Use of neuroleptics
Study of institutionalized elderly people in Montreal, Que

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ABSTRACT

OBJECTIVE To determine the prevalence of neuroleptic use in long-term care institutions in the greater Montreal, Que, area and to estimate the extent of use of atypical neuroleptics.

DESIGN Cross-sectional study in which single-day chart reviews were conducted to evaluate the prevalence of use of conventional and atypical neuroleptics.

SETTING Ten long-term care institutions in the greater Montreal area.

PARTICIPANTS Two thousand, four hundred sixty residents aged 65 years or older living in 10 long-term care institutions in and around Montreal.

MAIN OUTCOME MEASURES Single-day medication profiles compiled by institutions' pharmacists.

RESULTS Among patients in the 10 participating institutions, use of neuroleptics ranged from 15% to 37% with a mean of 25.2% (620/2460). Atypical neuroleptics were prescribed to 15.6%, conventional neuroleptics to 7.6%, and a combination of both to 2.0% of the 2460 patients.

CONCLUSION Use of neuroleptics was relatively prevalent, and there was wide use of atypical neuroleptics in Montreal-area long-term care institutions. There is little information on the safety and efficacy of these medications for institutionalized elderly people.

EDITOR'S KEY POINTS

- Family doctors frequently use neuroleptics to treat institutionalized elderly patients' behavioural problems despite the risk of extrapyramidal symptoms.
- This study in Montreal found that, overall, 26% of residents were prescribed neuroleptics: 16% atypical neuroleptics, 8% conventional neuroleptics, and 2% a combination of both.
- The most commonly prescribed neuroleptics were risperidone (52%), haloperidol (36%), and olanzapine (13%).
- Newer atypical neuroleptics appear to be widely prescribed, even though there is limited evidence of their efficacy. They might be chosen, however, because of a lower incidence of extrapyramidal symptoms.

Utilisation des neuroleptiques
Étude chez des vieillards de centres d'hébergement à Montréal, Qué.

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RÉSUMÉ

OBJECTIF Déterminer la prévalence d'utilisation des neuroleptiques dans certains centres d'hébergement à long terme du grand Montréal et estimer celle des neuroleptiques atypiques.

TYPE D'ÉTUDE Étude transversale dans laquelle on a consulté les dossiers d'une seule journée pour évaluer la prévalence d'utilisation des neuroleptiques classiques et atypiques.

CONTEXTE Dix centres d'hébergement à long terme du grand Montréal.

PARTICIPANTS Deux mille quatre cent soixante personnes de 65 ans et plus vivant dans 10 centres de soins de longue durée de Montréal ou des environs.

PRINCIPAUX PARAMÈTRES ÉTUDIÉS Les profils médicamenteux d'une seule journée établis par le pharmacien du centre.

RÉSULTATS L'utilisation des neuroleptiques chez les patients des 10 institutions participantes variait de 15 à 37%, avec une moyenne de 25,2% (620 sur 2460). Sur les 2460 patients, 15,6% avaient reçu des neuroleptiques atypiques, 7,6% des neuroleptiques classiques et 2% une combinaison des deux.

CONCLUSION Dans ces centres de soins de longue durée du grand Montréal, la prévalence d'utilisation des neuroleptiques était relativement élevée, notamment pour les neuroleptiques atypiques. On possède peu de données sur la sécurité et l'efficacité de ces médicaments chez les personnes âgées hébergées dans ces institutions.

POINTS DE REPÈRE DU RÉDACTEUR

- Le médecin de famille prescrit souvent des neuroleptiques aux patients âgés des centres d'hébergement qui présentent des troubles du comportement et ce, malgré les risques d'éffets extrapyramidaux.
- Cette étude montréalaise révèle que dans l'ensemble, 26% des patients hébergés recevaient des neuroleptiques: 16% des neuroleptiques atypiques, 8% des neuroleptiques classiques et 2% un combinaison des deux.
- Les neuroleptiques les plus souvent prescrits étaient la rispéridone (52%), l'halopéridol (36%) et l'olanzapine (13%).
- Les nouveaux neuroleptiques atypiques sont apparemment prescrits de façon judicieuse, malgré le peu de preuve de leur efficacité. Leur choix pourrait toutefois dépendre du fait qu'ils entraînent moins d'effets extrapyramidaux.

In Canada, 50% of elderly people with dementia are institutionalized.[1,2] More than 90% of them have behavioural disorders, particularly when they are at moderate-to-severe stages of dementia.[3] Although the efficacy of neuroleptics for treating behavioural disorders in dementia has been shown to be modest,[4] these medications are still widely used for this indication.[5,6]

Some studies comparing neuroleptics with placebo show improvement in hallucinations, agitation, and resistance to care among patients treated with neuroleptics.[7] According to studies completed in the United States in the 1980s and early 1990s, one quarter to one third of residents in nursing homes were prescribed conventional neuroleptics (CNs).[7-9]

Haloperidol is the most commonly used CN. Serious adverse effects have been seen with use of CNs, particularly in frail institutionalized elderly patients. These medications can induce sedation; hypotension; anticholinergic effects; cardiovascular, gastrointestinal, and endocrinologic problems; hypersensitivity reactions; and extrapyramidal signs.[10] Extrapyramidal signs are attributable to the antidopaminergic properties of neuroleptics. They include parkinsonism, akathisia, dystonia, and dyskinesia. According to population studied, methodology, and type of neuroleptics used, various studies report a prevalence of extrapyramidal signs ranging from 5% to 67% among elderly patients prescribed CNs.[11] These side effects can come on suddenly or appear insidiously, generally within the first 30 days of use.

Atypical neuroleptics (ANs) (risperidone, olanzapine, quetiapine, and clozapine) were introduced in the 1990s. They show less affinity for dopaminergic receptors and greater affinity for serotonergic receptors.[11,12] These pharmacodynamic properties could result in greater efficacy and fewer side effects for young schizophrenic patients.[11,13-17]

Quality of evidence

We searched PubMed, Ovid Citations, and Current Contents for randomized controlled trials carried out among elderly patients that evaluated the efficacy and safety of ANs. We identified only three studies using the key words dementia, Alzheimer's disease, Lewy body disease, psychotic disorders, behavior disorders, pharmacotherapy, drugs, antipsychotic agents, atypical antipsychotics, randomized controlled trial, placebo, and double-blind method.[18-20] These three trials suggested that ANs were superior to placebo but had modest efficacy. The only trial comparing a CN with an AN showed that haloperidol, risperidone, and placebo had similar efficacy.[18]

De Deyn et al[18] and Katz et al[19] reported a prevalence of extrapyramidal signs ranging from 7% to 22%, depending on type of neuroleptic used and dose given. Street et al[20] found no significant differences in prevalence of extrapyramidal signs among elderly subjects taking placebo, and 5 mg, 10 mg, and 15 mg of olanzapine. Results reported in these three trials are insufficient to prove there is a real difference in prevalence of extrapyramidal signs among elderly patients prescribed ANs or CNs.

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Objectives of study

The objectives of this study were to describe neuroleptic use and to estimate the extent of use of ANs in long-term care institutions in Montreal, Que. Greater knowledge of actual patterns of neuroleptic prescribing in long-term care institutions could help identify areas of continuing medical education for physicians and could be used as a starting point for development of Canadian guidelines on use of neuroleptics.

METHODS

Ten long-term care institutions in the greater Montreal, Que, area were randomly selected from among the Collaborative Research Network in long-term care, which consists of 17 institutions. This was a convenience sample, but it represented one third of Montreal's long-term care institutions. The survey was conducted between October 2000 and April 2001. All residents aged 65 and older living in the participating institutions were included in the study. This study was approved by the research ethics committee of l'Institut universitaire de gériatrie de Montréal and by the research ethics committee or the committee of physicians, dentists, and pharmacists of each participating institution.

For each institution, the pharmacist was asked to provide data from a single-day medication profile for each neuroleptic user. These profiles included the date of the profile corresponding to the date of data extraction by the pharmacist; characteristics of patients, including date of birth, sex, and date of admission to the institution; and data on neuroleptic prescriptions, including generic name, date of prescription, dose, frequency, and route of administration. Use of the following medications were also recorded, as they can influence presence of extrapyramidal signs: antiparkinsonian agents, such as levodopa; antidepressants; benzodiazepines; sedatives; cholinesterase inhibitors; anticonvulsants; lithium; and anticholinergic agents, such as procyclidine.

The prevalence of neuroleptic use by those 65 or older was determined for each institution first, and then the mean prevalence was calculated for the 10 institutions. With this approach, each institution had equal weight, regardless of size. We also calculated the mean prevalence of neuroleptic users, using the total number of residents in the 10 institutions as a denominator. These two approaches were used to evaluate whether size of institution influenced estimates of prevalence. The prevalence of use of CNs, ANs, or a combination of both types (CN+AN) was estimated for each institution and for the 10 institutions overall. Use of medications that can influence presence of extrapyramidal signs was also analyzed. For comparing our results with those of previous studies, dose and duration of treatment were estimated only for neuroleptics prescribed on a regular basis and administered orally.

In the context of this study, we could not verify whether neuroleptics prescribed only as needed (PRN) were administered or not. Only neuroleptics prescribed on a regular basis were considered in the analysis. Mean daily doses of neuroleptics used on a regular basis were calculated and compared with maximum geriatric daily doses recommended by the United States Omnibus Budget Reconciliation Act (OBRA-87) legislation: 4 mg for haloperidol, 2 mg for risperidone, 10 mg for olanzapine, and 200 mg for quetiapine.[21] We compared our results with American guidelines since no Canadian guidelines on neuroleptic prescribing in long-term care were available. Duration of treatment was analyzed according to a binary method; 180 days or more was considered a long duration of treatment.

The association between type of neuroleptic prescribed and characteristics of residents (age, sex, length of stay, and use of other medications) was analyzed using multinomial logistic regressions to determine which factors were related to use of CNS, ANs, or CN+AN. The association between medications that can influence presence of extrapyramidal signs and characteristics of residents were analyzed using logistic regression. Logistic regressions were also used to analyze the association between high doses of neuroleptics and characteristics of residents and the association between duration of treatment and characteristics of residents. All analyses were adjusted considering the institutions as fixed factors.[22]

RESULTS

Our sample was composed of eight public institutions and two private institutions caring for a total of 2460 residents. Three institutions had fewer than 150 beds, four had between 150 and 300, and the other three had more than 300 beds. Four institutions were affiliated with universities.

Prevalence of neuroleptic use

The mean prevalence of neuroleptic use calculated from the prevalence in each of the 10 institutions was 25.8% ± 6.3% (range 15% to 37%). The mean prevalence of neuroleptic use among all 2460 residents was 25.2% (620/2460). These results show that the size of the institution had little influence on the mean prevalence of neuroleptic use. Therefore, for the rest of the analysis, mean prevalence was based on the 620 neuroleptic users. Mean age of neuroleptic users was 84 years (range 65 to 102 years); more women (75%) than men were prescribed neuroleptics. Mean length of stay in an institution was 2.5 years (range 6 days to 23 years).

For the 620 neuroleptic users, 757 prescriptions were identified for an average of 1.22 prescriptions per resident. **Figure 1** shows the proportion of residents receiving ANs, CNs, or AN+CN. **Table 1** shows the number of residents prescribed each type of neuroleptic. No resident in our sample was prescribed clozapine.

Risperidone was most frequently prescribed (52%), followed by haloperidol (36%), olanzapine (13%), and quetiapine (7%). The most common combinations (n = 46) were one of the three ANs prescribed on a regular basis with haloperidol PRN. Risperidone appeared in 41% of these combinations, olanzapine in 26%, and quetiapine in 13%.

Figure 2 shows the distribution of other psychotropic drugs among neuroleptic users. Benzodiazepines were the most frequently prescribed (31%), followed by antidepressants (22%). Only 32% of neuroleptic users were not using these medications. Overall, 79% of neuroleptics were prescribed on a regular basis and 21% PRN. Almost half (46%) the haloperidol prescriptions, but only 13% of the risperidone prescriptions, were PRN.

Doses

Daily doses of risperidone, haloperidol, olanzapine, and quetiapine were evaluated, since they were the most frequently prescribed (543 prescriptions, 92% of our sample). **Table 2**[21] shows the mean daily dose, standard deviation, range of dose given, and proportion of residents receiving high doses. High dose was defined as above the maximum daily dose recommended in OBRA-87. Quetiapine was most

Figure 1. Prevalence of neuroleptic use according to type: *N = 2460*
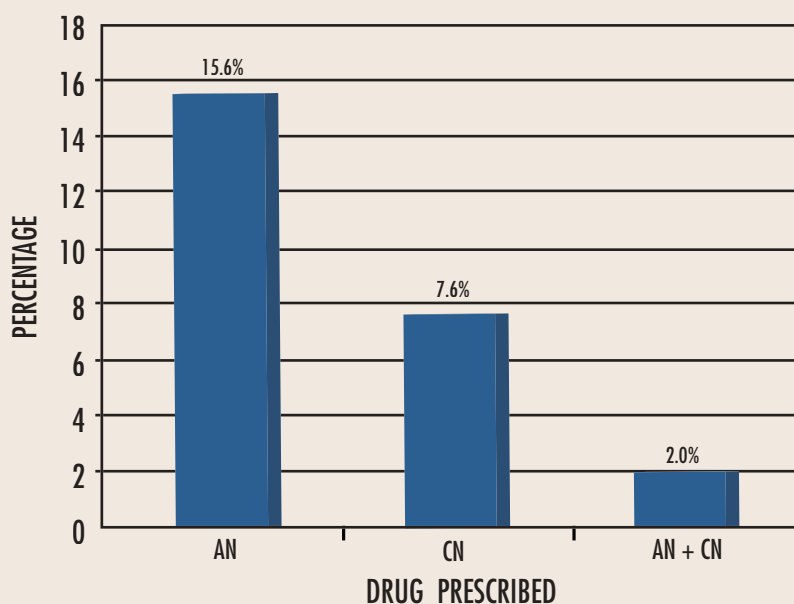
AN—atyptical neuroleptics, CN—conventional neuroleptics.

Table 1. Relative frequencies of use of conventional and atypical neuroleptics: *N =620.*

NEUROLEPTIC DRUG	NO. OF RESIDENTS USING DRUG* (%)
CONVENTIONAL NEUROLEPTICS	
Haloperidol	222 (36)
Loxapine	34 (5.5)
Prochlorperazine	6 (1.0)
Thioridazine	5 (0.8)
Perphenazine	4 (0.6)
Pimozide	4 (0.6)
Trifluoperazine	2 (0.3)
Fluphenazine decanoate	1 (0.2)
Thioproperazine	1 (0.2)
ATYPICAL NEUROLEPTICS	
Risperidone	320 (51.6)
Olanzapine	82 (13.2)
Quetiapine	46 (7.4)

Some patients were taking more than one drug.

Table 2. Daily neuroleptic dose prescribed: *N = 543 prescriptions*.

NEUROLEPTIC DRUG (MAXIMUM DOSE*)	MEAN DAILY DOSE (SD)	RANGE	% OF RESIDENTS RECEIVING HIGH DOSES
Haloperidol (4 mg)	1.3 (± 1.7 mg)	0.25-10 mg	4.3
Risperidone (2 mg)	1.0 (± 0.7 mg)	0.125-4.5 mg	4.9
Olanzapine (10 mg)	5.4 (± 4.4 mg)	1.25-30 mg	7.5
Quetiapine (200 mg)	79.8 (± 84.9 mg)	12.5-375 mg	10.9

Maximum daily dose according to the OBRA-87 (Omnibus Budget Reconciliation Act).[21]

also estimated for all oral neuroleptics prescribed on a regular basis (n = 590). Results show that 19% of neuroleptic prescriptions had been initiated within 30 days preceding the study, 39% were active in a range of 30 days to 180 days, and 42% had been ongoing for 180 days and more.

Results were adjusted considering the institutions as fixed factors. For comparisons between types of neuroleptics, CN users were considered the reference group. Compared with CN users, AN users were more likely to have a shorter length of stay in an institution (odds ratio [OR] 0.67, 95% confidence interval [CI] 0.57 to 0.80), were less likely to be prescribed medications used to treat extrapyramidal

likely to be prescribed at a dose exceeding the maximum recommended geriatric daily dose (10.9%), followed by olanzapine (7.5%), risperidone (4.9%), and haloperidol (4.3%). Duration of treatment was
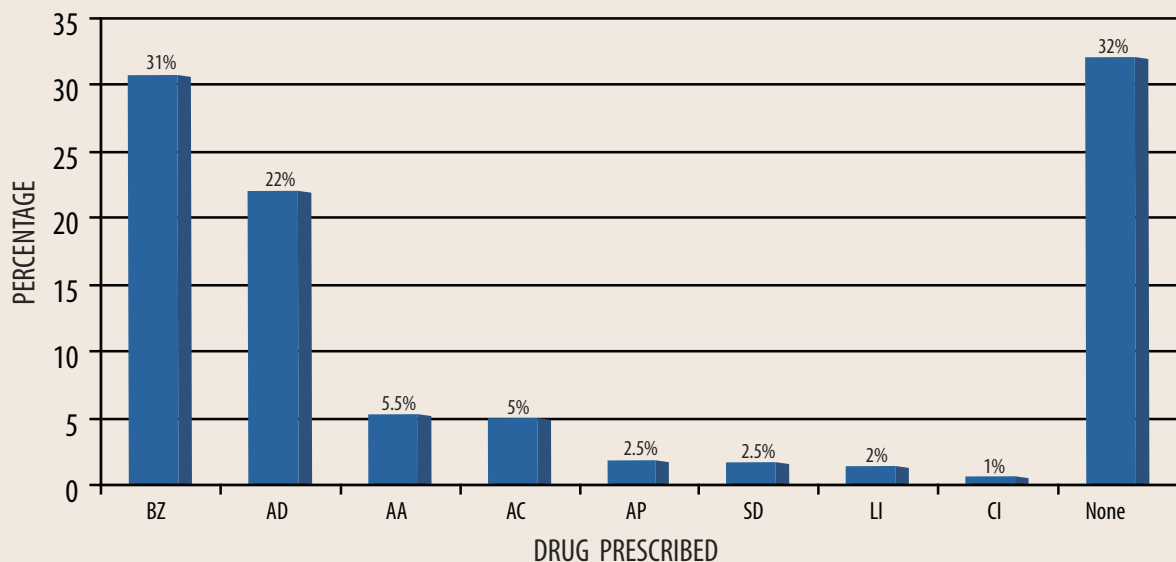

AA—anticholinergic agents, AC—anticonvulsants, AD—antidepressants, AP—antiparkinsonian agents, BZ—benzodiazepines, CI—cholinesterase inhibitors, LI—lithium, SD—sedatives.

signs (OR 0.27, 95% CI 0.12 to 0.62), and were relatively younger (OR 0.97, 95% CI 0.95 to 1.00) (**Table 3**). We created various multiple logistic regression models to identify characteristics that would make patients more likely to be taking psychotropic drugs other than neuroleptics. Increasing age was the only factor associated with decreased risk of receiving antidepressants (OR 0.97, 95% CI 0.94 to 0.99), benzodiazepines (OR 0.74, 95% CI 0.95 to 99), and medications used to treat extrapyramidal signs (OR 0.90, 95% CI 0.86 to 0.95).

Table 3. **Multiple logistic regression model comparing atypical neuroleptic users with conventional neuroleptic users:** *Conventional neuroleptic users were the reference group.*

PATIENT CHARACTERISTICS	ODDS RATIO	95% CONFIDENCE INTERVAL
Male sex	0.80	0.51-1.24
Age	0.97	0.95-1.00
Benzodiazepine use	1.17	0.76-1.81
Using medication for extrapyramidal signs	0.27	0.12-0.62
Antidepressant use	1.26	9.78-2.02
Length of stay	0.67	0.57-0.80

Likelihood of receiving high doses of neuroleptics was inversely related to age (OR 0.91, 95% CI 0.86 to 0.96) (**Table 4**). Patients prescribed high doses were eight times more likely to receive medications used to treat extrapyramidal signs (OR 8.02, 95% CI 2.50 to 25.76).

Table 4. **Multiple logistic regression model to identify patient characteristics associated with use of high-dose neuroleptics**

PATIENT CHARACTERISTICS	ODDS RATIO	95% CONFIDENCE INTERVAL
Male sex	1.04	0.43-2.55
Age	0.91	0.86-0.96
Benzodiazepine use	1.54	0.64-3.74
Dopamine derivative use	8.02	2.50-25.76
Antidepressant use	1.25	0.54-3.40
Use of atypical antipsychotics	2.06	0.60-7.07
Length of stay	1.35	0.95-1.92
Duration of treatment	1.00	0.75-1.34

Duration of treatment

Another multiple logistic regression model was used to predict factors associated with treatment exceeding 180 days. Results are shown in **Table 5**. Relatively younger users were less likely to receive neuroleptics for a long period (OR 0.97, 95% CI 0.95 to 1.00), and AN users were less likely to have a long duration of treatment (OR 0.47, 95% CI 0.31 to 0.72). Longer stay in an institution (OR 1.60, 95% CI 1.34 to 1.88) was related to a higher probability of having a long duration of treatment with neuroleptics.

Table 5. **Multiple logistic regression model to identify patient characteristics associated with duration of treatment with neuroleptics exceeding 180 days**

PATIENT CHARACTERISTICS	ODDS RATIO	95% CONFIDENCE INTERVAL
Male sex	0.95	0.62-1.47
Age	0.97	0.95-1.00
Use of atypical antipsychotics	0.47	0.31-0.72
Length of stay	1.59	1.34-1.88

DISCUSSION

In this cross-sectional study, the mean prevalence of neuroleptic use among institutionalized elderly people was 25.2%. Our sample was a convenience sample and does not necessarily represent all Montreal's institutionalized elderly residents. Nevertheless, it represents one third of all residents. Use of PRN prescriptions was almost exclusively for haloperidol and risperidone. This is likely due to their pharmacokinetic properties (both medications reach their peak concentration rapidly) and to the fact that they are both available in small and variable doses. Conn et al,[5] in an Ontario study, reported a prevalence of neuroleptic prescriptions of 29.8% among 436 nursing home residents and of 20.3% among 442 residents of a veterans' institution, but of only 14.8% among 1405 residents living in homes for the aged.

Overall, neuroleptic use in Canada is comparable to use in other countries,[5,6,23-30] but is somewhat higher than in the United States since implementation of OBRA-87. **Table 6**[5,6,23-30] shows neuroleptic use among nursing home residents in various countries. Only studies published after 1990 were considered because use of neuroleptics has changed markedly in the United States since implementation of OBRA-87.

Table 6. Prevalence of neuroleptic use among nursing home residents in various countries since 1989

COUNTRY	STUDY	TYPE OF INSTITUTION	MEAN % OF RESIDENTS USING NEUROLEPTICS
Denmark	Tybjerg and Gulmann, 1992[29]	Nursing homes	20
Australia	Snowdon et al, 1995[27]	Nursing homes	27.4
Austria	Wancata et al, 1997[30]	Nursing homes	32.1*
United States	Borson and Doane, 1997[23]	Geriatric care facilities	13.3
United States	Tobias and Pulliam, 1997[28]	Nursing facilities	14.2
Sweden	Schmidt et al, 1998[6]	Nursing homes	32.6
Norway	Ruths et al, 2001[26]	Nursing homes	23
Spain	Garolera et al, 2001[24]	Nursing homes	21.0
United Kingdom	Oborne et al, 2002[25]	Nursing homes	24.5
Canada	Conn et al, 1999[5]	Nursing homes	29.8
Canada	Champoux et al (this study)	Nursing homes	25.2

Newly admitted patients only.

Use despite modest efficacy

Our study shows wide use of neuroleptics despite their modest efficacy. This finding might reflect the lack of more effective treatment. The distress experienced by demented residents with behavioural disorders and their caregivers can partly explain this high use. According to our clinical experience, once physicians initiate neuroleptic treatment, the drugs are prescribed for very long periods, often until patients die, without considering trying to reduce or stop the medication.

We also found physicians were prescribing ANs despite the lack of scientific evidence to support this practice. The frailty of institutionalized patients could explain why physicians switch to ANs; they are safer.

Among the three trials we found in our literature search,[18-20] only one compared a CN (haloperidol) to an AN (risperidone).[18] The efficacy of the two drugs appeared to be similar, but presence of extrapyramidal signs was lower with risperidone (15% of patients) than haloperidol (22%) ($P < .05$).

In our study, the proportion of residents receiving high doses of neuroleptics was relatively low. Perhaps physicians practising in long-term care institutions are aware of the increased risks of side effects when prescribing for this frail population. About 42% of neuroleptic users, however, had active

prescriptions for 180 days or more. This rather long duration of treatment raises concern since neuroleptics' long-term efficacy in this population has not been evaluated. Moreover, clinical trials conducted over short periods report that CNs have only modest effects on elderly people's behavioural disorders[31-33] and that prolonged exposure to neuroleptics could increase risk of developing extrapyramidal signs, especially tardive dyskinesia.[34-37]

The newer ANs were prescribed relatively more frequently (62.1%) despite a lack of information on use of these medications for institutionalized elderly patients and their relatively high cost compared with CNs.

Other drugs prescribed to neuroleptic users

Benzodiazepines were prescribed to 31% of neuroleptic users. Considering that both medications can affect mobility and increase risk of falls in frail elderly people, this relatively frequent combination raises concern. Among the antidepressants prescribed to 22% of patients, 60% were selective serotonin reuptake inhibitors, such as sertraline and paroxetine, both of which can cause extrapyramidal signs. We also found concurrent use of antiparkinsonian and anticholinergic agents in neuroleptic users; high-dose neuroleptic users were more likely to receive anticholinergic agents. It was impossible to determine whether these residents suffered from Parkinson disease or had side effects from neuroleptics. Such confusion could result in addition of dopaminergic drugs.[38]

Reducing doses or discontinuing neuroleptics

Whenever possible, reducing the dose or discontinuing the neuroleptic should be considered.[38] Use

of CNs is strongly related to use of anticholinergic agents, but use of AN+CN is not. This difference could be explained by the fact that CNs in combination were prescribed only PRN.

Older residents seem protected against long duration of treatment with neuroleptics, high doses of neuroleptics, and use of medications that can affect presence of extrapyramidal signs. Nevertheless, a prolonged stay in a long-term care institution increases the probability of receiving CNs and of using neuroleptics for more than 180 days. This could be because CN users were probably initially treated with CNs and were never switched to newer neuroleptics.

Limitations

It was impossible to ascertain how often PRN medications were actually administered without an extensive, time-consuming review of each resident's chart because the information was collected through institutions' computerized pharmacy databases. Second, it was impossible to determine whether residents using neuroleptics were suffering from dementia or any other psychiatric disorders, such as schizophrenia. We hope that other studies will address the many unanswered questions about institutionalized seniors' use of neuroleptics.

Conclusion

Results of our study have shed light on use of neuroleptics in Montreal long-term care institutions and on use of medications that can affect the presence of extrapyramidal signs. Prevalence of use of neuroleptics continues to be relatively high (25.2%) among institutionalized elderly people; use of ANs is extensive (62.1%) even though little information exists about the safety and efficacy of these medications in this population.

Contributors

Dr Champoux *conceived and designed the study, analyzed and interpreted the data, drafted the article, and gave final approval to the version to be published.* **Dr Monette, Ms Monette, Dr Galbaud du Fort,**

Dr Wolfson, *and* **Mr Le Cruguel** *made substantial contributions to the concept and design of the study, critically revised the article, and gave final approval to the version to be published.*

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