Education and Use of Dementia Drugs: A Register-Based Study of Over 600,000 Older People

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Key Words

Elderly, Sweden · Drug register · Dementia drugs · Education

Abstract

Background/Aims: Low education has been shown to be a risk factor for dementia. However, little is known about the association between educational level and dementia drugs.

Methods: We conducted a register-based study in Sweden of 645,973 people aged 75–89 years. Data on age, sex, type of residential area (urban/rural), dispensed drugs and education were analyzed from people aged 75–89 years registered in the Swedish Prescribed Drug Register during July to October 2005. The 3 main outcome measures were dispensed dementia drugs, cholinesterase inhibitors (donepezil, rivastigmine and galantamine) and memantine. **Results:** Dementia drugs were used by 3% of the study population, cholinesterase inhibitors by almost 3% and memantine by 0.4%. High education was associated with dementia drugs (OR: 1.26; 95% CI: 1.19–1.34 for ≥ 15 years of education compared with ≤ 9 years), cholinesterase inhibitors (OR: 1.25; 95% CI: 1.17–1.33 for ≥ 15 years of education compared with ≤ 9 years) and, especially, memantine (OR: 1.46; 95% CI: 1.26–1.68 for ≥ 15 years of education compared with ≤ 9 years), after adjustment for age, sex, type of residential area and number of dispensed drugs. **Conclusion:** The results indicate that there may be inequalities in the use of dementia drugs among el-

derly Swedes. Future research is required to explain why educational level has the opposite relationship to dementia drugs than to dementia diagnosis.

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Introduction

Dementia is one of the most common diseases in the elderly and a major cause of disability and mortality, resulting in human, social and economical costs. The problems related to dementia are expected to intensify because of the increasing number of elderly in the world [1, 2]. Alzheimer's disease accounts for about two thirds of all dementia cases [3].

In the 1990s, the cholinesterase inhibitors (donepezil, rivastigmine and galantamine) were introduced for treatment of mild to moderate Alzheimer's disease. Some years later, the NMDA receptor antagonist memantine was available for treatment of moderate to severe Alzheimer's disease [2], although the exact indication for memantine varies between different countries [4]. However, the dementia drugs are controversial [5], due to discussions about their clinical benefits [3, 6, 7] and arbitrariness in prescribing [4, 8, 9]. A recent review and meta-analysis concluded that dementia drugs have a limited effect, but their use is still justified given the current lack of other effective treatments [10].

Low education has been shown to be a risk factor for dementia [11–15]. The exact pathway between low education and dementia is not established, however, several interpretations have been suggested, such as increasing neocortical synaptic density and more effective coping with dementia symptoms among higher-educated people [12]. In contrast, a recent study from the UK reported that elderly with higher education are more likely to use dementia drugs [16]. Consequently, the dementia drugs may not be reaching all potential patients and there may exist an inequality in the use of these drugs.

We wanted to investigate whether there exists an inequality in use of dementia drugs by analyzing data from the new Swedish Prescribed Drug Register, which contains information on all dispensed prescriptions in Sweden [17]. This drug register provides unique possibilities for studying drug use among the elderly.

The aim of this study was to investigate the association between educational level and dementia drugs in a large sample of older people in Sweden.

Materials and Methods

Study Population

The Swedish Prescribed Drug Register contains individual-based data on all dispensed prescriptions to the whole population of Sweden (about 9 million inhabitants). The data collection is administered by the state-owned National Corporation of Swedish Pharmacies and then transferred to the National Board of Health and Welfare [17].

The Swedish Prescribed Drug Register for the time period July to October 2005 was individually linked by personal identification numbers to the national education register, which is updated yearly by Statistics Sweden and includes information on the highest formal education of each Swedish citizen aged 15–74 years [18]. In Sweden, the maximum quantity of drugs prescribed is for 90 days of supply. Thus, the study period of 4 months ought to include most prescriptions for regularly used drugs, such as dementia drugs. The information on education was collected from years 1990, 1997, 2000 and 2004, and, consequently, individuals ≥ 90 years did not have complete information on education in the register and were therefore excluded. Also 2.3% (15,405/661,797) of the individuals aged 75–89 years with missing data on education were excluded, together with 419 individuals with missing data on municipality of residence. Finally, data on age, sex, type of residential area (urban/rural), dispensed drugs and education were analyzed from 645,973 individuals aged 75–89 years.

Definitions

Dementia drugs were identified by the Anatomical Therapeutic and Chemical classification system [19]: donepezil (N06DA02), rivastigmine (N06DA03), galantamine (N06DA04) and memantine (N06DX01). Cholinesterase inhibitors were defined as use of any of the dementia drugs donepezil, rivastigmine or galantamine.

Education was coded into 5 groups according to the Swedish educational system [20]: ≤ 9 years of education (elementary school; used as reference), 10–11 years (high school), 12 years (high school), 13–14 years (graduate education) and ≥ 15 years (graduate and postgraduate education).

Age was categorized into 3 groups: 75–79 (reference), 80–84 and 85–89 years.

Number of dispensed drugs was divided into 4 categories: 1–4 (reference), 5–9, 10–14 and ≥ 15 drugs.

Type of residential area was classified according to a scale by Statistics Sweden in 6 categories of so-called homogeneity regions (H1–H6) depending on the population density and the number of inhabitants in the nearest vicinity of the main city in that municipality [21]. According to this official homogeneity region classification, the 2 highest-density categories (H1, H2) include only the largest cities in Sweden: Stockholm, Göteborg and Malmö/Lund. H3 consists of municipalities with $>90,000$ inhabitants within a 30-km radius from the centre of that municipality. H4 includes municipalities with $>27,000$ but $<90,000$ inhabitants from the centre of that municipality and also $>300,000$ inhabitants within a 100-km radius from the same centre. H5 is identical to H4 except that there are $<300,000$ inhabitants from the centre of the municipality. Finally, H6 consists of municipalities with $<27,000$ inhabitants within a radius of 30 km from the municipality centre. H1–H3 were classified as urban (reference) and H4–H6 as rural areas [22].

The study was approved by the ethics board in Stockholm (Dnr 2006/948-31).

Statistical Analysis

Logistic regression was used to study the association between the explanatory variables (age, sex, number of dispensed drugs, type of residential area and education) and dementia drugs. The results are shown as odds ratios (ORs) with 95% confidence intervals (CIs). SPSS 14.0 for Windows (SPSS Inc., 1989–2005) was used for the analyses.

Results

The mean age among the 645,973 elderly was 81 years, 60% were women, 65% lived in urban areas, and 61% had ≤ 9 years of formal education (table 1). Dementia drugs were dispensed for 3% of the study population, cholinesterase inhibitors for almost 3% and memantine for 0.4% (table 2). Moreover, among the individuals aged 75–79 years dementia drugs were dispensed for 2.2%, among 80–84 years for 3.4% and among 85–89 years for 3.7%.

In the logistic regression analyses (table 3), high education was associated with dementia drugs (OR: 1.26; 95% CI: 1.19–1.34 for ≥ 15 years of education compared with ≤ 9 years), cholinesterase inhibitors (OR: 1.25; 95% CI: 1.17–1.33 for ≥ 15 years of education compared with ≤ 9 years) and, especially, memantine (OR: 1.46; 95% CI: 1.26–1.68 for ≥ 15 years of education compared with ≤ 9 years), after adjustment for age, sex, type of residential

Table 1. Characteristics of the elderly study population (n = 645,973), Sweden, 2005

	n	%
Age		
75–79 years	267,700	41.4
80–84 years	232,837	36.0
85–89 years	145,436	22.5
Sex		
Men	257,750	39.9
Women	388,223	60.1
Type of residential area		
Urban	422,522	65.4
Rural	223,451	34.6
Dispensed drugs		
1–4	237,510	36.8
5–9	248,917	38.5
10–14	110,245	17.1
≥15	49,301	7.6
Education		
≤9 years	394,731	61.1
10–11 years	138,770	21.5
12 years	44,016	6.8
13–14 years	29,484	4.6
≥15 years	38,972	6.0

area and number of dispensed drugs. There was a positive gradient across the educational levels in the association with dispensed dementia drugs.

Moreover, the elderly women had a higher probability of use of cholinesterase inhibitors (OR: 1.14; 95% CI: 1.10–1.18 for women compared with men), yet, not of memantine (OR: 0.97; 95% CI: 0.90–1.05 for women compared with men), after adjustment for age, type of residential area, number of dispensed drugs and education. Living in a rural area was associated with cholinesterase inhibi-

Table 2. Dispensed dementia drugs in the elderly study population (n = 645,973), Sweden, 2005

	n	%
Total dementia drugs		
≥1 dispensed dementia drug	19,266	3.0
Specific types of dementia drug		
≥1 dispensed cholinesterase inhibitor	17,355	2.7
Dispensed memantine	2,751	0.4

Table 3. Adjusted ORs with 95% CIs for dispensed dementia drugs in the elderly study population (n = 645,973), Sweden, 2005

	Total dementia drugs	Cholinesterase inhibitors	Memantine
Age			
75–79 years	ref.	ref.	ref.
80–84 years	1.49 (1.44–1.55)	1.49 (1.44–1.55)	1.33 (1.22–1.45)
85–89 years	1.59 (1.53–1.65)	1.58 (1.52–1.65)	1.33 (1.20–1.46)
Sex			
Men	ref.	ref.	ref.
Women	1.12 (1.09–1.16)	1.14 (1.10–1.18)	0.97 (0.90–1.05)
Type of residential area			
Urban	ref.	ref.	ref.
Rural	1.20 (1.17–1.24)	1.23 (1.19–1.27)	1.00 (0.92–1.09)
Dispensed drugs			
1–4	ref.	ref.	ref.
5–9	2.07 (1.99–2.15)	2.03 (1.95–2.12)	2.74 (2.45–3.06)
10–14	2.64 (2.53–2.76)	2.54 (2.43–2.66)	3.86 (3.43–4.35)
≥15	2.28 (2.16–2.42)	2.16 (2.04–2.29)	3.91 (3.39–4.51)
Education			
≤9 years	ref.	ref.	ref.
10–11 years	1.09 (1.05–1.13)	1.09 (1.05–1.14)	1.05 (0.95–1.15)
12 years	1.18 (1.11–1.25)	1.19 (1.12–1.27)	1.18 (1.02–1.38)
13–14 years	1.20 (1.12–1.28)	1.21 (1.13–1.30)	1.33 (1.13–1.58)
≥15 years	1.26 (1.19–1.34)	1.25 (1.17–1.33)	1.46 (1.26–1.68)

tors (OR: 1.23; 95% CI: 1.19–1.27 for rural compared with urban areas), however, not with memantine (OR: 1.00; 95% CI: 0.92–1.09 for rural compared with urban areas), after adjustment for age, sex, number of dispensed drugs and education. Increasing number of dispensed drugs was clearly associated with memantine (OR: 3.91; 95% CI: 3.39–4.51 for ≥ 15 drugs compared with 1–4 drugs), after adjustment for age, sex, type of residential area and education. However, the association for cholinesterase inhibitors was not as straightforward.

Discussion

Main Findings

The results suggest that elderly with a high level of formal education have a higher probability of being dispensed dementia drugs, especially memantine, than the lower-educated elderly. Conversely, low education is a known risk factor for dementia [11–15]. High education has also been associated with faster cognitive decline after dementia diagnosis [23, 24]. Our finding is in concordance with a recent study on dementia drugs from the UK, where treatment with these drugs was biased towards individuals with higher education [16]. The lower-educated elderly may have problems with paying for dementia drugs; however, prescribed drugs are subsidized to a great extent in Sweden in order to level out socioeconomic differences. Two other debated drugs, statins (lipid-lowering drugs) [25, 26] and hormone replacement therapy [27, 28], have also been suggested to be used to a higher extent among the more socioeconomically advantaged. It seems like higher-educated elderly more often use newer and more expensive drugs than lower-educated elderly [29]. People with higher education may be more aware of treatment alternatives and may have developed better communication skills [26] and, thus, be more likely to be prescribed dementia drugs. Also, better-educated elderly and their family members may have greater expectations of health care and may be more likely to have adopted news about dementia treatments [25]. In general, though, drug use is more frequent among people with lower socioeconomic status, which implies that those in the greatest medical need use most medicines [30].

Moreover, the association with high education was stronger for memantine than for the cholinesterase inhibitors. Again, this may be due to the higher probability for higher-educated elderly to use newer drugs than lower-educated elderly, and memantine was introduced

on the Swedish market after the cholinesterase inhibitors. Alternatively, this finding may be an expression of severity of disease [31]; memantine is licensed for moderate to severe Alzheimer's disease, and the cholinesterase inhibitors for mild to moderate Alzheimer's disease.

Living in a rural area was associated with being dispensed cholinesterase inhibitors. This might reflect regional differences in physicians' therapy traditions [9, 32] or actual differences in the prevalence of dementia between rural and urban areas [33].

The prevalence of dementia drugs in this study population was 2% for the age of 75–79 years, 3% for 80–84 years and 4% for 85–89 years. In contrast, the prevalence of dementia in Sweden has been estimated at 9% for the age of 75–79 years, 20% for 80–84 years and 23% for 85–89 years [34], and 19% for Alzheimer's disease among people aged ≥ 77 years [35]. Two studies on dementia drugs from the UK also reported that treatment with dementia drugs was much lower than expected from known prevalence rates [9] and a large proportion of the eligible population was not prescribed these drugs [16].

Limitations

Only information from people aged 75–89 years who were registered in the Swedish Prescribed Drug Register during July to October 2005 and with complete data were used, which corresponds to about 89% (645,973/725,035 [36]) of the population aged 75–89 years in Sweden. A selection bias could be present in this study if the elderly aged 75–89 years not registered in the Swedish Prescribed Drug Register during July to October 2005 had a higher education than those included, which may result in an overestimation of the probability for the higher-educated elderly of being dispensed dementia drugs. However, the distribution of education among the elderly in this study corresponds rather well with previous papers on elderly Swedes [11, 12]. The excluded 15,824 people aged 75–89 years with missing data on education or municipality of residence had a mean age of 82 years, 65% were women, and 2.4% used dementia drugs.

Further, the Swedish Prescribed Drug Register does not include data on over-the-counter drugs, herbal drugs and drugs used in hospitals and is incomplete with regard to drugs used in nursing homes, which may lead to an underestimation of the drug use.

Dementia diagnoses were not included in this study. However, confounding by indication is less likely to explain the association between high education and demen-

tia drugs, since high education has been connected to lower risk of dementia [11–15].

Moreover, the analyses of the association between education and dementia drugs were not adjusted for other measurements of socioeconomic status or comorbidity, which may act as confounders. Nevertheless, education is a strong determinant of employment and income [37], and number of dispensed drugs may be regarded as an overall measure of comorbidity [38, 39].

Finally, dispensed drugs are not synonymous with prescribed drugs. Hence, the prescription of dementia drugs in Sweden may be higher than the estimated frequency of dispensed dementia drugs in this study.

Conclusion

Sweden has a health care system with presumably equal access to medical care. However, this study indicates that there may be inequalities in the use of dementia drugs among elderly Swedes.

Future research is required to explain why educational level has the opposite relationship to dementia drugs than to dementia diagnosis.

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