Psychotropic drug use in a group of Dutch nursing home patients with dementia: many users, long-term use, but low doses


Introduction

Dementia is a progressive disease. The main symptoms are memory dysfunctions, disturbances of judgement, and, at a later stage, aphasia, agnosia, and apraxia [1,2]. In addition, ‘non-cognitive’ or behavioural symptoms are often observed, such as personality disorders, delusions, or depression [2]. Behavioural disturbances can be a major source of distress and a burden for patients and/or their caregivers. Sometimes patients have to be institutionalized in a nursing home because of serious behavioural disturbances.

Dutch psychogeriatric nursing homes offer an environment that is tolerant of behavioural problems. A multidisciplinary team including a specially trained ‘Dutch nursing home doctor’ generates an individual management plan to approach this problematic behaviour. Psychotropic drugs are only prescribed if these approaches are no longer effective. Our investigation has shown behavioural disturbances in 70% of a group of nursing home patients with dementia. Agitation, negativism, depression, anxiety, psychosis, and aggression were most frequently observed. If there is a need for pharmacotherapeutic intervention, neuroleptics, benzodiazepines, and antidepressants have an important role in the alleviation of these symptoms [3].

There are few data available about the prescription of psychotropic drugs in Dutch nursing homes. Data indicate that 28-41% of the patients are treated with psychotropics [4], of which 27-31% are treated with neuroleptics [5-7], 8-22% with benzodiazepines [6-8], and 2-7% with antidepressants [7]. Data from international literature indicate that 26-87% of patients suffering from dementia are treated with at least one psychotropic drug [9-13]. Neuroleptics are prescribed in 12-47% of patients [6,7,10-15], benzodiazepines in 9-24% of patients [10-13], and antidepressants in 7-11% of patients [10-13].

Elderly people, and in particular those who suffer from dementia, are very susceptible to the side-effects of psychotropics and this warrants reservation in prescription. A high percentage of patients are reported to experience side-effects of neuroleptics such as sedation, extrapyramidal symptoms, and postural hypotension [6,12,16-19].

In 1984 doctors of ‘Joachim en Anna’ nursing home developed a protocol for the rational prescription of neuroleptics [20]. On the basis of receptor–antagonism profiles, five relatively ‘safe’ neuroleptics were chosen [20]. Haloperidol was proposed as the drug of first choice for the treatment of psychotic behaviour (delusions and hallucinations) with agitation. Bromperidol was prescribed for the treatment of psychosis without agitation, and pimpernel for the treatment of aggression, negativism, and disturbances of diurnal rhythm. Zuclopenthixol was prescribed for the treatment of so-called ‘aspecific’ behavioural disturbances (mostly combi-
nations of psychosis, aggression, anxiety, and nega-
tivism) and dehydrobenzperidol for interventions of
short duration, for example, to prepare patients for
invasive treatments like catheterization [20]. In 1990
this schedule was evaluated, with special attention
being paid to efficacy and side-effects [6]. The cur-
rent study addressed, in detail, the prescription of
neuroleptics, benzodiazepines, and antidepressants,
and changes in prescription patterns during the last
12 years. The aim of the study was to assess the use
of psychotropic drugs in this nursing home with
regard to the type of drug, the number of patients
treated, the duration of use and dosage, changes in
these aspects of psychotropic drug use between

Methods

Patients
The study was a retrospective analysis of medical
records. All patients with dementia according to
DSM-III-R criteria [1] who were admitted to the
“Joachim en Anna” nursing home in Nijmegen, the
Netherlands, between 1 January 1980 and 31
December 1989 were included in the study. Follow-
up data were collected until death or the end of the
registration period in April 1992. Methods of data
collection have been described previously [21 22].

“Joachim en Anna” is a nursing home with
250 beds. Most patients suffer from dementia. All
patients are initially admitted on the same ward. In
the first 6 weeks of institutionalization a full medical
and neuropsychological examination is carried out.
Afterwards patients are referred to one of the long-
stay wards, where patients with a similar stage of
dementia live together.

Psychotropic drug use
Psychotropic drug use was continuously registered
from the day of admission. Data were obtained from
the medication list of the medical record. Each time
pattern (time window or risk window) of drug ex-
posure, including one single dosage, was registered
[23-25]. A time pattern of drug exposure was de-
efined as an uninterrupted period of usage of the
same drug. A change of dose between times was not
considered a new time pattern.

Drugs were classified by means of the Anatomical
Therapeutic Chemical (ATC) classification system
[26]. The ATC system uses five levels of classification.
The first, second, and third levels refer to an an-
atomical group with two therapeutic subgroups. The
fourth level refers to the chemical/therapeutic sub-
group, and the fifth level refers to the active com-
ponent [26]. For example, the code N05AF05 stands
for zuclopenthixol. In this study we used the fourth
level. Drug dosages were expressed according to
the defined daily dose (DDD) methodology rec-
ommended by the WHO Drug Utilization Research
Group for pharmacoepidemiological research [27]. In
addition (mean) actual prescribed doses were re-
corded (PDD) and the ratio PDD to DDD was cal-
culated. A PDD/DDD ratio < 1 indicates that the drug is
prescribed in a lower dosage than recommended; a
ratio > 1 indicates that the prescribed dosage is
higher than recommended. For example, the DDD
for haloperidol is 8 mg per day. When a mean of
2 mg per day is prescribed, the PDD/DDD ratio is
0.25. Furthermore whether a drug was withdrawn or
continued at admission or whether the drug was
administered during institutionalization was re-
corded.

Side-effects mentioned in the medical records were
classified with the International Classification of
Health Problems in Primary Care (ICPPPC)-2-defined
[28]. The code 9952 (side-effect medical agent cor-
rectly administered in proper dosage) was supple-
mented with codes for medication group and type of
side-effect [28].

To investigate changes in psychotropic prescrip-
tion time patterns throughout the time patients were
admitted, it was studied whether the prescription of
neuroleptics after 1984 was consistent with the pro-
ocol. Changes in the percentage of patients treated
and in the duration of usage were investigated by
dividing the study population into 10 cohorts (one
cohort for each year). For a proper comparison,
figures were corrected for the time that patients
spent in the nursing home. Changes were studied by
means of linear regression analysis [29].

Results
During the study period 890 patients with dementia
were admitted to the nursing home, of whom 102
survived until April 1992; 70% of the patients were
women. The mean time spent in the nursing home
was 2.2 years, with a range from 0 to 10.6 years.
A total of 3,294 time patterns of psychotropic drug
exposure were registered. 204 drugs were with-
drawn on the day of admission. Therefore this study
is based on the 3,090 remaining time patterns. A
mean of 4.5 time patterns per user was registered
(range 1-35 time patterns per user). In Table 1, the
number of time patterns, the mean duration of drug
exposure, the mean daily dose, and the PDD/DDD
ratio are listed for the drugs that were actually ad-
ministered during institutionalization (3,090 time
patterns). Neuroleptics, benzodiazepines, and anti-
depressants accounted for 58, 32, and 9% of the
time patterns, respectively. Because time patterns
vary in duration, these percentages do not give valid
information about the contribution of neuroleptics,
benzodiazepines, and antidepressant to the prescri-
bing pattern.

The nine most frequently prescribed drugs were
zuclopenthixol, haloperidol, pipamperone, oxaze-
pam, nitrazepam, lormetazepam, trazodone, amitriptyline, and doxepin (Table 1). These covered about 70% of all time patterns prescribed. For almost all drugs the mean PDD was much lower than the DDD. For neuroleptics 25% of the DDD was prescribed, while for benzodiazepines and antidepressants this was 50% and 33%, respectively (Table 1).

During institutionalization more than 75% of the study population received one or more psychotropics (Table 2). Most patients were treated with a neuroleptic, 50% of the patients received a benzodiazepine, and 20% received an antidepressant. Also combinations of medications were frequently prescribed. A neuroleptic in combination with a benzodiazepine was administered in 252 patients. 142 patients received two neuroleptics at the same time (Table 2).

In general, psychotropics were prescribed for a long period. The median duration of the time patterns was 245 days. It has to be noted that a time pattern was ended when a patient died or when the registration period ended. More than 50% of the users of psychotropic drugs had a time pattern of drug exposure for 50 to 100% of their time spent in the nursing home.

More side-effects were associated with the use of neuroleptics than with the use of benzodiazepines or antidepressants (Table 3). One or more side-effects were observed in 50% of the patients who used neuroleptics. Excessive sedation was the most frequently reported problem in the medical records.

After 1984, a neuroleptic that was not included in the schedule was prescribed only thirteen times. Drugs such as levomepromazine, properciiazine, thioridazine, alimemazine, promazine, perazine, and chlorpromazine almost totally disappeared from the prescription list.

Neither the total percentage of psychotropic drug used (expressed as neuroleptics, benzodiazepines, and antidepressants) nor the duration of usage changed throughout the time patients were admitted. Most figures showed fluctuations without a statistically significant rising or falling trend.

**Discussion**

At any time during institutionalization in this nursing home, more than 75% of the patients with dementia were prescribed a psychotropic drug. Neuroleptics

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**Table 1** Number of drug–time patterns (n = 3090), mean duration of exposure, mean daily dose and prescribed daily dose-defined daily dose (PDD/DDD) ratio of the prescribed psychotropics during institutionalization

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Number of time patterns</th>
<th>Mean duration (days)</th>
<th>Mean dose (mg)</th>
<th>Mean PDD/DDD ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroleptics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Zuclopenthixol</td>
<td>600</td>
<td>135</td>
<td>5.4</td>
<td>0.18</td>
</tr>
<tr>
<td>• Haloperidol</td>
<td>330</td>
<td>123</td>
<td>1.5</td>
<td>0.19</td>
</tr>
<tr>
<td>• Pipamperone</td>
<td>291</td>
<td>149</td>
<td>33.6</td>
<td>0.17</td>
</tr>
<tr>
<td>• Alimemazine</td>
<td>179</td>
<td>146</td>
<td>24.0</td>
<td>0.80</td>
</tr>
<tr>
<td>• Bromperidol</td>
<td>124</td>
<td>153</td>
<td>1.4</td>
<td>0.14</td>
</tr>
<tr>
<td>• Dehydrobenzperidol</td>
<td>105</td>
<td>85</td>
<td>4.2</td>
<td>0.28</td>
</tr>
<tr>
<td>• Propercliazine</td>
<td>62</td>
<td>94</td>
<td>13.4</td>
<td>0.27</td>
</tr>
<tr>
<td>• Sordinol</td>
<td>44</td>
<td>119</td>
<td>12.7</td>
<td>0.13</td>
</tr>
<tr>
<td>• Thioridazine</td>
<td>21</td>
<td>112</td>
<td>57.6</td>
<td>0.19</td>
</tr>
<tr>
<td>• Perazine</td>
<td>17</td>
<td>42</td>
<td>53.6</td>
<td>0.54</td>
</tr>
<tr>
<td>• Promazine</td>
<td>12</td>
<td>101</td>
<td>52.2</td>
<td>0.17</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Oxazepam</td>
<td>497</td>
<td>130</td>
<td>15.8</td>
<td>0.32</td>
</tr>
<tr>
<td>• Temazepam</td>
<td>210</td>
<td>101</td>
<td>11.8</td>
<td>0.59</td>
</tr>
<tr>
<td>• Lormetazepam</td>
<td>137</td>
<td>136</td>
<td>1.0</td>
<td>1.01</td>
</tr>
<tr>
<td>• Nitrazepam</td>
<td>90</td>
<td>129</td>
<td>4.0</td>
<td>0.81</td>
</tr>
<tr>
<td>• Diazepam</td>
<td>50</td>
<td>46</td>
<td>10.9</td>
<td>1.08</td>
</tr>
<tr>
<td>Antidepressants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Trazodone</td>
<td>112</td>
<td>176</td>
<td>109.9</td>
<td>0.37</td>
</tr>
<tr>
<td>• Amitriptyline</td>
<td>56</td>
<td>160</td>
<td>33.5</td>
<td>0.45</td>
</tr>
<tr>
<td>• Doxepin</td>
<td>51</td>
<td>190</td>
<td>25.8</td>
<td>0.26</td>
</tr>
<tr>
<td>• Mianserin</td>
<td>47</td>
<td>163</td>
<td>19.7</td>
<td>0.33</td>
</tr>
<tr>
<td>• Mapritiline</td>
<td>10</td>
<td>545</td>
<td>51.4</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Not listed are levomepromazine, sulpiride, clorpromazine, chlorprothixene, flurazepam, chlordiazepoxide, flunitrazepam, lorazepam, nomifensine, clomipramine, imipramine, lithium carbonate, and promethazine. These medications were each prescribed less than 10 times.
Table 2 Number of patients treated with neuroleptics, benzodiazepines, and antidepressants, parallel prescriptions*, and median duration of exposure expressed in days

<table>
<thead>
<tr>
<th></th>
<th>Patients (n = 890)</th>
<th>Median duration of exposure (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>At least 1 time pattern for a psychotropic</td>
<td>683</td>
<td>77</td>
</tr>
<tr>
<td>At least 1 time pattern for a neuroleptic</td>
<td>554</td>
<td>62</td>
</tr>
<tr>
<td>At least 1 time pattern for a benzodiazepine</td>
<td>456</td>
<td>51</td>
</tr>
<tr>
<td>At least 1 time pattern for an antidepressant</td>
<td>199</td>
<td>22</td>
</tr>
<tr>
<td><strong>Parallel prescription</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 neuroleptics</td>
<td>142</td>
<td>16</td>
</tr>
<tr>
<td>2 benzodiazepines</td>
<td>45</td>
<td>5</td>
</tr>
<tr>
<td>2 antidepressants</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>1 neuroleptic + 1 benzodiazepine</td>
<td>252</td>
<td>28</td>
</tr>
<tr>
<td>1 benzodiazepine + 1 antidepressant</td>
<td>74</td>
<td>8</td>
</tr>
<tr>
<td>1 neuroleptic + 1 antidepressant</td>
<td>91</td>
<td>10</td>
</tr>
<tr>
<td>1 neuroleptic + 1 benzodiazepine + 1 antidepressant</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

* Parallel prescription means that one or more drugs were prescribed at one time.

were most frequently prescribed, followed by benzodiazepines and antidepressants. Psychotropic drugs usually were prescribed for long-term use but in a relatively low dose. All these figures reflect the prescribing policy of one team of Dutch nursing home doctors. Therefore the results cannot be generalized to all Dutch nursing home patients.

The results are difficult to compare with international data. In this study, data were registered continuously, while most other studies have a cross-sectional design. Most studies do not report dosage and duration of use. The fact that the PDD was much lower than the internationally agreed DDD can be explained by the advanced age of these nursing home patients. Changes in pharmacodynamics and pharmacokinetics in elderly people increase the risk of cumulation and therefore the dosage has to be adjusted [30]. In addition, elderly people, and especially those with an organic brain syndrome, have a higher end-organ sensitivity for psychotropic drugs [30]. These and other mechanisms account for most of the observed side-effects. In particular, neuroleptics caused side-effects which led to adjustment of the dose or even withdrawal of the drug. It has to be mentioned that patients were not systematically checked for signs of sedation, extrapyramidal signs, or other symptoms. Therefore the figures reported here are most likely an underestimation of the real frequency and only express the recognized side-effects.

Neuroleptics can be effective in very low doses [6 17]. Willekens-Bogaers and coworkers found in their evaluation study that in 69% of their patients, who were also included in our investigation, psychosis, and/or behavioural disturbances could be reduced to an acceptable level [6]. This agrees with the finding of Schneider and coworkers. They concluded in their meta-analysis that neuroleptics were of benefit to

Table 3 Percentage of patients showing side-effects of antidepressants (n = 556), neuroleptics (n = 457), and benzodiazepines (n = 199)

<table>
<thead>
<tr>
<th>Side-effect*</th>
<th>Antidepressants</th>
<th>Neuroleptics</th>
<th>Benzodiazepines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation</td>
<td>41</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Gait disorder</td>
<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Falling</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Extrapyramidal signs</td>
<td>9</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Cardiovascular problem</td>
<td>3</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>Paradox reactions</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>50</td>
<td>15</td>
<td>14</td>
</tr>
</tbody>
</table>

* More than one side-effect could be observed per patient.
frequent changes of type of drugs can be explained by symptoms change with time.

When there is a need for dopamine as well as serotonin receptor antagonism, treatment with two neuroleptics can be a rational choice for treatment of agitation, negativism, and anxiety, and so the target symptoms change with time.

The prescription of combinations of drugs may indicate the complexity of symptomatic treatment of behavioural problems in these patients. Prescription of a neuroleptic in combination with a benzodiazepine can be a rational choice for treatment of agitation in the daytime and sleep disturbance during the night. But prescription of two neuroleptics at one time indicates difficulties in managing behaviour. When there is a need for dopamine as well as serotonin receptor antagonism, treatment with two neuroleptics can be a rational therapy. Recent studies show that extrapyramidal side-effects can be reduced by using these combinations of drugs. "Start low and go slow" during the search for the correct dosage.

The number of time patterns per patient and the wide range in these patterns reflect a continuous search for the right and most effective drug. The prescription of combinations of drugs may indicate the complexity of symptomatic treatment of behavioural problems in these patients. Prescription of a neuroleptic in combination with a benzodiazepine can be a rational choice for treatment of agitation in the daytime and sleep disturbance during the night. But prescription of two neuroleptics at one time indicates difficulties in managing behaviour. When there is a need for dopamine as well as serotonin receptor antagonism, treatment with two neuroleptics can be a rational therapy. Recent studies show that extrapyramidal side-effects can be reduced by using these combinations of drugs. "Start low and go slow" during the search for the correct dosage.

Conclusion

Despite a tolerant setting and multidisciplinary therapeutic approach, most of the patients in this psychogeriatric nursing home manifested behaviour for which psychotropics were prescribed. Psychotropics were prescribed for a long period but in a relatively low dosage. Side-effects were frequently observed during the search for the correct dosage.

References

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