Research Report

Treatment Patterns of Patients with All-Cause Dementia in Russia

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Abstract.
Background: Studies on prevalence or the therapy of dementia are rare or non-existent in Russia.
Objective: The purpose of this study was to analyze the prescription patterns of antidementia therapy in Russia in 2018.
Methods: This retrospective cross-sectional study was based on the IQVIA Russia LRx database, which covers approximately 11% of all patients enrolled in federal or regional reimbursement state healthcare programs. We descriptively analyzed the proportions of patients treated with antidementia drugs, antipsychotics, antidepressants, and benzodiazepines.
Results: A total of 12,051 dementia patients were available for analysis. Of those, 6,394 patients had a vascular dementia (VaD) diagnosis, while 3,413 were diagnosed with dementia in other diseases (DOD), 1,128 with Alzheimer's disease (AD), and 1,116 with unspecified dementia (UD). The therapy with the highest patient proportion was antipsychotics, with 74% of VaD patients, 73% of UD patients, and 47% of DOD patients receiving these drugs. The proportion of patients treated with antidementia drugs was 68% in AZ, 56% in VaD, 45% in UD, and only 9% in DOD. Antidepressants were a relatively rare therapy in dementia patients (between 4% and 12%), and 30% of DOD patients received benzodiazepines, while the proportions of patients receiving this therapy class in other dementias was low (7–10%). Most patients were treated with old-generation drugs.
Conclusion: The proportion of older drugs prescribed in Russia is higher than in Western Europe, which may likely be due to their low prices, resulting in a higher chance for successful health insurance reimbursement claims.

Keywords: Antidepressants, antipsychotics, benzodiazepine, dementia, Russia

INTRODUCTION

Dementia is a neuropsychiatric disorder caused by neurodegeneration that leads to a progressive loss of cognitive functions [1]. A recently published systematic review and meta-analysis reported the age- and sex-standardized prevalence rate of dementia in Europe to be 7.1% [2]. Russia is a country with about 145 million inhabitants, and about 12% of them are 65 or older [3]. In 2010, Russia was estimated to be among the nine countries with the highest number of people with dementia [4, 5].

Therapy patterns of dementia patients constitute an important research subject, and in recent years, several studies focusing on this issue have been published in different countries throughout the world [6–12]. Russia has essentially not yet been covered by research, and studies on prevalence or the therapy of chronic diseases like dementia are rare or non-existent.

Therefore, the goal of this retrospective study was to analyze the prescription patterns of antidementia therapy in Russia in 2018.

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Table 1
Basic characteristics of dementia patients in this study

Variable	Vascular dementia (ICD- 10: F01)	Dementia in other diseases classified elsewhere (ICD- 10: F02)	Alzheimer's disease (ICD-10: G30)	Unspecified dementia (ICD-10: F03)
N	6,394	3,413	1,128	1,116
Age (Mean, SD)	74.6 (13.1)	53.2 (18.7)	67.2 (17.4)	70.2 (17.7)
Male	40.8	53.0	37.2	31.7
Female	59.2	47.0	62.8	68.3
Treating physician				
Neuropsychiatrist	93.0	84.0	68.5	93.1
General practitioner	4.1	6.7	24.2	3.9
Others	2.9	9.3	7.3	3.0
Category of disability				
I (mild)	40.1	11.4	28.3	43.9
II (moderate)	45.7	47.5	46.3	44.1
III (severe)	14.2	41.1	25.4	12.0

METHODS

This retrospective cross-sectional study was based on the IQVIA Russia LRx database, which covers approximately 11% of all patients enrolled in federal or regional reimbursement state healthcare programs. The data is properly anonymized (in accordance with Federal Law 152, which is similar to the EU General Data Protection Regulation) and allows for longitudinal tracking of each patient via a unique patient ID. Other data attributes include age, sex, diagnosis, and prescription information (therapy with the indication of trade name, molecule, drug form, dosage, manufacturer, region in which the drug was dispensed, prescription period), and prescriber specialty.

Outpatients with dementia, including vascular dementia (VaD) (ICD-10: F01), dementia in other diseases (DOD) (ICD-10: F02), Alzheimer's disease (AD) (ICD-10: G30), and unspecified dementia (UD) (ICD-10: F03), who received prescriptions in the time period between January 2018 and December 2018, were included in our analyses. We analyzed the following therapy classes (based on the anatomical classification of pharmaceutical products published by the European Pharmaceutical Market Research Association (EphMRA)): antidementia drugs (ATC: N07D), antipsychotics (ATC: M05A), antidepressants (ATC: N06A), and benzodiazepines (N05 C).

We separately analyzed the proportions of dementia patients treated with each of four antidementia drugs: donepezil, galantamine, memantine, and rivastigmine, as well as the proportions of patients treated with several antipsychotics, antidepressants, and benzodiazepines.

This study is of a descriptive nature, and no hypotheses were tested. All analyses were carried out using SAS version 9.4.

RESULTS

In total, 12,051 dementia patients who were seen by 1,325 physicians and received medication therapy were available for analysis. Of those, 6,394 patients had a VaD diagnosis, while 3,413 were diagnosed with DOD, 1,128 with AD, and 1,116 with UD. The mean age varied between 53.2 years in DOD and 74.6 years in VaD patients. The proportion of females was highest in the UD group (68.3%) and lowest in the DOD group (47.0%). The majority of patients were treated by neuropsychiatrists (Table 1).

The proportion of defined therapy classes in dementia patients is shown in Figure 1. The therapy with the highest patient proportion was antipsychotics, with 74% of VaD patients, 73% of UD patients, and 47% of DOD patients receiving these drugs. The proportion of patients treated with antidementia drugs was 68% in AZ, 56% in VaD, 45% in UD, and only 9% in DOD. Antidepressants were a relatively rare therapy in dementia patients (between 4% and 12%), and 30% of DOD patients received benzodiazepines, while the proportions of patients receiving this therapy class in other dementias was low (7%-10%).

Among patients treated with antidementia drugs, memantine had the highest shares (between 46% in AD patients and 62% in UD patients), followed by galantamine (from 21% in UD patients to 41% in
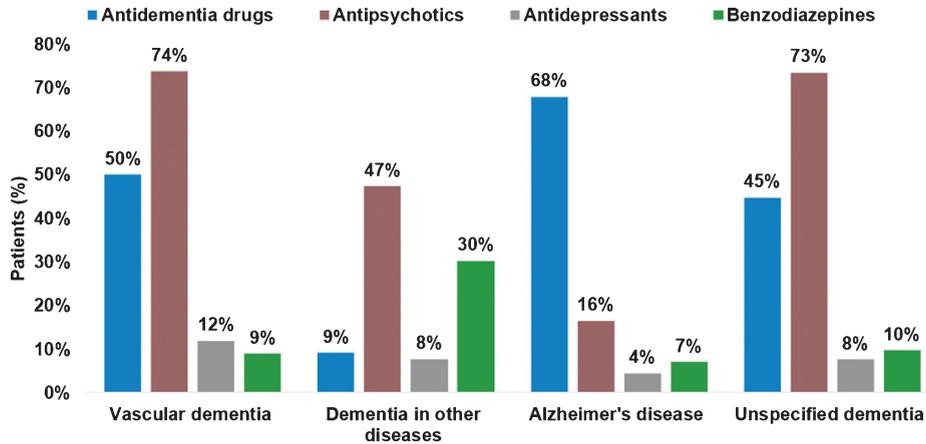
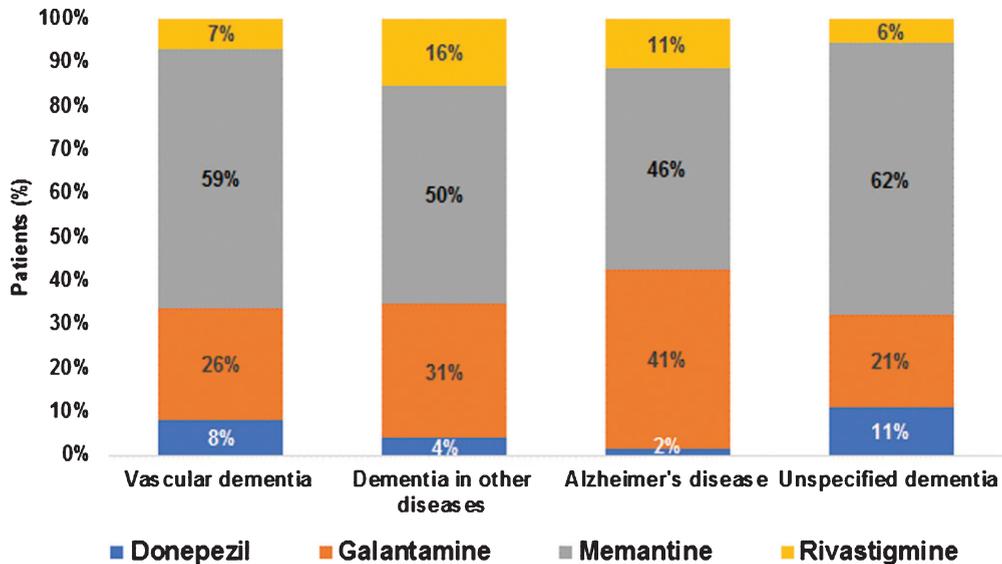Fig. 1. Therapy classes prescribed to dementia patients in Russia in 2018.

Fig. 2. Drugs prescribed to dementia patients in Russia in 2018.

AD patients). Both donepezil and rivastigmine were prescribed much less frequently (Fig. 2).

Antipsychotic therapy strongly differed between patients within the four dementia groups studied herein. In VaD patients, chlorprothixene (49% of patients treated with antipsychotics), haloperidol (27%), and quetiapine (21%) were the three must frequently prescribed drugs. The same drugs were frequently given to UD patients (chlorprothixene 48%, haloperidol 21%, and quetiapine 20%). In DOD patients, chlorpromazine (36%) and thioridazine (28%) were the most frequently prescribed, while in AD patients, quetiapine (34%) and thioridazine (23%) were prescribed more often.

About 20 different antidepressants were prescribed. Amitriptyline (28%) and fluvoxamine (23%) were the only drugs with a proportion of at least 20% in VaD patients, and paroxetine (21%) and amitriptyline (20%) the only ones with a proportion of at least 20% in UD patients. Amitriptyline was the only frequently prescribed antidepressant In DOD and AD patients (62% in DOD, 36% in AD).

Phenozepam was the only frequently used drug when dementia patients received benzodiazepines

(83% in VaD, 76% in DOD, 80% in AD, and 86% in UD patients).

DISCUSSION

In this retrospective study of about 12,000 individuals with dementia, the treatment classes used differed between dementia types. Patients in Russia with dementia types that mainly occur in elderly patients (i.e., VaD and AD) were relatively young (67 years in the AD and 75 years in the VaD group). For example, in Germany, the average age of dementia patients was 81 years [13, 14], while in Poland, the proportion of dementia patients aged ≥ 75 years was about 76% [15]. The reason for this difference may be the relatively low life expectancy in Russia (65.5 years in men, 76.5 years in women), especially in non-central and rural regions [3, 16].

In Russia, 58% of VaD and 68% of AD patients received antidementia drugs. These shares were higher than in Germany (47%) [17]. However, a valid comparison is not possible since all diagnosed dementia patients in Germany were used as denominator and, in Russia, dementia patents with at least one prescription for dementia were classified, resulting in the overestimation of the prevalence rates. A prevalence of dementia therapy of about 50% can be assumed, so the prevalence of antidementia drug use in dementia patients is about 30% and thus in line with the value reported by Vasenina et al. [18].

When discussing the possible reasons for the treatment behavior of non-university-based physicians in non-English-speaking countries, it is important to understand which sources these physicians use to be informed about evidence-based medicine studies. In Russia, the first line consists of Russian scientific journals. Publications on dementia are often published in the *Zhurnal Nevrologii i Psikhiatrii imeni S.S. Korsakova*.

Memantine is the most frequently prescribed antidementia drug in Russia. This drug was the subject of several studies published in Russian in this country, which have shown some therapy benefits for dementia patients [19–22]. The efficacy and safety of galantamine, which is frequently used in Russia, was also demonstrated [23–25].

In Russia, antipsychotics were often prescribed to dementia patients. This result is not surprising, as a similar situation was observed in Germany [26], where 47.7 % of patients with dementia were treated with antipsychotics. Moreover, diagnosis of VaD was positively associated with therapy initiation. In line with the Germany study, the prevalence of antipsychotic use in Russia was highest in VaD patients. Explaining why antipsychotics like chlorprothixene, haloperidol, quetiapine, chlorpromazine, and thioridazine were more frequently prescribed than other drugs is difficult. Four of these drugs (chlorprothixene, haloperidol, chlorpromazine, and thioridazine) are old-generation antipsychotics that were introduced many decades ago and have low prices, thus gaining a higher share in the reimbursement segment. Studies from Russia on antipsychotic use in elderly patients are lacking, but several studies have been published in Europe and the U.S. For example, in a large retrospective study, the mortality risk in older adults was found to be increased for haloperidol and decreased for quetiapine and olanzapine [27]. Schmedt et al. reported a higher risk of death in patients treated with haloperidol, levomepromazine, and zuclopenthixol compared to risperidone. Lower risks were observed for quetiapine, prothipendyl, olanzapine, tiapride, clozapine, perazine, and flupentixol [28].

The proportion of benzodiazepine prescriptions in dementia patients in Russia was very similar to that in Germany (10%) [29]. However, the prescribed drugs differ from country to country (phenazepam in Russia, diazepam in Germany). Phenazepam is a benzodiazepine developed about 50 years ago in the former USSR, and its toxicity is considered to be lower than that of other benzodiazepines. This drug has often been prescribed in Russia for anxiolytic, sedative-hypnotic, or anti-epileptic uses [30].

Amitriptyline was the antidepressant most frequently prescribed to antidementia patients in Russia. In a claims data analysis from Germany, amitriptyline was dispensed more often than other tricyclic antidepressants [31]. However, amitriptyline has been a potentially inappropriate medication for elderly patients for years and is included in international PRISCUS (Latin for "old and venerable") lists [32]. Again, amitriptyline is an old-generation antidepressant with a low price and a good chance in the reimbursement segment.

This study is the first using Russian data representing the therapy patterns of dementia patients. However, it is subject to several limitations that should be mentioned at this point. The first limitation is the short time period the investigation covers. A longer time period was not possible as LRx data in Russia are only available from 2018 onward. Second, the 11% coverage of the LRx database is relatively

limited and does not include many regions. Third, the LRx database does not include any information on the reasons for the physicians' decisions in terms of antidementia drugs or antipsychotic prescriptions in dementia patients. Fourth, the database lacks information on the severity of the disease and additional disease details. For example, in DOD patients, no information was available on what the other diseases were (Parkinson's disease, epilepsy, multiple sclerosis, etc.). Fifth, no information about urban and rural areas was available, which could play an important role in the treatment of dementia. Nevertheless, the main strength of this study is that the LRx database contains real-world data and large patient numbers, which allowed for an estimation of the prevalence of antidementia prescriptions in Russia.

The drug classes prescribed to dementia outpatients in Russia do not considerably differ from those given in Europe. However, the proportion of older drugs in Russia is higher than in Western Europe; this finding is probably due to the low prices of older drugs, resulting in a higher chance for successful health insurance reimbursement claims.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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