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Primary data analysis on the use of antidementia drugs in German patients with Alzheimer's disease across all severity stages of the disease

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Introduction

Alzheimer's disease (AD) is one of the most common neurodegenerative diseases in the elderly with more than 600.000 patients in Germany. Curative therapies for AD are lacking. Earlier studies showed positive effects of antidementia drugs (ADDs) on the patients' cognition, the ability to perform activities of daily living, and the global clinical impression. Current guidelines of the German neurological and psychiatric associations recommend a symptomatic treatment of mild to moderate dementia with acetylcholine esterase inhibitors and memantine for patients with moderate to severe AD. Earlier studies showed that the prescription rate of ADDs in German dementia patients ranges from 42% to 52% with a lower use among nursing home inhabitants. Most previous studies assessed the use of ADDs in Germany on the basis of claims data, not containing information on patients' severity of dementia and further clinical status. Therefore, we used primary data to evaluate the prescription of ADDs according to the patients' cognitive status as measured with the Mini-Mental Status Examination (MMSE). Additionally, we hypothesized that the prescription of ADDs is associated with the patients' clinical status and socio-demographic characteristics such as age, gender, living situation, and level of care.

Patients and Methods

In this cross-sectional study, 395 community-dwelling (n = 272) and institutionalized (n = 123) patients with AD were consecutively recruited from five study sites in Marburg-Biedenkopf, Germany. The use of ADDs was identified by the ATC-codes N06DA02 (donepezil), N06DA03 (rivastigmine), N06DA04 (galantamine), and N06DX01 (memantine). Patients were classified into four dementia severity groups depending on their MMSE score: mild cognitive deficits (27 - 30 pts.), mild dementia (20 - 26 pts.), moderate dementia (10 - 19 pts.), and severe dementia (0 - 9 pts.). The further clinical assessment comprised the patients' ability to perform activities of daily living (Alzheimer's Disease Cooperative Study-Activities of Daily Living, ADCS-ADL), the presence of neuropsychiatric symptoms (Geriatric Depression Scale, GDS and Neuropsychiatric Inventory, NPI), and the health-related quality of life (HrQoL). Patients' HrQoL was assessed with the generic EuroQol Instrument (EQ-5D index and EQ VAS) and the disease-specific QoL-AD (Quality of Life-Alzheimer's Disease). First, we evaluated the unadjusted bivariate associations between the use of ADDs and the patients' socio-demographic and clinical status. Finally , we included the independent variables in a multiple logistic regression model.

Results

The majority of the study population were female (63.2%) and community-dwelling (68.9%). ADDs were prescribed in 46.6% of all participants and less often in nursing home inhabitants compared to community-dwelling patients (38.2% vs. 50.4%, Chi²-test: p = 0.025). In bivariate analyses, patients using ADDs reported significantly less depressive symptoms as measured with the GDS (29.9% vs. 38.4%, Chi²-test: p = 0.038) and a higher HrQoL according to the QoL-AD (Mann-Whitney U test: p = 0.029) and the EQ-5D index (Mann-Whitney U test: p = 0.001). Patients not treated with ADDs scored non-significantly higher in the NPI (Mann-Whitney U test: p = 0.587) and lower in the ADCS-ADL (Mann-Whitney U test: p = 0.563). The majority of patients (79.3%) medicated with ADDs were treated by neurologists or psychiatrists. The multiple regression analysis showed that patients treated by neuropsychiatric specialists had a higher chance of receiving ADDs (OR 2.467, 95% CI: 1.288 – 4.726) as well as those with mild to moderate dementia (OR 3.752, 95% CI: 1.166 – 12.080 and OR 3.526, 95% CI: 1.431 – 8.688). Additionally, ADDs were less often prescribed in patients in the statutory health insurance compared to privately insured participants (49.2% vs. 71.4%, Chi²-test: p = 0.025; OR 0.309, 95% CI: 0.098 – 0.957). Additionally, 39% of the patients with mild cognitive deficits (MMSE 27 - 30) and 48% of the mild demented patients (MMSE 20 - 26) received memantine.

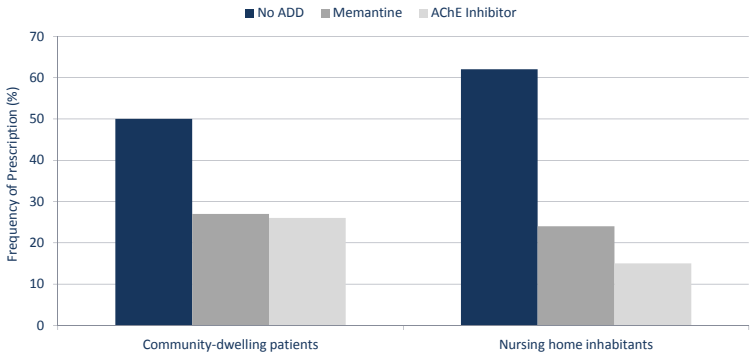

Figure 1: Prescription of acetylcholine esterase inhibitors and memantine depending on the patients' living situation.

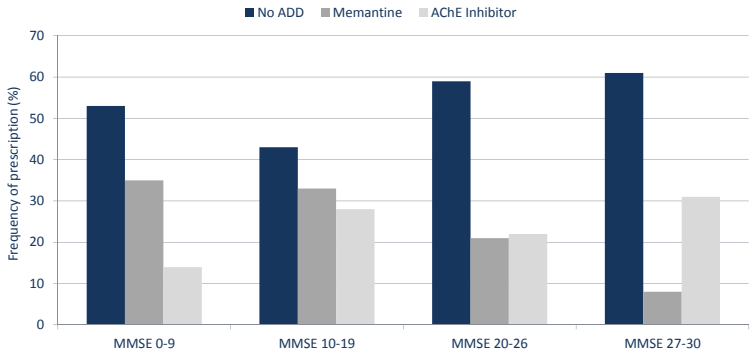

Figure 2: Prescription of antidementia drugs with regard to the patients' severity of dementia.

Multiple logistic regression analysis of associations between the prescription of antidementia drugs (dependent variable) and the patients' socio-demographic and clinical status.

Variable	Regression Coefficient	Standard Error	Odds Ratio	95%-Odds Ratio Confidence Interval	p-value
Age	0.005	0.018	1.005	0.971 – 1.041	0.768
Gender Female Male	 - 0.271	 0.289	 0.763	 0.433 – 1.346	 0.350
Living Situation Nursing Home Community-dwelling	 0.498	 0.399	 1.646	 0.753 – 3.595	 0.212
Outpatient Treatment No Specialist Neuropsychiatric Specialist	 0.903	 0.332	 2.467	 1.288 – 4.726	 0.006
Health Insurance Private Statutory	 - 1.185	 0.582	 0.309	 0.098 – 0.957	 0.042
Care Level, n (%) None (Reference) Level I Level II or III	 0.203 - 0.458	 0.353 0.472	 1.226 0.632	 0.613 – 2.448 0.251 – 1.596	 0.565 0.332
MMSE (points) 27-30 (Reference) 20-26 10-19 0-9	 1.322 1.260 0.260	 0.597 0.460 0.382	 3.752 3.526 1.297	 1.166 – 12.080 1.431 – 8.688 0.613 – 2.745	 0.027 0.006 0.496
GDS score	0.017	0.034	1.017	0.952 – 1.086	0.618
QoL-AD score	0.055	0.037	1.057	0.982 – 1.137	0.138
EQ-5D index	0.852	0.571	2.344	0.766 – 7.175	0.136
EQ VAS	- 0.003	0.009	0.700	0.979 – 1.014	0.700

MMSE: Mini-Mental Status Examination. GDS: Geriatric Depression Scale. QoL-AD: Quality of Life - Alzheimer's Disease. EQ-5D: EuroQol - 5 Dimensions. EQ VAS: EuroQol Visual Analogue Scale. Hosmer-Lemeshow-test: p = 0.260. Nagelkerkes R^2 .176.

Conclusion

The use of ADDs in the study population was low and partly inappropriate, whereas only the MMSE was used for the clinical evaluation of the patients' dementia severity. Especially, reasons for a significant lower prescription of ADDs among institutionalized patients should be further evaluated. The treatment with ADDs can be restricted by medical reasons (contraindications, interactions, adverse events, etc.), the patients' adherence to the medication, and an insufficient implementation of guideline recommendations in the healthcare institutions (including general practitioners, neurologists, psychiatrists). However, attending physicians, dementia patients and their caregivers should be educated about benefits and risks of a treatment with ADDs. Additionally, a higher use of ADDs among privately insured patients potentially hints at an economic/budgetary impact on the decision to prescribe ADDs. Due to the regionally restricted design, the sample size, and the consecutive recruitment, our study does not allow for a representative conclusion regarding the prescription prevalence of ADDs in Germany.

Bohlken J et al. Pharmacotherapy of dementia in Germany: Results from a nationwide claims database. *Eur Neuropsychopharmacol* 2015; 25(12): 2333-2338
Wuebbeler M et al. Antidementia drug treatment in dementia networks in Germany: use rates and factors associated with treatment use. *BMC Health Serv Res* 2015; 15: 205
Wucherer D et al. Antidementia drug treatment in people screened positive for dementia in primary care. *J Alzheimers Dis* 2015; 44(3): 1015-1021
Van den Bussche H et al. Antidementia drug prescription sources and patterns after the diagnosis of dementia in Germany: results of a claims data-based 1-year follow-up. *Int Clin Psychopharmacol* 2011; 26(4): 225-231.

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