6 July 1995 to 18 December 1995, all study patients received zuclopenthixol acetate for rapid tranquillisation. Finally, as we observed that the zuclopenthixol acetate group contained more patients than the haloperidol group, a second haloperidol phase began on 19 December 1995 and continued until the study ended on 5 January 1996. Patients from the two haloperidol phases were pooled to form a single haloperidol group. One patient who was on the ward during a crossover period and was exposed to both drugs was excluded from the study.

The dose of study drug was at the discretion of ward staff, within previously agreed *British*

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National Formulary guidelines, since patients vary in their response to neuroleptics. This should have ensured that all patients received the optimum drug dose. Lorazepam could also be used for rapid tranquillisation, in conjunction with the study drug, if considered necessary. Our intention was that the study should interfere as little as possible with routine clinical practice. Therefore, all other aspects of patient management (including maintenance neuroleptic medication, treatment of extra-pyramidal side-effects, use of low-stimulus environment, special nursing, etc) were at the discretion of ward staff.

As our previous study showed that costs related to patient violence (special nursing, staff time to manage violent incidents and the consequences of violence) comprised 93% of the unit's variable costs (Hyde & Harrower-Wilson, 1995) the current study measured only these costs, plus the cost of the study drugs.

The Psychiatric Studies in Aggression Database (PSAD) was used to record information for each patient, including demographic details, diagnosis, nursing and medical staff involvement, dose of study drug and lorazepam and details of violent incidents (using the Staff Observation Aggression Scale (SOAS) questionnaire (Palmstierna *et al*, 1987)). All patients were assessed using the Psychiatric Symptom Assessment Scale (PSAS; Berthot & LaPierre, 1989) and Social Dysfunction and Aggression Scale (SDAS; Wistedt *et al*, 1990) scales on admission, daily for the first seven days, and then weekly thereafter. Medication side-effects (drowsiness, tremor, rigor, dystonia, akathisia, visual disturbances and orofacial movements) were rated at the same times, on a three-point scale (0=absent, 1=mild, 2=severe). The ratings for all seven side-effects were summed to produce an overall score (minimum score=0, maximum score=14).

Nursing staff employment costs (including basic salary, overtime and enhancement payments, pension contributions, superannuation fees, employers' National Insurance costs, annual holiday, sickness absenteeism and study leave) were taken as a weighted mean across all staff grades, and totalled £9.29 per working hour. Medical staff employment costs were calculated separately for each grade of doctor. Damage to property and injury to people during violent incidents were recorded on the SOAS questionnaire and costs calculated at the end of the study using manual records. Drug prices were taken from the *British National Formulary*, March 1995 edition.

At the end of the study, a questionnaire was circulated to all 21 nursing staff on the PICU asking which of the two study drugs they preferred and why. Their preference was rated on a three-point scale (greatly preferred, slightly preferred or no preference), and they were then given five drug attributes (length of action; speed of action; quality of sedation; reduction in the number of injections; and reduced side-effects) and asked to rank these in order of their importance in determining their drug preference.

Findings

Sixteen patients met the study criteria during the haloperidol periods (of a total of 116 patients admitted) and 26 during the zuclopenthixol acetate period (of a total of 64 patients admitted). We are unable to account for this difference in recruitment rate. The groups differed slightly in demographic characteristics, although none of the differences was statistically significant (Table 1). Mean PSAS, SDAS and SOAS scores were similar in both groups (Table 1). Thus, there was no clinical evidence that either group was more psychotic or more violent than the other.

The dose of zuclopenthixol acetate ranged from 25 to 150 mg, and the dose of haloperidol from 5 to 30 mg. During the study period, the 26 zuclopenthixol acetate patients received a total of 5600 mg of zuclopenthixol acetate (mean of 215.4 mg per patient), and the 16 haloperidol patients received a total of 680 mg of haloperidol (mean of 42.5 mg per patient). The maximum number of doses required for any one patient over the study period was seven in the zuclopenthixol acetate group and 11 in the haloperidol group.

The two groups did not differ in their scores for medication side-effects. In the zuclopenthixol acetate group the mean overall side-effect score was 0.55 (range 0–1.42) and in the haloperidol group the mean was 0.50 (range 0–1.45). The use of oral procyclidine (the only medication used for control of side-effects) also revealed no difference between the groups. The procyclidine dose ranged from 5 to 10 mg in both groups, and the mean total dose administered per patient over the study period was 33.5 mg in the zuclopenthixol acetate group and 31.9 mg in the haloperidol group. It should be noted that patients were also receiving maintenance neuroleptic treatment at the discretion of their consultants, and it was not possible to differentiate between extrapyramidal side-effects due to maintenance neuroleptics and those due to the study drugs.

There was no difference between the groups in the mean number of violent incidents recorded per patient; rapid tranquillisation was required 36 times in the haloperidol group and 59 times in the zuclopenthixol acetate group, a mean of 2.3 incidents per patient in both groups. There was also no difference in the requirement for concomitant lorazepam, required in 71% of the incidents in the zuclopenthixol acetate group

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Table 1. Patient characteristics

	Haloperidol group (*n*=16)		zuclopenthixol acetate group (*n*=26)	
Demography				
Mean age, years	34		31	
Number (%) male	15	(94)	20	(77)
Number (%) admitted informally	2	(13)	2	(8)
Number (%) with forensic history	3	(19)	10	(38)
Number (%) Caucasian	13	(81)	19	(73)
Diagnosis				
Schizophrenia	11	(69)	15	(58)
Mania	1	(6)	3	(12)
Manic depression (mixed/rapid cycling)	3	(19)	4	(15)
Substance misuse	1	(6)	2	(8)
Other acute psychosis	0		2	(8)
Clinical assessment				
Mean PSAS score per patient, all ratings (s.d.)	25	(10.51)	28	(9.67)
Mean SDAS score per patient, all ratings (s.d.)	6	(3.83)	6	(2.61)
Mean SOAS score per patient, all violent incidents (s.d.)	4.75	(1.62)	4.51	(1.86)

PSAS, Psychiatric Symptom Assessment Scale; SDAS, Social Dysfunction and Aggression Scale; SOAS, Staff Observation Aggression Scale.

and 69% in the haloperidol group. The dose of lorazepam employed ranged from 2–4 mg in both study groups. The total cumulative dose over the study period was 114 mg in the zuclopenthixol acetate group (mean of 4.4 mg per patient), and 193 mg in the haloperidol group (mean of 12.1 mg per patient). However, the apparent increase in lorazepam use during the haloperidol phase was due mainly to high use in one patient and probably does not represent a real difference.

Three incidents in the haloperidol group resulted in damage to property, compared with four in the zuclopenthixol acetate group; the number of incidents resulting in injury to people were seven and nine respectively. Injuries in all cases were minor, and the costs incurred negligible (a total of £409.74 for the whole unit during the study period, of which £100 was accounted for by replacement of spectacles broken in one incident). There were 15 successful absconding attempts in the haloperidol group and 25 in the zuclopenthixol acetate group. None resulted in damage or injury and in most cases the patients returned of their own volition. The costs of absconding were also negligible, totalling £111.71 over the study period.

Over twice as many patients in the haloperidol group required special nursing as in the zuclopenthixol acetate group (31 compared with 12%).

The total costs of rapid tranquillisation, replacement of damaged property and special nursing are shown in Table 2.

Twenty fully completed questionnaires were returned. All the nursing staff preferred to use zuclopenthixol acetate for rapid tranquillisation. The main reasons for their choice were: reduction in the number of injections required (7 replies); longer duration of action (5 replies); speed of action; and better quality of sedation (4 replies each).

Comment

So far as we are aware, this is the first study to investigate the effect of different medications for rapid tranquillisation on overall costs. The mean variable cost per patient was substantially lower in the zuclopenthixol acetate group than in the haloperidol group. Indeed, the total variable cost for the whole zuclopenthixol acetate group was lower than the total variable cost for the whole haloperidol group, despite the larger number of patients in the zuclopenthixol acetate group (26, compared with 16 in the haloperidol group). The main reason for this was the lower use of special nursing in the zuclopenthixol acetate group, indicating that use of zuclopenthixol acetate may be able to reduce the need for special nursing in some patients. Zuclopenthixol acetate has a longer duration of action than aqueous formulations, with one dose remaining active for up to three days (Baastrup *et al*, 1993). This may mean that patients receiving rapid tranquillisation with zuclopenthixol acetate are slower to return to a state of agitation and therefore require less high-intensity nursing. More stable neuroleptic levels may also be achieved, and Yeasavage (1982) has reported an inverse correlation between danger-related events and neuroleptic levels in patients with schizophrenics.

Zuclopenthixol acetate was preferred over haloperidol by all the nursing staff on our unit.

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Table 2. Total costs, £

	Total cost in group		Mean cost per patient	
	Haloperidol (*n*=16)	zuclopenthixol acetate (*n*=26)	Haloperidol (*n*=16)	zuclopenthixol acetate (*n*=26)
Rapid tranquillisation cost				
Drug cost	44.62	608.76	2.79	23.41
Nursing time cost	614.84	1116.66	38.43	42.95
Medical time cost	120.00	208.17	7.50	8.01
Total rapid tranquillisation cost	779.46	1933.59	48.72	74.37
Replacing damaged property	310.00	220.00	19.38	8.46
Special nursing	12 708.72	10 033.20	794.30	385.89
Total	13 798.18	12 186.79	862.40	468.72

In contrast to the report by Omérov *et al* (1995) we did not observe any difference in the frequency of violent incidents between the two patient groups. This may reflect differences between the studies in factors such as: patient type, ward environment, patient management or definition of violence. It may also reflect the observed differences in patient characteristics between our two patient groups, which were marked although not significant. An earlier two-year study on our unit found that patients of non-Caucasian ethnic background were more likely to use physical (as well as verbal) threat, and patients with a forensic history were more likely to use more violent means of attack (Hyde, 1998). Both non-Caucasians and forensic patients in the present study were concentrated in the zuclopenthixol acetate group, which also contained a higher proportion of patients detained under the 1983 Mental Health Act, and it is possible that as a result this group had a greater tendency to violence than the haloperidol group. Against this, however, is the observation that both groups had similar scores on the psychiatric rating scales used.

Zuclopenthixol acetate may have the potential to reduce the requirement for special nursing in psychiatric intensive care, which is costly and stressful for both staff and patients. Further research in this area is called for.

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*Clive E. Hyde, *Consultant Psychiatrist*, Colina Harrower-Wilson, *Divisional Manager Psychiatric Nursing* and Paul E. Ash, *Clinical Nursing Officer, Department of Psychiatry, Withington Hospital, Nell Lane, West Didsbury, South Manchester M20 2LR*

*Correspondence