Efficacy and Tolerability of Moclobemide in Comparison with Placebo, Tricyclic Antidepressants, and Selective Serotonin Reuptake Inhibitors in Elderly Depressed Patients: A Clinical Overview

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Objective: To review the efficacy and safety of moclobemide in comparison with TCAs (for our purposes, “TCAs” will represent tricyclic and tetracyclic antidepressants, including maprotilin and mianserin) and selective serotonin reuptake inhibitors (SSRIs) in elderly depressed patients.

Methods: The efficacy data reviewed were obtained from the following sources: 1) results of published studies in the elderly; 2) data on patients aged ≥ 60 years extracted from all available controlled trials in adults (≥ 18 years) in which moclobemide was compared with TCAs or SSRIs; and 3) the adverse events were extracted for patients aged ≥ 60 years from the safety database of all available comparative short-term studies with moclobemide versus TCAs, SSRIs, or placebo and of long-term studies with moclobemide.

Results: The data show that moclobemide is an effective antidepressant in depressed patients aged ≥ 60 years. The response rate to moclobemide was 50% to 55% in this population. Moclobemide was more effective than placebo and was of similar efficacy to the TCAs and the more recently introduced SSRIs. The tolerability of moclobemide was rated as “very good” or “good” in almost 90% of these patients, which was better than the tolerability of TCAs and similar to that of SSRIs. Patients without any adverse events were more frequently found in the moclobemide group than in those treated with TCAs (P < 0.01) or SSRIs (P < 0.01). Adverse events of the anticholinergic type were more frequent with TCAs than with moclobemide (P < 0.001), and nausea was found 3 times more frequently with SSRIs than with moclobemide (P < 0.01).

Conclusions: Moclobemide is an effective and well-tolerated antidepressant for the treatment of elderly depressed patients.

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Key Words: efficacy, safety, antidepressant, moclobemide, elderly, long-term treatment

Depression is common in the elderly. The estimated prevalence of depression in people over age 65 is about 10% to 15% (1,2). Depression in elderly patients is managed in most cases pharmacologically and by psychological counselling. Drug treatment in the elderly is difficult, however, being complicated by, among other things, concomitant diseases and age-related physiological changes, which influence the pharmacokinetics and metabolism of drugs. Until recently, antidepressant drug treatment was restricted to the TCAs, which are often associated with side effects, including myocardial toxicity, and cardiovascular and anticholinergic effects (3–5). Manela found that “the overwhelming majority
(90%) of depressed subjects were not taking antidepressants” (2, p S184). Only in recent years have better-tolerated therapeutic agents become available, notably the SSRIs, (for example, fluvoxamine and fluoxetine) and the reversible selective inhibitors of monoamine oxidase isoenzyme A (RI-MAs) (for example, moclobemide).

The new RIMA moclobemide has been shown to be well tolerated and effective in adults (6–9). The benign side effect profile of moclobemide and its low potential for adverse drug interactions, as well as the fact that the pharmacokinetics of moclobemide are age-independent (10), may offer special advantages in the treatment of elderly patients. This publication reviews the available evidence from studies of elderly depressed patients specifically as well as data on elderly patients included in studies of adult depressives.

Methods

This review includes all published studies with moclobemide in elderly depressed patients. In addition, results of patients ≥ 60 years were extracted from the manufacturer data base of all available moclobemide studies in adults (≥ 18 years).

Results of Published Studies of Moclobemide in the Elderly

The results will be reviewed study by study. The methods used in the published studies of moclobemide in elderly patients with major depression are not described here, since they have been published elsewhere. Key information is provided below, however.

Data from Elderly Patients (≥ 60 Years) Extracted from Moclobemide Studies with a Broad Age Range (≥ 18 Years)

Data from different studies against TCAs or SSRIs were pooled. Patients were allocated to treatment for a period of 4 or 6 weeks depending on the study protocol. In most cases, patients were given the standard recommended dosages, as follows: moclobemide 300 to 600 mg/day, TCAs 100 to 200 mg/day, fluoxetine 20 to 40 mg/day, fluvoxamine 100 to 200 mg/day. Efficacy was assessed using the Hamilton Depression Rating Scale (HDRS). Response was defined as an improvement of 50% or more in the total score on the HDRS (17 items) between baseline and the last available endpoint (on day 42 or earlier). Response was also evaluated using the investigator’s rating of overall efficacy at the endpoint (Clinical Global Impression [CGI]) according to “very good/good” or “very much improved/much improved.” All patients with at least one postbaseline assessment were included in the analysis. Overall tolerability was evaluated from the investigator’s rating at the end of the study according to “very good” (no side effects) or “good” (side effects did not interfere with patient’s activities).

Adverse Event Profile

The data pool summarizes the adverse events from all available comparative short-term moclobemide studies in depression. From this data pool, which contained 11 325 depressed patients as of June 1995, the adverse events of all patients aged ≥ 60 years are reported here. All adverse events occurring in at least one treatment group (moclobemide, placebo, TCA, SSRI) in a frequency of 5% or higher were considered. The duration of treatment was 6 weeks in the majority of the studies, and the target dose range of moclobemide was 300 to 600 mg/day. In addition, all available long-term data from moclobemide studies were included.

Results

Table 1 gives an overview on all available double-blind comparative studies of moclobemide in the elderly as well as the pooled data on elderly patients extracted from comparative studies against TCAs and against SSRIs in adults (≥ 18 years).

Comparisons with Placebo

The efficacy of moclobemide in the elderly was compared with that of placebo in 2 studies (11,12). In the study by Roth and others (11), the primary objective was to determine whether treatment for 6 weeks with moclobemide at a dose of 400 mg/day in elderly depressed patients with cognitive decline produced a greater amelioration of depressive symptoms and behaviour than placebo as measured by the HDRS, the Sandoz Clinical Assessment Geriatric scale (SCAG), and the Physician’s Clinical Assessment of Efficacy.

Six hundred and ninety-four elderly patients with symptoms of depression and cognitive decline participated in a double-blind trial in which they were randomly allocated to treatment with either moclobemide or placebo for 42 days. Five hundred and eleven patients met DSM-III criteria for dementia and were also depressed (DEM+D group); 183 did not meet DSM-III criteria for dementia but met the criteria for DSM-III major depressive episode and also suffered from cognitive decline (MDE+CD group).

For the 183 patients suffering from major depression and cognitive decline (MDE+CD), the total scores of the 17-item HDRS at study baseline were the same in both treatment groups (mean ± SD 23.5 ± 5.3 in both groups). The time course of the mean improvement in the HDRS scores of both treatment groups is shown in Figure 1. Differences between moclobemide and placebo were statistically significant (t test, \( P < 0.05 \)) from day 21 on. A greater portion of moclobemide-treated patients (52%) improved by 50% or more from baseline than placebo-treated patients (25%, \( P < 0.001 \)). The results of the Physician’s Clinical Assessment of Efficacy also favoured moclobemide (improvement with moclobemide 62% versus placebo 51%).
The mean total scores of the SCAG scale decreased during treatment to a significantly greater extent in the moclobemide group (change of −17 points) than in the placebo group (change of −10 points, \( P < 0.01 \)).

The 511 patients in the DEM+D group showed a rather high mean HDRS score at baseline (24.5 ± 5.3), and the cognitive impairment was pronounced (MMSE 20.2 ± 4.8, SCAG factor 1 13.5 ± 3.9). The changes in HDRS, SCAG factor 1, and Mini-Mental State Examination (MMSE) showed moclobemide to be superior to placebo (\( P < 0.01 \)). At week 6, significantly more patients treated with moclobemide were responders (HDRS ≥ 50%: moclobemide 56%, placebo 36%).

Tolerability was independent of diagnostic classification. In 92% of the placebo patients and in 88% of the moclobemide patients the tolerability rating was “excellent” or “good.” Premature termination rates due to adverse events were 8.4% on moclobemide and 4.7% on placebo.

The second comparison of moclobemide and placebo in elderly depressed patients was provided in a double-blind randomized study of moclobemide (400 mg/day fixed dose), nortriptyline (± 75 mg/day flexible dose, adapted to reach 50 to 170 ng/mL), and placebo (12). Following a 4- to 14-day drug-free run-in period, 109 elderly patients suffering from a major depressive episode were randomized to receive 1 of the 3 treatments for 7 weeks, but only 50% of the patients completed the 7-week treatment. The reasons for premature termination were predominantly intolerance of nortriptyline and inefficacy of moclobemide or placebo.

The remission rates at the end of treatment (week 7 or earlier) were 33% for nortriptyline, 23% for moclobemide, and 11% for placebo. Remission was defined as an end-of-treatment score less than 10 on the 17-item HDRS. The difference between moclobemide and placebo was not statistically significant; the difference between nortriptyline and placebo almost reached statistical significance (\( P = 0.05 \)). A secondary analysis carried out on the 54 patients who completed the full 7-week study resulted in significantly higher
remission rates for the active drugs versus placebo (11%), that is, nortriptyline 60% ($P < 0.01$) and moclobemide 53% ($P < 0.01$).

Overall tolerability was reported to be “excellent” or “good” in 83% of patients on moclobemide as compared with 74% of patients on placebo and 37% on nortriptyline. Nortriptyline was significantly less well tolerated than placebo ($P < 0.002$) or moclobemide ($P < 0.001$). Significantly more premature terminations due to intolerance occurred on nortriptyline (26.5%) compared with moclobemide (5.6%) ($P < 0.05$) or placebo (2.9%) ($P < 0.05$).

**Comparisons with TCAs**

Moclobemide was compared in elderly depressed patients in 4 further studies with 3 TCAs, namely, mianserin, maprotiline, and imipramine. All studies had the formal limitation of having recruited a rather small number of patients. Altogether, however, they further confirm the efficacy of moclobemide in elderly patients. In a study by Tiller and others (13), both drugs were well tolerated and side effects were minimal. Forty-one patients suffering from DSM-III major depressive episode were randomized to either moclobemide (300 to 600 mg/day) or mianserin (60 to 90 mg/day). Twenty-six patients (13 on moclobemide, 13 on mianserin) completed 4 weeks of treatment, and 20 patients (11 on moclobemide, 9 on mianserin) completed the 8-week treatment. The 24-item mean HDRS scores were similar at baseline, with 26 ± 6 points for the moclobemide group and 25 ± 5 points for the mianserin group. Both drugs significantly reduced HDRS total scores. Sequential analysis as well as unpaired comparisons found no significant difference between the 2 drugs.

The second study (14) also compared moclobemide with mianserin in elderly patients (≥ 60 years) with a DSM-III diagnosis of major depressive episode. Eighty eligible patients were randomized to either moclobemide 300 to 500 mg/day or mianserin 75 to 125 mg/day for 4 weeks. The baseline ratings on the 24-item HDRS were similar for moclobemide (23.4 ± 4.4) and mianserin (22.5 ± 4.2). Four weeks of treatment resulted in a mean reduction of HDRS score by 52% in each group. The overall assessment of efficacy was “good” or “very good” for somewhat more than 60% of the patients in each group, and tolerability was rated as “very good” or “good” in more than 85% of patients in each group.

De Vanna and others (14) also studied 39 inpatients over 60 years of age who were randomized after a 7-day washout to treatment with moclobemide (150 to 300 mg/day) or maprotiline (75 to 150 mg/day) for 6 weeks. Patients met criteria for ICD-9–defined endogenous or neurotic depression and scored 20 or more points on the 24-item HDRS. Baseline HDRS scores were similar (moclobemide 33 ± 6 and maprotiline 29 ± 4). At the end of treatment, HDRS scores declined 85% in both groups compared with baseline. The overall assessment of efficacy was over 90% “good” or “very good” in both groups, and general tolerability was rated “very good” or “good” in 80% of the moclobemide and 75% of the maprotiline cases.

In another recent study (15), 30 patients suffering from major depression ($n = 24$) or from a depressive episode of bipolar disorder ($n = 6$) were randomized to treatment with moclobemide (400 to 600 mg/day) or imipramine (75 to 100 mg/day). HDRS total scores were similar at baseline (moclobemide: 27 ± 5 and imipramine 24 ± 4), and were steadily reduced over 60 days in both groups. Moclobemide resulted in a mean HDRS reduction of 51% compared with 45% with imipramine (Benton-Test, digit-symbol substitution test). Cognitive performance was significantly ameliorated after 30 and 60 days of treatment with moclobemide, but not with imipramine. Tolerability results favoured moclobemide over imipramine, particularly with respect to anticholinergic side effects.

In the data pool of controlled moclobemide studies in elderly and younger patients with major depression, data on 223 elderly patients receiving moclobemide were available for comparison with those of 228 elderly patients on TCAs. Response rates (defined previously) for moclobemide were 50% using the 17-item HDRS and 55% using the CGI; these rates were similar to the response rates obtained with TCAs (56% on the HDRS and 57% on the CGI).

Overall tolerability was rated as “very good” or “good” in 85% of elderly patients on moclobemide compared with 68% on TCAs ($P < 0.0001$).

**Comparisons with SSRIs**

Moclobemide has been compared with fluvoxamine in a double-blind study of elderly patients who had a severe depressive episode (16). Forty patients received moclobemide 300 to 450 mg/day or fluvoxamine 100 to 200 mg/day for 4 weeks. The mean total score on the Montgomery Asberg Depression Rating Scale (MADRS) showed a steady decline in both treatment groups, and this decline was significantly more pronounced in the moclobemide group than in the fluvoxamine group ($P = 0.009$). Furthermore, the CGI efficacy rating was “very good” or “good” in 84% of the moclobemide patients and in 55% of the fluvoxamine patients. General tolerability was excellent under both treatment conditions: 100% of patients on moclobemide and 95% on fluvoxamine were rated as having “very good” or “good” tolerance to treatment.

Altamura and Aguglia (17) reported results from a double-blind study in 68 elderly patients with major depression or dysthymia. Moclobemide (400 mg/day) and fluoxetine (20 mg/day) were of comparable efficacy. At the end of the 6-week treatment period, the mean reduction of the HDRS total score was 56% in patients treated with moclobemide and 50% in patients treated with fluoxetine (not significant). Altamura and Aguglia did not use the CGI to measure effi-
Efficacy and Tolerability of Moclobemide

Table 2. Incidence of adverse events (%) in elderly patients reported in double-blind, 6-week trials of moclobemide versus placebo

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Moclobemide (n = 502)</th>
<th>Placebo (n = 483)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth</td>
<td>7.4</td>
<td>6.0</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>8.4</td>
<td>6.2</td>
</tr>
<tr>
<td>Headache</td>
<td>8.4</td>
<td>11.4</td>
</tr>
<tr>
<td>Nausea</td>
<td>5.6</td>
<td>3.5</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5.4</td>
<td>4.3</td>
</tr>
<tr>
<td>Constipation</td>
<td>4.4</td>
<td>3.1</td>
</tr>
<tr>
<td>Tremor</td>
<td>1.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Agitation, nervousness</td>
<td>10.4</td>
<td>10.8</td>
</tr>
<tr>
<td>Sleepness, tiredness</td>
<td>5.0</td>
<td>6.2</td>
</tr>
<tr>
<td>Sweating</td>
<td>0.6</td>
<td>1.2</td>
</tr>
<tr>
<td>None</td>
<td>59.6</td>
<td>62.7</td>
</tr>
</tbody>
</table>

Table 3. Incidence of adverse events (%) reported in double-blind, 6-week trials of moclobemide versus TCAs

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Moclobemide (n = 423)</th>
<th>TCA (n = 480)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth</td>
<td>14.4</td>
<td>34.6</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>12.8</td>
<td>6.5</td>
</tr>
<tr>
<td>Headache</td>
<td>9.2</td>
<td>7.5</td>
</tr>
<tr>
<td>Nausea</td>
<td>5.7</td>
<td>5.6</td>
</tr>
<tr>
<td>Dizziness</td>
<td>8.0</td>
<td>10.6</td>
</tr>
<tr>
<td>Constipation</td>
<td>4.7</td>
<td>9.2</td>
</tr>
<tr>
<td>Tremor</td>
<td>5.9</td>
<td>11.3</td>
</tr>
<tr>
<td>Agitation, nervousness</td>
<td>11.6</td>
<td>7.5</td>
</tr>
<tr>
<td>Sleepiness, tiredness</td>
<td>7.1</td>
<td>12.7</td>
</tr>
<tr>
<td>Sweating</td>
<td>4.0</td>
<td>10.4</td>
</tr>
<tr>
<td>None</td>
<td>40.9</td>
<td>32.5</td>
</tr>
</tbody>
</table>

Efficacy and tolerability; however, better tolerability was reported for moclobemide, particularly in its lower incidence of gastrointestinal side effects.

In the data pool of controlled moclobemide studies in adult patients with depression, data from 81 elderly patients on moclobemide were available for comparison with those from 82 patients on fluoxetine. The response rates using the CGI were 49% with moclobemide and 51% with fluoxetine. The response rates were similar according to a 50% or greater improvement in the HDRS: 47% of patients treated with moclobemide and 49% of patients treated with fluoxetine improved.

The Adverse Event Profile

The adverse event data base (short term of 4 to 6 weeks) for moclobemide available to the manufacturer in June 1995 included 11385 cases treated with moclobemide or with comparative drugs or placebo. Of these, 1054 patients treated with moclobemide were aged 60 years or older.

Comparative data from patients treated with placebo (n = 483), TCAs (n = 480) or SSRIs (n = 134) are also presented here. It is of interest to see that the incidence of adverse events with moclobemide is to some extent higher in controlled studies against TCAs than in placebo-controlled studies. This finding can be partially explained by methodological differences in collecting adverse events (several TCA-controlled studies used a semistructured interview with checklists to collect adverse events, whereas most of the other studies collected signs and spontaneously reported adverse events); the finding may also indicate that clinicians are to some extent influenced in their judgement by expectations based on the known side effects of TCAs.

Many of the adverse events recorded during the treatment of patients suffering form depression (dry mouth, insomnia, fatigue, nervousness, headache) are also found in untreated depressed patients; although not pathognomonic, these symptoms are frequently found during depression. The real adverse event incidence can therefore be best established in studies comparing an antidepressant drug with placebo. Nearly 1000 cases are available for this purpose (Table 2).

Nearly 2 out of 3 patients (62.7%) who received placebo were reported to have been free of treatment-emergent adverse events during the whole trial. For moclobemide, this frequency was only slightly lower, at 59.6%. The difference does not reach statistical significance, at 59.6%. The difference does not reach statistical significance. Agitation or nervousness, headache, insomnia, and dry mouth were the most frequently found adverse events in both placebo- and moclobemide-treated elderly patients. For none of these adverse events was significantly different frequency found in moclobemide- or placebo-treated patients. Since the observed population approaches 1000, we may posit with some certainty that in elderly patients, the frequency of these adverse events with moclobemide is similar to the frequency with placebo ($\beta < 0.1$).

The comparison with TCAs (Table 3) shows clear advantages for moclobemide. More patients receiving moclobemide did not report any adverse events during treatment ($P < 0.01$). Most important is the difference in anticholinergic adverse events: not only dry mouth, constipation, tremor, and sweating but also sleepiness or daytime tiredness were found more often with TCAs ($P < 0.01$). By contrast, insomnia was more frequent with moclobemide ($P < 0.01$), and nervousness just failed ($P = 0.06$) to be significantly more frequent with moclobemide. Headache, nausea, and dizziness were found with a similar frequency in both groups.

In the comparisons of moclobemide with SSRIs (Table 4), both treatments were well tolerated, but more patients treated with moclobemide were free of adverse events ($P < 0.01$). With the SSRIs, 5 adverse events (nausea, headache, nervousness, dry mouth and insomnia) were found with a frequency $\geq 5$%; with moclobemide, only 2 adverse events (nervousness and headache) had the same frequency. Nausea
is 3 times more frequent in patients treated with SSRIs than in those treated with moclobemide ($P < 0.01$).

Adverse event incidence data for 566 elderly patients treated for longer than 6 weeks were included in the long-term safety data base. Approximately 60% of these individuals were treated for up to 6 months, approximately 20% for more than 6 and up to 12 months, and approximately 20% for longer than one year. The adverse events that occurred during the first 6 weeks of treatment were included in the short-term data base. Table 5, therefore, reports adverse events newly emerging after 6 weeks or persisting into the long-term period.

During long-term moclobemide treatment, lasting on average for more than 6 months, 2 out of 3 patients were completely free of any adverse event. The adverse event profile is very similar to short-term treatment, but at a lower level of frequency. This finding is remarkable, since the exposure time was approximately 5 times longer than the acute treatment phase. The incidence of sleep disturbance and constipation was reduced to approximately one-third; the incidence of tremor, agitation, and sweating was reduced to half (see Table 5).

**Discussion**

The data obtained from the studies presented here are consistent and clearly demonstrate that moclobemide is an effective and well-tolerated antidepressant in elderly depressed patients. In this patient population, moclobemide has been shown to be more efficacious than placebo and of comparable efficacy to the established TCAs and the SSRIs. A metaanalysis of moclobemide studies (18) compared the efficacy of moclobemide and reference antidepressants in elderly and younger patients. There was no significant difference in response rates between younger (62%) and elderly patients (65%). Elderly patients receiving comparator antidepressants responded significantly less well (58% total response rate, 20% had a very good response) than younger patients (62% total response rate, 29% had a very good response). In the study reported by Roth and others (11), the response rate to moclobemide was twice that to placebo. The response rate (52%) was similar to reported response rates for other antidepressants in the elderly. Gershon and others (19), who analyzed the results of studies published from 1964 to 1986 of antidepressant agents in elderly patients, found an overall response rate of 50% in elderly depressed patients. In the study by Nair and others (12), there was a clear superiority of both nortriptyline and moclobemide over placebo in the analysis of patients completing a sufficiently long period of treatment, namely, 7 weeks (Georgotos and others [20] have demonstrated that antidepressant treatment in the elderly requires as long as 7 weeks to be effective). Compared with a small placebo-controlled study of medically frail elderly patients in residential care settings by Katz and others (21), who found a 39.4% mean HDRS reduction on nortriptyline, the placebo-controlled study by Roth and others (11) showed a mean HDRS reduction of 51.4% for patients on moclobemide. In the latter study, 78.1% of patients were living in an institutional setting. The percentages of early termination due to side effects were 33.3% on nortriptyline in the Katz study (21) and 8.4% on moclobemide in the Roth study (11). In comparison with SSRIs, moclobemide in the elderly has been demonstrated to be at least as effective as fluoxetine (17) and fluvoxamine (16). Furthermore, Pancheri and others (15) found that moclobemide, but not imipramine, increased cognitive performance in elderly patients suffering from different forms of depression. Similar findings were obtained by Roth and others (11).

Since moclobemide does not bind to cholinergic receptors and does not produce sedative effects, it is not surprising that it did not cause deterioration of cognitive function in this elderly population. Elderly depressed patients are more sensitive to the anticholinergic and sedative effects of drugs than younger patients. This is a frequent reason for undertreatment
or no treatment of the elderly. Moclobemide at a dosage of 300 to 600 mg/day was well tolerated in the elderly across studies. Consistently (in more than 80% of the cases), the tolerability of moclobemide was rated “very good” or “good.” In controlled studies, moclobemide was tolerated better than TCAs and had comparable overall tolerability to that of the SSRIs. In the study by Nair and others (12), 5.6% of patients on moclobemide and 26.3% on nortriptyline dropped out because of adverse events. The percentage of premature terminations of treatment found for nortriptyline is of interest because some clinicians believe that this TCA is particularly well-suited for the treatment of elderly depressed patients (22). Kamath and others (23) found a drop-out rate due to side effects of 42% among nortriptyline or desipramine users and 39% among SSRI-treated patients. In contrast, in a recent qualitative analysis of the literature by Menting and others (24), the drop-out rates due to side effects of SSRIs were found to be significantly lower than the rates for TCA-treated subjects. Holman and others (25) reported a drop-out rate due to an adverse event of 12% for patients treated with fluoxetine. The rate of premature terminations of treatment with moclobemide was reported to be 8.4% by Roth and others (11). The update of safety data for the elderly depressed patients presented here shows similar numbers of patients free of adverse events on moclobemide and on placebo. Recent overview articles (26,27) reported moclobemide to be as well tolerated in elderly as in younger patients. Compared with SSRIs, moclobemide treatment resulted in significantly fewer adverse events, although both substances were tolerated well.

Nausea is significantly more frequent with SSRIs than with moclobemide.

The most recent update of safety data indicates that patients aged 60 years or older tolerate moclobemide at least as well as do younger patients. The absence of anticholinergic and sedative effects (19) is considered to be a major advantage for the treatment of depression in elderly patients. No specific adverse event occurred more often in elderly patients than in younger patients.

In the elderly, a comedication to treat organic disease, such as hypertension, coronary heart disease, diabetes, or rheumatic disease, was prescribed in more than 40% of the patients. These patients were at theoretical risk for interaction with moclobemide. The benign adverse event profile of moclobemide in the elderly indirectly confirms, therefore, the high specificity of moclobemide’s biochemical effect (28, 29).

Since many depressed patients undergo long-term treatment, a favourable side effect profile is of great importance for compliance with maintenance treatment. Our results regarding long-term moclobemide treatment are in full agreement with previously published data (30): no new adverse events appeared during the long-term period, and the frequency of adverse events was even substantially reduced compared with short-term treatment.

In conclusion, moclobemide is an effective and well-tolerated antidepressant for the treatment of elderly depressed patients.

Figure 1. HDRS 17 total score (means with 95% confidence limits) for elderly patients suffering from major depressive episode and cognitive decline. ITT population (Roth and others).

Clinical Implications

- Moclobemide is superior to placebo and of similar efficacy to the GCIs and the SSRIs in the treatment of elderly patients with major depression.
- In the elderly, moclobemide is of similar tolerability to placebo and is better tolerated than TCAs and marginally better tolerated than SSRIs.
- Moclobemide is safe during long-term treatment and when comedicated with drugs frequently used in the geriatric population.

Limitations

- The duration of the double-blind studies was 42 days, which may be too short to show maximum effect.
- Most of the studies were run as fixed dose trials.

References

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Résumen

Objectif : Examiner l’efficacité et l’innocuité du moclobémide par comparaison avec les ATT (pour notre propos, les « ATT » représenteront les antidépresseurs tricycliques et tétracycliques, notamment la maprotiline et la miansérine) et les inhibiteurs spécifiques du recaptage de la sérotonine (SSRI) chez les patients âgés dépressifs.

Méthodes : Voici les sources des données d’efficacité examinées : 1) résultats des études publiées sur les personnes âgées; 2) données sur les 60 patients extraites de tous les essais contrôlés disponibles chez les adultes (18 ans) où le moclobémide a été comparé aux ATT ou aux SSRI; et 3) on a extrait les effets indésirables chez les patients de 60 ans à partir de la base de données sur l’innocuité de toutes les études comparatives à court terme sur le moclobémide par rapport aux ATT, aux SSRI ou au placebo et aux études à long terme sur le moclobémide.

Résultats : Les données révèlent que le moclobémide est un antidépresseur efficace chez les patients dépressifs de 60 ans. Le taux de réponse au moclobémide était de 50 à 55 % dans cette population. Le moclobémide était plus efficace que le placebo et son efficacité était semblable à celle des ATT et des SSRI commercialisées plus récemment. La tolérance au moclobémide était jugée « très bonne » ou « bonne » chez près de 90 % de ces patients, ce qui est supérieur à la tolérance aux ATT et semblable à la tolérance aux SSRI. Les patients qui n’ont subi aucune réaction indésirable faisaient plus fréquemment partie du groupe moclobémide que des groupes traités aux ATT (P < 0,01) ou aux SSRI (P < 0,01). Les réactions indésirables de type anticholinergique étaient plus fréquentes avec les ATT qu’avec le moclobémide (P < 0,001), et on a constaté que les nausées étaient trois fois plus fréquentes avec les SSRI qu’avec le moclobémide (P < 0,01).

Conclusions : Le moclobémide est un antidépresseur efficace et bien toléré pour le traitement des patients âgés dépressifs.