

Trends in Medication Use Over 11 Years in Patients Presenting to a Rural and Remote Memory Clinic

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ABSTRACT: *Background:* Anticholinergic and sedating medications are generally contraindicated in those with cognitive decline. We examined trends in medication use by patients at initial presentation to a rural and remote memory clinic (RRMC) between March 2004 and June 2015 to determine whether patterns of medication use have changed. *Methods:* The first 444 patients seen at the RRMC between 2004 and 2015 were included in this analysis. Medication lists were collected at the patient's initial visit, and it was noted whether patients were taking anticholinergic or potentially sedating drugs. Statistical analysis (Spearman's correlation) was conducted to examine trends in medication use over time. *Results:* Patients were on a mean of 5.18 medications (standard deviation, 3.46). Ninety-one patients (20.5%) were taking at least one anticholinergic medication. There was a decline (25.0% in 2004 to 12.5% in 2014) in percentage of patients presenting with anticholinergic medications over the 11 years of this study (Spearman's correlation coefficient = -0.64 , $p=0.035$). The prevalence of drugs acting on the central nervous system trended toward an increase, but this was not statistically significant. Sixty-three patients (14.2%) presented to the RRMC already taking a cholinesterase inhibitor. *Conclusions:* The most encouraging statistic to come from this study is a decline in anticholinergic medication use in this rural population. Prescribers must be properly informed to ensure that the number of medications per patient does not continue to rise, that medications are used only as necessary, and that potentially deleterious medications are avoided.

RÉSUMÉ: *Tendances de consommation de médicaments sur plus de 11 ans par des patients ayant visité une clinique de la mémoire en régions rurales et éloignées.* *Contexte:* L'utilisation d'anticholinergiques et de sédatifs par des patients montrant un déclin des fonctions cognitives demeure généralement contre-indiquée. Afin de déterminer l'évolution relative à la consommation de ces médicaments, nous avons examiné, de mars 2014 à juin 2015, les tendances de consommation de patients visitant pour la première fois une clinique de la mémoire en régions rurales et éloignée. *Méthodes:* Les 444 premiers patients examinés dans la clinique de 2004 à 2015 ont été inclus dans cette étude. La liste des médicaments qu'ils prenaient a été dressée dès leur visite initiale. Nous avons noté en particulier dans quelle mesure ils consommaient des anticholinergiques et des médicaments aux possibles effets sédatifs. Au moyen de la corrélation de Spearman, nous avons également effectué une analyse statistique afin d'examiner les tendances de consommation de ces médicaments au fil du temps. *Résultats:* En moyenne, les patients consommaient 5,18 médicaments différents (écart type de 3,46). Quarante-vingt onze (91) patients (20,5%) consommaient au moins un anticholinergique. Au cours de la période de 11 ans visée par cette étude, nous avons observé une diminution du pourcentage (25,0% en 2004 contre 12,5% en 2014) de patients traités par un anticholinergique se présentant à la clinique (coefficient de corrélation de Spearman = $-0,64$; $p = 0,035$). La prévalence de la consommation de médicaments agissant sur le système nerveux central a, quant à elle, connu une tendance à la hausse mais cette dernière ne s'est pas révélée statistiquement significative. Enfin, soixante-trois (63) patients (14,2%) déjà traités par un inhibiteur de la cholinestérase se sont présentés à la clinique. *Conclusions:* Le fait que la consommation d'anticholinergiques au sein de cette population rurale ait diminué demeure la constatation la plus encourageante qui émerge de cette étude. Dans le même ordre d'idées, il incombe d'informer adéquatement les médecins prescripteurs pour s'assurer que le nombre de médicaments prescrits par patient cesse d'augmenter, que ces médicaments ne soient utilisés qu'en cas de nécessité et qu'on évite de prescrire ceux comportant des effets potentiellement néfastes.

Keywords: Alzheimer's, clinical pharmacology, cognitive impairment, dementia, degenerative diseases, memory, neurological practice, quality of care

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Anticholinergic medications have been shown to worsen cognition in the elderly and their use has been associated with lower Mini-Mental Status Examination (MMSE) scores.¹

The American Geriatric Society updated Beer's Criteria in 2012 to give prescribers insight into the potentially harmful properties of common medications with the goal of improving care for the

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elderly population.² Patients with Alzheimer's disease are even more susceptible to anticholinergic effects.³ Current literature maintains that benzodiazepines, opioids, and medications with anticholinergic properties are best avoided in the elderly unless absolutely essential because they have been shown to worsen cognition and can cause behavior change.¹⁻³ Prescribers must be aware that polypharmacy may affect cognition and should consider this when managing their patients.³

Saskatchewan, a western Canadian province, has a population of about one million, with nearly 40% of those people living in rural areas and small towns, defined as centers with fewer than 10,000 people.⁴ Rural centers tend to have higher elderly populations than urban areas, with about one in five people in a typical Saskatchewan town older than age 65.⁴ With a small population dispersed across the province, geographical access has been a critical barrier to equal access to care for people in rural communities.⁵ In 2006, nearly 17% of the rural population was older than age 65.⁴ As age increases, so does risk of dementia. In Canada, 14.9% of people older than age 65 have some form of dementia.⁶ To improve access to specialist diagnosis for rural patients, the Rural and Remote Memory Clinic (RRMC) was started in 2004. The initial visit involves assessment by a neurologist, neuropsychologist, physiotherapist, dietitian, and neuroimaging.⁷ At the end of the day, patients receive a diagnosis and treatment plan, including information about necessary follow-up via telehealth.^{8,9} Telehealth allows patients to receive the care they require without having to leave their home community, thus limiting the burden placed on caregivers and the health care system.^{7,8} The clinic is described in more detail elsewhere.⁷⁻⁹

In 2008, Steve et al analyzed the medication lists that 66 patients brought to their first visit at the RRMC.¹⁰ The focus of that article was on the prevalence of polypharmacy, anticholinergic medication use, and benzodiazepine use.¹⁰ They found that, at initial presentation, 24% of patients were taking an anticholinergic medication, 14% were taking a benzodiazepine, and the average number of medications per patient was 4.80 (standard deviation [SD], 3.66).¹⁰ However, it is important to quantify how physicians have changed their practices over time as more information about medication use and cognition has become available. The present study examined medication use by patients at presentation to the RRMC between March 2004 and June 2015 to see whether patterns of medication use have changed over time in patients with cognitive concerns.

METHODS AND ANALYSIS

The first 444 patients seen at the RRMC between March 2004 and June 2015 were included in this analysis. At each patient's first visit to the RRMC, patients (or their primary caregiver) are asked to bring a list of current medications. From the reports of the patient's initial assessment, medications were categorized based on their anticholinergic properties and it was noted if they were already taking a cholinesterase inhibitor.^{2,11} Medications considered anticholinergic included the American Geriatric Society's Updated Beer's Criteria and ranitidine in an effort to be consistent with Steve et al's paper and to form an accurate picture of trends over the 11-year period.^{2,10} We additionally catalogued medications with central nervous system effects (benzodiazepines, hypnotics, non-anticholinergic antidepressants,

antiepileptics, and lithium) and recorded each patient's total number of medications.^{2,3,12,13}

In an attempt to quantify polypharmacy, we totaled the number of medications at initial presentation. We excluded one patient in this analysis who presented on 27 medications and was considered an outlier, as the next closest patient had 15 medications on his or her list. For further analysis, we catalogued the score of the MMSE, which is administered during the initial clinic visit.⁸ The MMSE is a brief examination that provides a general measure of a patient's cognitive status rated on a 30-point scale, with a lower score indicating greater impairment.⁸

Patients were assigned to a 12-month period based on the date of their initial presentation. We then calculated prevalence of anticholinergic medication use, total medications, and medications with central nervous system effects for each period. Statistical analysis of these medication categories was conducted to examine trends in medication use over time. Percentages and frequencies were then calculated for each of these 12-month periods. Spearman correlation coefficient was used to measure the association between medication use and time. Ethics approval for this study was obtained from the Biomedical Research Ethics Board at the University of Saskatchewan.

RESULTS

Between March 2004 and June 2015, 444 patients were seen at the RRMC. Mean patient age was 77.4 years (SD=12.0). Mean MMSE at initial presentation was 22.4 (SD=5.8). The most frequent diagnosis (Table 1) at initial assessment was Alzheimer's disease (43.5%). Other common initial diagnoses were: mild cognitive impairment (15.3%), frontotemporal dementia (10.3%), Lewy body dementia (4.9%), vascular dementia (4.5%), and vascular/Alzheimer's dementia (2.7%).

Ninety-one patients (20.5%) were taking at least one anticholinergic medication (Table 2). Eighty patients (18.0%) were taking one anticholinergic medication, and eleven patients were taking two. Thirty-two of a total 193 patients with Alzheimer's disease were taking an anticholinergic medication

Table 1: Breakdown of diagnosis made at patient's initial visit (N = 444)

Diagnosis at initial visit	Number of patients	%
Alzheimer's disease	193	43.5
Mild cognitive impairment	68	15.3
Normal	60	13.5
Frontotemporal dementia	46	10.3
Lewy body dementia	22	4.9
Vascular dementia	20	4.5
Vascular/Alzheimer's dementia	12	2.7
Head injury	5	1.1

Other diagnoses (number of patients): corticobasal degeneration (3), hydrocephalus (3), medication side effects (2), depression (1), epilepsy (1), Fragile X-associated dementia (1), herpes encephalitis (1), hypoxic ischemic encephalopathy (1), multiple systems atrophy (1), Parkinson's dementia (1), posterior cortical atrophy (1), progressive supranuclear palsy (1), transient ischemic attacks (1).

Table 2: Breakdown of type of anticholinergic medications at initial presentation (N = 444)

Anticholinergic medications	Medication	Number of patients	%
Antihistamines	Ranitidine	31	6.7
	Diphenhydramine	4	0.9
	Hydroxyzine	3	0.7
	Loratadine	1	0.2
Antiparkinson agents	Benzotropine	2	0.4
Skeletal muscle relaxants	Cyclobenzaprine	2	0.4
Antipsychotics	Olanzapine	1	0.2
	Clozapine	1	0.2
	Prochlorperazine	2	0.4
Antidepressants	Paroxetine	30	6.7
	Amitriptyline	13	2.9
	Clomipramine	1	0.2
	Doxepin	1	0.2
	Imipramine	1	0.2
Antimuscarinics	Oxybutynin	7	1.6
	Tolterodine	3	0.7
Antispasmodics	Loperamide	1	0.2
	Scopolamine	1	0.2

Table 3: Number of current medications at initial clinic visit (N = 444)

Number of medications	Number of patients	%
0	40	9.0
≥1	405	91.0
≥2	372	83.6
≥3	339	76.2
≥4	297	66.7
≥5	251	56.4
≥6	193	43.4
≥7	146	32.8
≥8	107	24.0
≥9	72	16.2
≥10	49	11.0

(16.6%). Of the 91 patients that were taking an anticholinergic medication, 68 had some form of dementia or mild cognitive impairment (74.7%). Eleven of the 91 patients taking an anticholinergic medication were simultaneously taking a cholinesterase inhibitor (12.1%).

Patients were on an average of 5.2 medications each (n = 444; range, 0-15; SD, 3.46) (Table 3). Forty patients (9.0%) were on no medications, whereas 339 patients (89.7%) were taking three or more medications.

We also looked at trends in average number of medications taken over time (Figure 1). There was a weak positive correlation

between total medications per patient and time (Spearman's correlation coefficient = 0.11, p=0.017) as the average number of medications per patient increased from 5.3 in 2004 to 7.0 in 2014.

As shown in Figure 2, we saw a slight decline in percentage of patients presenting with anticholinergic medications over time (Spearman's correlation coefficient = -0.64, p=0.035).

There was no statistically significant relationship between use of medications that affect the central nervous system and time (Spearman's correlation coefficient = 0.09, p = 0.790) (Figure 3). Despite the lack of statistical significance, there appears to be an increase in the use of these medications between 2012 and

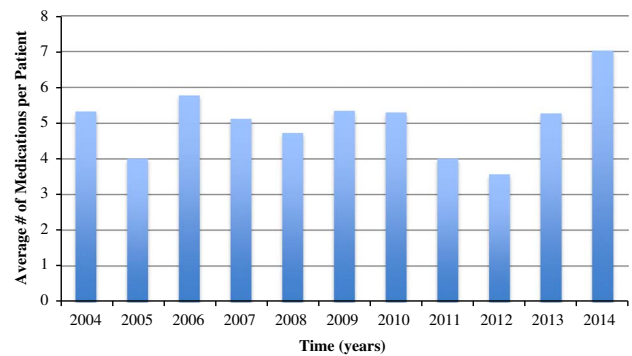


Figure 1: Average number of medications per patient by year of clinic operation.

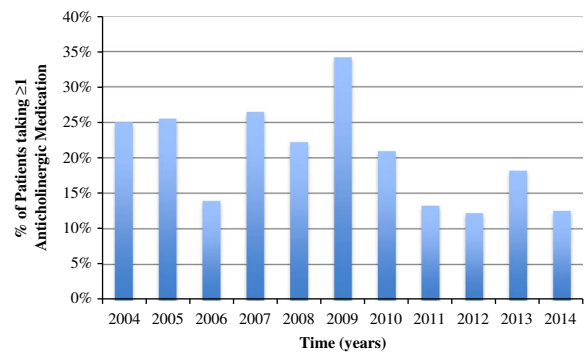


Figure 2: Percentage of patients taking at least one anticholinergic medication over time.

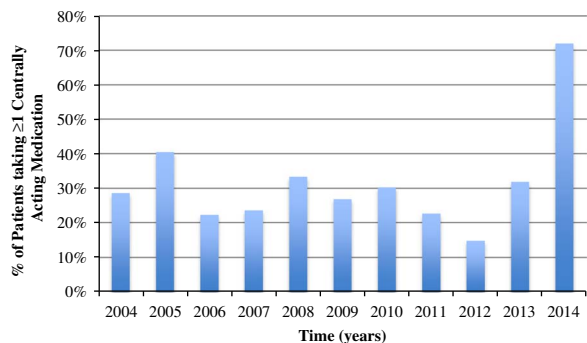


Figure 3: Percentage of patients taking at least one centrally acting medication over time.

2014. These medications include benzodiazepines, hypnotics, antidepressants (non-anticholinergic), and antiepileptics.^{2,3,12}

Sixty-three patients (14.2%) presented to the RRMC already taking a cholinesterase inhibitor.¹¹ Of these, eight (12.7%) were taking an anticholinergic medication concurrently. Thus, 1.8% (8/444) of patients presented on both an anticholinergic medication and a cholinesterase inhibitor simultaneously.

CONCLUSION

The most encouraging statistic to come from this study is a decline in anticholinergic medication use by the rural elderly population as they presented to the RRMC. Educating prescribers about the problems of prescribing anticholinergic drugs has been shown to be important for patients older than age 65 years.² This result suggests that prescribers are becoming more aware of the potentially harmful effects of anticholinergic medications in elderly populations.² Looking at specific medications, it is important to consider that some medications (eg, bladder medications)¹⁴ may still benefit the patient more than any inherent cognitive risk. However, the solution may be as simple as switching the prescription to a different drug within the same class.¹⁵ One example is paroxetine, a selective serotonin reuptake inhibitor antidepressant (6.7% of patients presented with it on their medication list).^{2,15} Other selective serotonin reuptake inhibitors have less anticholinergic activity and may be a better choice in elderly populations.^{2,15}

When Steve et al examined the prevalence of anticholinergic medication use at the RRMC in 2008, they found that 24.0% of the 66 patients they had seen were taking some form of anticholinergic medication.¹⁵ Of the 444 patients (including the initial 66 analyzed by Steve et al) who have now been seen at the RRMC, 20.5% were taking a medication with anticholinergic properties at initial presentation.

In 2004, Carrahan et al found that 35.4% of patients with a cholinesterase inhibitor on their prescription list also had an anticholinergic medication on their prescription list from their primary care physician.¹¹ The proportion of RRMC patients is lower than previously reported by Carrahan et al, in which only eight of the 63 patients (12.7%) who presented with a cholinesterase inhibitor on their medication list were also taking an anticholinergic medication.¹¹

Research has shown that polypharmacy may be associated with increased cognitive symptoms.^{3,13} Considering that patients were taking an average of 5.2 medications each, it is critical for caregivers to be aware of the possible impact that polypharmacy may have on a patient's cognition.^{3,13} Informed prescribing is essential to limit unnecessary side effects, particularly in patients with memory concerns.^{2,3,13} Prescribers must be properly informed to ensure that the number of medications per patient does not continue to rise, that

medications are only used when necessary, and that potentially deleterious medications are avoided.^{2,3,13}

DISCLOSURES

None of the authors have anything to disclose.

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