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# A DOUBLE-BLIND COMPARISON OF THE EFFICACY AND SAFETY OF PAROXETINE AND IMIPRAMINE IN THE TREATMENT OF DEPRESSION WITH DEMENTIA

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## ABSTRACT

*Objectives*. To compare the efficacy of paroxetine and imipramine prospectively in patients with coexisting depression and dementia.

*Methods*. An 8-week, double-blind, parallel group trial comparing paroxetine 20–40 mg/day with imipramine 50–100 mg/day in 198 patients aged 60 years or over with a Montgomery–Asberg Depression Rating Scale (MADRS) score $\geqslant 20$ and a Folstein mini-mental state evaluation score of 17–23 points after a 3- to 7-day placebo run-in period.

*Results*. Both paroxetine and imipramine reduced the MADRS and the Clinical Global Impression (CGI) severity-of-illness and global improvement scores at weeks 2, 4, 8 and at endpoint, with no significant differences between treatment groups at any timepoint (MADRS, $p \geqslant 0.368$; cgi, $p \geqslant 0.286$). There was a statistically significant difference in favour of paroxetine at both the week 4 and week 8 timepoints (analysis of variance, $p \leqslant 0.049$) in the Cornell scale for depression in dementia: at endpoint there was no significant difference between treatments ($p = 0.103$). Treatment-emergent adverse experiences were reported by 51.5% (51/99) of patients treated with paroxetine and 50.5% (50/99) of patients treated with imipramine. Anticholinergic adverse experiences (paroxetine 6.1%; imipramine 13.1%) and serious non-fatal adverse experiences (paroxetine 4.0%; imipramine 8.1%) were reported by more patients in the imipramine group than in the paroxetine group.

*Conclusions*. Paroxetine and imipramine were both effective in the treatment of depression in elderly subjects with co-existing dementia, and no significant differences were detected between the groups. There were trends suggesting that paroxetine was better tolerated than imipramine in terms of anticholinergic adverse experiences and serious non-fatal adverse experiences. © 1998 John Wiley & Sons, Ltd.

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Dementia, is almost exclusively an illness of the elderly; between 10% and 47% of the population are reported to have Alzheimer's disease by the age of 85 years (Evans *et al*., 1989; Rocca *et al*., 1986). Dementia is one of the major reasons for institutionalisation in the aged and has major economic cost implications. The association of depression with dementia has been recognised for a number of years and it has been estimated that approximately 40% to 50% of demented patients exhibit depressive symptoms at some stage during their illness (Wragg and Jeste, 1989). While treatment of the depressive symptoms does not directly influence the natural course of the dementia, amelioration of the depression frequently results in attendant improvements in cognitive function.

Tricyclic antidepressants (TCAs) such as imipramine and amitriptyline are among the oldest and most commonly used antidepressants. However, anticholinergic side effects which could be considered merely troublesome in the younger patient, can be more problematic in the elderly (Naranjo *et al*., 1995). The increased incidence of

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postural hypotension and daytime sedation can increase the risk of falls and hip fractures (Dunner, 1994).

The selection serotonin reuptake inhibitor (SSRI) paroxetine has demonstrated similar efficacy in younger depressed adults to the TCAs imipramine (Dunbar *et al*., 1991), amitriptyline (Bignamini and Rapisarda, 1992) and dothiepin (Shillingford *et al*., 1990), and has also been shown to be effective in the treatment of late-life depression (Dunbar, 1995). In comparison with the TCAs, paroxetine has an improved tolerability profile and is associated with fewer anticholinergic adverse effects (Jenner, 1992). Furthermore, when the behavioural effects of paroxetine were compared with dothiepin in 94 patients with major depression, cognitive function was impaired by dothiepin whereas paroxetine had no detrimental effect (Hindmarch, 1992).

The published literature on the treatment of depression in demented subjects is sparse. Imipramine did not improve the symptoms of depression over and above the placebo response in 28 demented patients who also met DSM-III criteria for depression (Reifler *et al*., 1989). In contrast, citalopram (Nyth *et al*., 1992) and maprotiline (Fuchs *et al*., 1993) have both demonstrated superiority over placebo in treating depressive symptoms in populations of elderly patients, although in the citalopram study not all patients had a concomitant diagnosis of dementia.

In order to evaluate the efficacy of paroxetine in the treatment of depression associated with dementia we have prospectively conducted an international, multicentre, comparative study of paroxetine and imipramine in a population of elderly depressed patients with a clinical diagnosis of dementia according to DSM-III-R criteria. The safety and tolerability of the two drugs, as well as their efficacy, were compared in this population.

## METHODS

This was a randomised, double-blind, multinational, parallel group study conducted at 34 centres in Australia, Germany, Austria, France, Italy and Switzerland. The study was conducted in accordance with Good Clinical Practice and the Declaration of Helsinki, and the protocol and statement of informed consent were approved by an Ethics Committee at each centre.

### *Entry criteria*

Patients of either sex, aged 60 years or over, with a clinical diagnosis of dementia according to DSM-III-R criteria were enrolled in the study. In addition, patients had to have a diagnosis of major/minor depression according to Research Diagnostic Criteria and a total score of at least 20 on the Montgomery Asberg Depression Rating Scale (MADRS) [Montgomery and Asberg, 1979], and have mild to moderate cognitive impairment supported by a score of 17–23 points on the Folstein mini-mental state evaluation (Folstein *et al*., 1975). Furthermore, a 'carer' (relative/nurse/warden etc) who had daily contact with the patient, and who could ensure that the study medication was taken, had to be identified.

Patients were excluded from the study if they had any severe co-existing disease or comorbid schizophrenia. Furthermore, patients who posed a current suicidal risk or who were known to abuse alcohol or illicit drugs were not included in the study. Exclusion criteria relating to previous psychotropic medication included the use of depot neuroleptics in the previous 6 months, lithium or electroconvulsive therapy in the past 8 weeks, and oral neuroleptics in the previous 2 weeks. Patients were also excluded if they had taken monoamine oxidase inhibitors in the previous 3 weeks, tri- or tetracyclic antidepressants in the past 7 days, or an SSRI in the previous 4 weeks. Treatment with benzodiazepines could be continued only if stabilised for at least 7 weeks prior to screening, and in one centre patients were also excluded if they had taken tryptophan in the previous 7 days. Patients who were currently receiving oral anticoagulants or type IC antiarrhythmics or who had received any investigational compound in the past 3 months were also excluded as were patients with clinically significant electrocardiogram or laboratory values at screening or baseline. In addition, patients with a history of hypersensitivity to TCAs, or patients unable to cooperate with study procedures due to the severity of their behavioural disturbance were also excluded.

### *Study medication*

Following screening, patients entered a 3- to 7-day placebo run-in phase, after which they were randomised to receive either paroxetine or imipramine under double-blind conditions for 8 weeks.

Each patient took one capsule of active drug or placebo in the morning and evening, except at the

highest dose level for each treatment group which involved two capsules in the morning and one in the evening. Patients in the paroxetine group took 20 mg each morning for the first 2 weeks of the study. According to the patients' clinical response at the end of week 2, the dose could be increased to 30 mg/day and at the end of week 4 could be further increased to 40 mg paroxetine daily, maintained at the same level as before, or decreased according to the patients' response and tolerability. In the imipramine group patients took 25 mg each evening for 3 days, then 50 mg/day as a divided dose (25 mg in the morning, 25 mg in the evening) for 11 days, and then in the subsequent 2 weeks 75 mg/day (25 mg in the morning, 50 mg in the evening). At the end of week 4 the dose of study medication could be increased to 100 mg imipramine daily (50 mg in the morning, 50 mg in the evening), maintained at the same level as before or decreased according to the patients' response and tolerability. The only concurrent psychotropic medication permitted during the active treatment was chloral hydrate on an as needed basis and benzodiazepines if they had been initiated and stabilised at least 7 weeks before the screening visit.

### *Efficacy and tolerability assessments*

Following screening, clinical assessments were made at baseline and after 1, 2, 4 and 8 weeks of active treatment. At each visit MADRS, Clinical Global Impression (CGI) severity-of-illness and global improvement scores (Guy, 1976), and the Gottfries, Brane, Steen (GBS) Scale (Gottfries *et al*., 1982) were assessed. In addition, the Cornell scale for depressive symptoms in dementia patients (Alexopoulos *et al*., 1988) was assessed at the end of weeks 4 and 8.

The primary efficacy parameters were the changes in MADRS and CGI severity-of-illness scale at endpoint (the latest timepoint at which at least 70% of the intention-to-treat population remained). This was after 8 weeks in this study.

Secondary efficacy variables included an analysis of the total scores on the CGI global improvement scale (on which 1 represents very much improved an 7 very much worse), the change from baseline in the GBS scale total score, and the Cornell Scale for depressive symptoms in dementia patients (assessments based on a 3-point scale for 19 questions). Compliance was checked at each visit by a routine capsule count, and any concurrent medication noted. Patients were also asked a non-leading question to elicit details of treatment-emergent adverse experiences. Serious adverse experiences were defined as any experience which was fatal, life threatening, disabling or incapacitating, or resulted in a hospital stay or prolonged hospitalisation or was associated with a congenital abnormality, carcinoma or overdose. Observed and spontaneously reported events were also noted, and sitting blood pressure and heart rate measured. At the week 8 visit, or earlier if the patient withdrew prematurely, a physical examination was undertaken, and samples were obtained for laboratory tests.

### *Statistical methods*

This study was designed to detect a difference of 6.0 points in the MADRS score, with a 90% power and significance level of 0.05. Allowing for an attrition rate of 40%, it was planned that 200 patients would be randomised to active treatment.

Endpoint data were generated from the last available on-treatment assessment for each patient. The endpoint was taken as the visit at which at least 70% of the intent-to-treat population (randomised patients with at least one valid on-treatment efficacy assessment) remained. The CGI severity-of-illness scores were compared using Cochran-Mantel-Haenszel chi-square tests, all the other efficacy variables were analysed by analysis of variance (ANOVA). A variable representing each country was constructed and examined for significance of treatment by country interaction. No significant interaction was detected. Therefore, the interaction term was not included in the model. The Cochran-Mantel-Haenszel chi-square test was also used to compare the incidence of emergent adverse experiences.

## RESULTS

### *Treatment groups*

A total of 216 patients entered the placebo run-in phase of the study. Of these, 198 patients were randomised to one of the treatment groups: 99 received paroxetine and 99 received imipramine. The baseline characteristics of the 198 who formed the intent-to-treat population are presented in Tables 1 and 2, and a summary of patients at each dose level is presented in Table 3. The majority of patients in the study were female, with the paroxetine group consisting of slightly more

Table 1. Demographic characteristics of intent-to-treat population

| | | Paroxetine ($n = 99$) | Imipramine ($n = 99$) |
|---|---|---|---|
| Sex | Male | 17 (17.2%) | 27 (27.3%) |
| | Female | 82 (82.8%) | 72 (72.7%) |
| Age (years) | Range | 59–98 | 59–97 |
| | Mean | 76.6 | 76.6 |
| Race | Caucasian | 99 (100%) | 98 (99.0%) |
| | Other* | 0 | 1 (1.0%) |
| Weight (kg) | Mean (SD) | 69.1 (9.6) | 73.1 (13.8) |

*Other includes Black, Asian, Oriental, other.

females than the imipramine group. The other demographic characteristics were equally balanced between the groups with a mean age of 76.6 years in both groups and all patients,with the exception of one, being Caucasian. Approximately, three-quarters of the patients had one or more concurrent illnesses or abnormal physical signs at screening, the most common relating to the cardiovascular system and the locomotor system. The duration of the present episode of depression was less than 6 months for the majority of patients, with approximately 60% of both treatment groups having already received treatment, principally with benzodiazepines or standard antidepressants.

Six of the randomised patients (three paroxetine, three imipramine) were excluded from the intent-to-treat efficacy dataset, as they had not received any valid on-treatment efficacy evaluations (one of the three paroxetine patients had a valid CGI assessment which was included in the efficacy dataset).

Twenty-five patients (25.3%) randomised to paroxetine and 26 (26.3%) randomised to imipramine withdrew prematurely from the study. The reasons for patient withdrawal are presented in Table 4.

Table 3. Maximum daily dose of study medication in the intent-to-treat population

| Paroxetine ($n = 99$) | | Imipramine ($n = 99$) | |
|---|---|---|---|
| dose (mg) | $n$ (%) patients | dose (mg) | $n$ (%) patients |
| | | 25 | 1 (1.0) |
| 20 | 60 (60.6) | 50 | 65 (65.7) |
| 30 | 29 (29.3) | 75 | 24 (24.2) |
| 40 | 10 (10.1) | 100 | 9 (9.1) |

*Note:* 25 mg imipramine group represents patients who did not complete the up-titration phase.

### *Efficacy*

Both paroxetine and imipramine reduced the mean MADRS total score in the intent-to-treat population at weeks 2, 4, 8 and at endpoint, indicating a progressive improvement in depressive symptoms (Fig. 1). There were no statistically significant differences between the two treatment groups at any time point ($p \geqslant 0.368$). At endpoint there was a mean reduction from baseline of

Table 2. Baseline psychiatric characteristics of intent-to-treat population

| | | Paroxetine ($n = 99$) | Imipramine ($n = 99$) |
|---|---|---|---|
| Duration of present depressive episode | $\leqslant 6$ months | 66 (66.6%) | 71 (71.7%) |
| | $> 6$ months | 33 (33.3%) | 28 (28.3%) |
| Previous treatment for current episode | | | |
| | Any | 60 (60.6%) | 58 (58.6%) |
| | Benzodiazepines | 38 (38.4%) | 42 (42.4%) |
| | Bi/tri/tetracyclic antidepressants | 22 (22.2%) | 25 (25.3%) |
| Previous history of depression | | 44 (44.4%) | 48 (48.5%) |
| MADRS score (mean ± SD)* | | 28.2 ± 4.7 | 28.1 ± 5.3 |
| CGI severity of illness score (mean ± SD)† | | 4.8 ± 0.8 | 4.6 ± 0.8 |
| Folstein mini-mental state evaluation (mean ± SD)‡ | | 19.6 ± 2.0 | 20.2 ± 1.9 |

*Three patients in each group had missing data.
†Two paroxetine patients and three imipramine patients had missing data.
‡Data from 79 paroxetine and 81 imipramine patients.
MADRS, Montgomery Asberg Depression Rating Scale.
SD, standard deviation.
CGI, clinical global impression.

Table 4. Reasons for withdrawal

| | Paroxetien ($n = 99$) | Imipramine ($n = 99$) |
|---|---|---|
| Lack of efficacy/relapse | 1 (1.0%) | 2 (2.0%) |
| Lack of efficacy + adverse events | 5 (5.1%) | 4 (4.0%) |
| Significant adverse events | 12 (12.1%) | 12 (12.1%) |
| Lack of patient compliance | 0 | 2 (2.0%) |
| Patient lost to follow up | 1 (1.0%) | 1 (1.0%) |
| Protocol violation | 2 (2.0%) | 1 (1.0%) |
| Concurrent disease | 0 | 1 (1.0%) |
| Death | 1 (1.0%) | 1 (1.0%) |
| Other* | 3 (3.0%) | 2 (2.0%) |

*For paroxetine patients 'other' reasons were: family stopped treatment, study medication stopped by nurse in error, reason not recorded in the case record (CRF). For the imipramine patients: patient went to health resort, reason not recorded on CRF.

12.6 (SD, 10.0) in the paroxetine group, compared with 11.8 (SD, 10.0) in the imipramine group (Table 5). Efficacy was also assessed using the mean change from baseline in the CGI severity-of-illness score. There was a very similar decrease in severity-of-illness scores at each successive time interval for both treatment groups (Fig. 2), and at endpoint there was a mean change from baseline of −1.3 in both the paroxetine and imipramine groups (Table 5). Comparison of the two treatment groups showed no statistically significant differences at any timepoint ($p \geqslant 0.286$). Similarly, the mean CGI improvement scores were analysed at endpoint and at weeks 2, 4, and 8. At endpoint there was a mean improvement score of 2.7 in both treatment groups (Table 5). The Cornell Scale for depression in dementia patients was analysed at weeks 4, 8 and at endpoint (Fig. 3). There was a significant difference in favour of paroxetine at both the week 4 and week 8 timepoints (ANOVA, $p \leqslant 0.049$) although there was no significant difference between the groups at endpoint ($p = 0.103$) (Table 5).

Table 5. Changes in efficacy variables at endpoint in intent-to-treat population

| | Paroxetine | | Imipramine | |
|---|---|---|---|---|
| | *n* | Mean (SD) | *n* | Mean (SD) |
| MADRS total score mean change | 96 | −12.6 (10.0) | 96 | −11.8 (10.0) |
| CGI severity of illness mean change | 97 | −1.3 (1.5) | 96 | −1.3 (1.5) |
| CGI improvement score | 97 | 2.7 (1.5) | 96 | 2.7 (1.6) |
| Cornell rating scale | 86 | −8.9 (6.7) | 86 | −7.1 (7.5) |
| GBS total score | 96 | −11.7 (18.1) | 96 | −12.0 (19.6) |

MADRS, Montgomery Asberg Depression Rating Scale.
CGI, clinical global impression.
GBS, Gottfries, Brane, Steen Scale.

Attendant improvements in aspects of dementia were assessed by the GBS scale scores. There was a steady improvement in GBS total score at each timepoint during the study and the change from baseline at endpoint was −11.7 in the paroxetine group and −12.0 in the imipramine group (Table 5). There was no significant difference between the two treatment groups at any timepoint ($p \geqslant 0.651$).

*Tolerability*

Treatment-emergent adverse experiences were reported by 51.5% of patients treated with

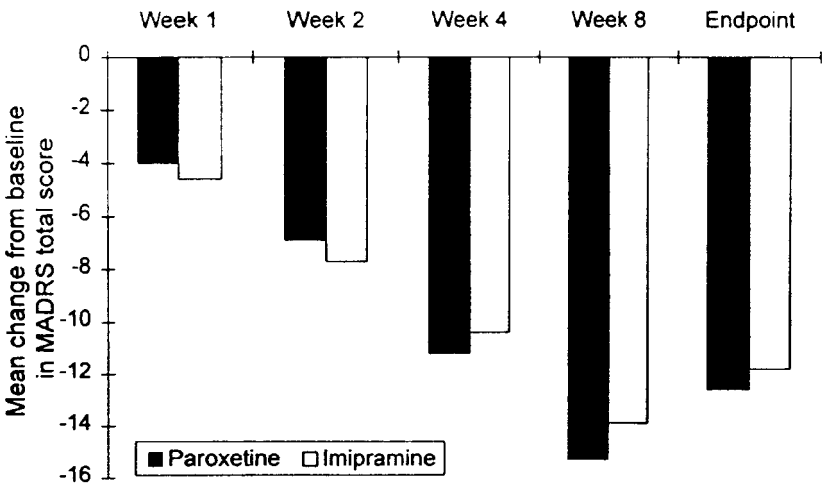


Fig. 1. The mean changes from baseline in MADRS total score during the study

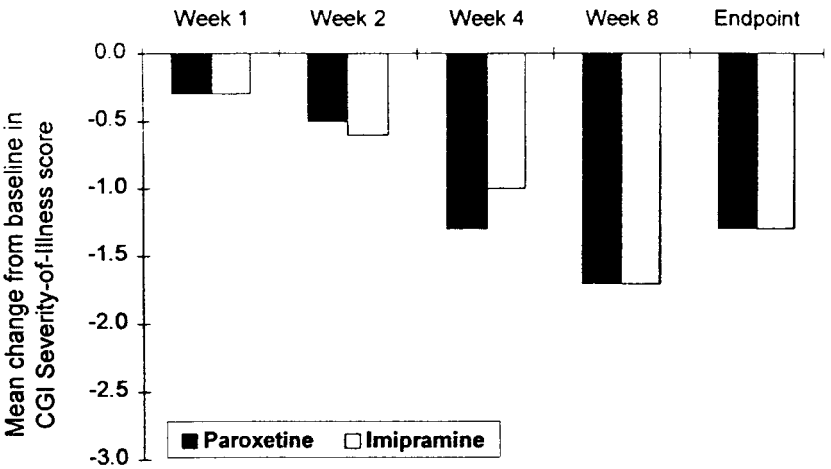


Fig. 2. The mean change from baseline in CGI severity of illness score during the study

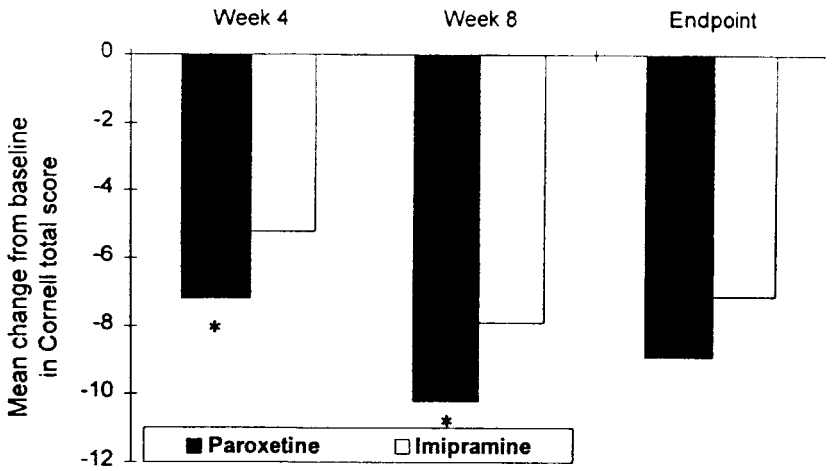


Fig. 3. The mean change from baseline in Cornell total scores during the study

paroxetine and 50.5% of patients treated with imipramine ($p = 0.82$) (Table 6). The body systems most frequently affected in both groups were the digestive system and the nervous system. The most common emergent experiences in the paroxetine group were trauma, somnolence, nausea and insomnia, while in the imipramine group, patients most frequently reported trauma, dry mouth, somnolence and confusion. Adverse experiences occurring in $\geqslant 5\%$ of patients in either group are presented in Table 7.

Serious non-fatal emergent adverse experiences were also reported in more patients in the imipramine group compared with the paroxetine group (paroxetine 4.0%; imipramine 8.1%). In the paroxetine group all the serious adverse experiences were considered by the investigator to be probably unrelated to study treatment, while in the imipramine group three patients had serious adverse experiences which were considered to be probably related to study treatment (severe costal fracture and severe pleural effusion [1], agitation [1], suicide attempt [1]). The patient with the severe costal fracture and pleural effusion experienced acute respiratory failure due to the pleural effusion and died. The patient's death was considered by the investigator to be probably related to study treatment.

Overall 18.2% of paroxetine-treated patients and 17.2% of imipramine-treated patients withdrew

Table 6. Summary of adverse experiences (AE) occurring in patients in either treatment group (intent-to-treat population)

| | Paroxetine ($n = 99$) | Imipraminie ($n = 99$) | $p$-value |
|---|---|---|---|
| Patients with at least one treatment-emergent AE | 51 (51.5%) | 50 (50.5%) | 0.820 |
| Anticholinergic-emergent AE | 6 (6.1%) | 13 (13.1%) | NT |
| Severe emergent AE | 24 (24.2%) | 22 (22.2%) | NT |
| Serious emergent AE (not including deaths) | 4 (4.0%) | 8 (8.1%) | NT |
| Withdrawals due to AE | 18 (18.2%) | 17 (17.2%) | NT |
| AE considered to be treatment-related | 3 (3.0%) | 8 (8.1%) | NT |

AE, adverse event.
NT, not tested.

Table 7. Treatment emergent adverse experiences occurring in $\geqslant 5\%$ of patients in either treatment group (intent-to-treat population)

| Adverse experience | Paroxetine ($n = 99$) | Imipramine ($n = 99$) |
|---|---|---|
| Trauma | 10 (10.1%) | 11 (11.1%) |
| Somnolence | 8 (8.1%) | 7 (7.1%) |
| Nausea | 5 (5.1%) | 1 (1.0%) |
| Insomnia | 5 (5.1%) | 2 (2.0%) |
| Dry mouth | 3 (3.0%) | 10 (10.1%) |
| Confusion | 2 (2.0%) | 6 (6.1%) |
| Asthenia | 2 (2.0%) | 5 (5.1%) |

because of adverse experiences. This difference was not tested statistically.

Three deaths occurred during the study; one paroxetine patient died from congestive heart failure and a further paroxetine patient died following severe haematemesis and haemorrhagic shock. One imipramine patient committed suicide (not with the study drug). All these deaths were considered unrelated to study treatment. A further three deaths (two paroxetine, one imipramine) occurred between 12 and 64 days after active medication had stopped. Both the deaths in the paroxetine group were considered unrelated to study treatment. However, the death in the imipramine group was considered probably related to study treatment (see above).

There were no differences between the groups with respect to mean values or changes at endpoint for the vital signs data. Furthermore, no changes of clinical significance were noted in the laboratory data for either group.

## DISCUSSION

The elderly psychiatric patient presents several challenges to the clinician as treatment is frequently complicated by psychological and physical changes related to ageing. Furthermore, the elderly have often been excluded from clinical trials as problems relating to the prevalence of concurrent medical illness, the use of concomitant medications and altered pharmacodynamics can confound the interpretation of efficacy assessments and more importantly can place these patients at a higher risk of adverse effects. While these are all valid reasons for a cautious approach to the recruitment of the elderly into clinical trials, they have led to a paucity of information concerning the efficacy and tolerability of psychotropic medications in the older population. As the proportion of elderly patients in the population continues to increase, with those aged 85 years and older comprising the fastest growing segment (Lebowitz and Cohen, 1992), issues relating to the availability and appropriate use of psychotropic medications in elders, many of whom will also suffer from dementia, have become of increasing importance.

This comparative double-blind, clinical trial has compared the efficacy and tolerability of the SSRI, paroxetine, with the TCA imipramine in the treatment of depression associated with dementia and has demonstrated that both agents are similarly effective. In our study there was no evidence of a significant difference in efficacy between paroxetine (20–40 mg/day) and imipramine (50–100 mg/day) for the treatment of the symptoms of depression. Though it might be argued that the maximum dose of imipramine was relatively low, higher doses might well have evoked more serious adverse effects. Moreover, the recommended daily dose of imipramine in elderly patients in the UK is 30–50 mg/day. Nevertheless, the design of the study did not include measurement of imipramine plasma levels. Furthermore, in the study of Reifler *et al.* (1989), no separation between imipramine and placebo was noted and therefore the lack of a placebo cell in the present study prevents a clear separation between active treatment and placebo response. Overall the only difference in efficacy between the treatments was in the Cornell scale for depression in dementia, for which there was a statistically significant difference favouring paroxetine at the week 4 and week 8 assessment. The Cornell scale is a clinician-rated scale of depressive symptoms especially designed for assessing dementia

patients. The scale performs equally well in rating depressive symptoms regardless of level of severity of cognitive impairment, and is sensitive to both major and minor depression (Teri and Logsdon, 1995). That paroxetine improved the Cornell rating scale for depression to a significantly greater extent than imipramine at two of the three timepoints is an interesting finding, which warrants further verification in a larger study group.

Although there were few significant differences between paroxetine and imipramine in the treatment of the symptoms of depression, the comparison of treatment-emergent adverse experiences suggested that paroxetine may have a more favourable profile than imipramine. In particular, serious emergent adverse experiences were reported in twice as many patients in the imipramine group compared with the paroxetine group (8.1% and 4.0%, respectively), and anticholinergic adverse experiences were reported by more than twice as many patients in the imipramine group as in the paroxetine group (13.1% and 6.1%, respectively). These latter findings are consistent with previous comparisons of paroxetine with imipramine (Dunbar *et al*., 1991; Claghorn and Feighner, 1993; Cohn and Wilcox, 1992) and other TCAs (Hutchinson *et al*., 1991). Patients with dementia, as typified by Alzheimer's disease, often have a deficit in the cholinergic system, and therefore may be especially prone to developing confusion because of anticholinergic activity. An association, between drugs with anticholinergic effects, such as TCAs, and delirium in the elderly has been noted in several epidemiological studies (Francis *et al*., 1990). It is therefore interesting to note that more patients in the imipramine group reported confusion as an emergent adverse experience than in the paroxetine group (6.1% and 2.0%, respectively).

The adverse experiences reported by paroxetine-treated elders were similar to those seen in previous clinical trials with this drug, although the incidence of nausea (5.1%), somnolence (8.1%) and insomnia (5.1%) was lower in the present trial. This may reflect the fact that over 60% of patients in both treatment groups remained on the lowest dose level of drug (paroxetine 20 mg/day and imipramine 50 mg/day) throughout the study.

That the relative incidence of serious adverse experiences and anticholinergic adverse experiences was not tested statistically is a limitation of this study. However, these statistical tests were not included in the initial plan of the study and it was considered inappropriate to re-open the database retrospectively to conduct these analyses. These preliminary results suggest that paroxetine may have a better tolerability profile than imipramine in an elderly population with dementia.

In conclusion, there was no difference in efficacy between paroxetine and imipramine in the treatment of patients with depression associated with dementia over the 8-week study period. However, there was an indication with the Cornell rating scale for depression that at weeks 4 and 8 paroxetine may have an advantage over imipramine. There were also indications that paroxetine had a more favourable tolerability profile, with fewer patients experiencing anticholinergic adverse experiences and serious non-fatal adverse experiences.

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