The use of benzodiazepines in the REMIND cohort: a cross- sectional study in elderly people with cognitive complaints

*Giulia Grande[1], Simone Pomati[1], Irene Tramacere[2], Claudio Mariani[1], Graziella Filippini[3] and the REMIND Study Group (**RE**te **M**ilanese **IN**tegrata per le **D**emenze)*

[1] Center for Research and Treatment on Cognitive Dysfunctions, Institute of Clinical Neurology, Department of Clinical Sciences, "Luigi Sacco" Hospital, University of Milan, Milan, Italy
[2] Unit of Neuroepidemiology, I.R.C.C.S. Foundation, Carlo Besta Neurological Institute, Milan
[3] Scientific Direction, I.R.C.C.S. Foundation, Carlo Besta Neurological Institute, Milan.

Background and aim:

Evidence are not conclusive to impute to benzodiazepines (BDZ) a negative impact on cognition, mainly depending on the different setting and study design.

We aimed to evaluate the use of BDZ in the cohort of the REMIND study. The REMIND (REte Milanese Integrata per le Demenze) study was funded by the Ministry of Italian Health, approved by the Lombardy Region Health Office[1] and operationalized by the Milan Health Authority[2] *(Percorso Preventivo- Diagnostico-Terapeutico- Assistenziale- Riabilitativo, PDTAR, per la popolazione e i pazienti con demenza ASL Milano, 2011).* The REMIND study is a 3-year pragmatic population-based prospective cohort study in Milan which aims to implement an Integrated Care Pathway (ICP) for people with dementia.

Materials and methods:

From April 2013 to March 2014, 4249 subjects with first cognitive complaints were evaluated by 353 General Practitioners (GPs). The GPs collected several socio-demographic and clinical data at baseline and they administered the Mini Mental State Examination (MMSE) to the participants. All 353 GPs underwent a strict training for the correct performance of the MMSE, in order to gain the highest level of reliability of the score.

Drug history was collected and the BDZ score was created (BDZ=0, receiving no BDZ drugs; BDZ= 1, receiving at least one BDZ drug).

The outcome of the present study was the cognitive impairment intended as scoring less than 24 at the MMSE (raw score).

Results:

Out of 4249 subjects, 782 (18.4%) received at least one BDZ drug.

As shown in table 1, subjects with BDZ score=1 were older (78.2 ± 7.6 vs. 76.7 ± 8.3; p<0.001) and were more frequently female (81.2% vs. 18.8%; p<0.001). No statistically significant differences were observed for what concern education and MMSE score.

Table 2 shows that subjects taking BDZ drugs did not have a statistically significant higher risk to be cognitively impaired, as defined by scoring less than 24 at the MMSE (crude OR: 0.98; 95% CI 0.81-1.19).

To assess the association between cognitive impairment and the use of BDZ, a multivariate analysis was used in order to adjust for the covariates (table 3). In the multivariate analysis, no statistically significant differences were found between subjects who took BDZ drugs and the risk of cognitive impairment (OR= 0.90, 95% CI 0.73-1.11).

Table 1

Baseline characteristics of the whole sample of subjects and by BDZ score

	Tot = 4249	BDZ score = 0 N = 3467 (81.6)	BDZ score = 1 N = 782 (18.4)	P
Age				
45- 60 yrs, N (%)	165 (3.9)	143 (4.1)	22 (2.8)	
61- 70 yrs, N (%)	667 (15.7)	583 (16.8)	84 (10.7)	**< 0.001**
71- 80 yrs, N (%)	1859 (43.8)	1510 (43.6)	349 (44.6)	
> 80 yrs, N (%)	1558 (36.6)	1231 (35.5)	327 (41.9)	
Mean ± SD	77.0 ± 8.2	76.7 ± 8.3	78.2 ± 7.6	**< 0.001**
Gender				
Female, N (%)	2822 (66.4)	2187 (63.1)	635 (81.2)	**< 0.001**
Male, N (%)	1427 (33.6)	1280 (36.9)	147 (18.8)	
Education				
< 3 yrs, N (%)	69 (1.6)	55 (1.6)	14 (1.8)	
3- 5 yrs, N (%)	1339 (31.5)	1089 (31.4)	250 (32.0)	0.966
6- 8 yrs, N (%)	1177 (27.7)	957 (27.6)	220 (28.1)	
9- 13 yrs, N (%)	1177 (27.7)	967 (27.9)	210 (26.8)	
> 13 yrs, N (%)	487 (11.5)	399 (11.5)	88 (11.3)	
Mean ± SD	8.9 ± 4.2	8.9 ± 4.6	8.7 ± 4.1	0.455
MMSE score				
≥ 24, N (%)	3441 (80.9)	2806 (80.9)	635 (81.2)	0.454
< 24, N (%)	808 (19.1)	661 (19.1)	147 (18.8)	
Mean ± SD	26.1 ± 3.6	26.1 ± 3.6	26.2 ± 3.4	0.334

Table 2

Crude OR and 95% CI of scoring below 24 at the MMSE according to the BDZ score

	Crude OR	95% CI
BDZ score 0	1	
BDZ score 1	0.98	0.81 - 1.19

Table 3

OR and 95% CI of scoring below 24 at the MMSE in relation to the BDZ score adjusted for demographic variables

	OR	95% IC
Age		
45- 60 yrs	1	
61- 70 yrs	0.94	0.56- 1.57
71- 80 yrs	1.60	0.99- 2.57
> 80 yrs	1.82	1.13-2.93
Gender		
Male	1	
Female	2.59	2.13- 3.14
Edication		
< 3 yrs	1	
3- 5 yrs	0.80	0.42- 1.52
6-8 yrs	0.83	0.63- 1.10
9- 13 yrs	0.89	0.67- 1.18
> 13 yrs	0.93	0.71- 1.24
BDZ score		
Score = 0	1	
Score = 1	0.90	0.73- 1.11

Conclusion:

About one fifth of the population of the present study with first cognitive complaints received BDZ medication in the primary care setting. In the present study, we did not find any association between BDZ use and a worst performance in the MMSE score.

The conflicting results from various longitudinal studies suggest that further investigation are needed in order to better understand the role of BDZ use and the impairment in cognitive performance.

[1] Determinazione in merito all'organizzazione in rete e criteri di riconoscimento delle strutture dedicate alle demenze. Direzione Generale Sanità. Regione Lombardia. Decreto N. 9942 del 5/10/2009

[2] Percorso Preventivo- Diagnostico- Terapeutico- Assistenziale- Riabilitativo (PDTAR) per la popolazione e i pazienti con demenza ASL Milano, 2011.

http://intranet.asl.milano.it/_asl/Alzheimer/Default.htm

REte Milanese INtegrata per le Demenze

IN COLLABORAZIONE CON
ISTITUTO NEUROLOGICO CARLO BESTA
Regione Lombardia
ASL Milano
Ministero della Salute

Grants of the Italian Ministry of Health (RF-2010-2318922) and of the Milan HA (Clinical Governance 2013)