

POPULATION ATTRIBUTABLE RISK OF HIP FRACTURES IN ANTIDEPRESSANT USERS IN HUNGARY AND ESTIMATION OF THE RELEVANT COST CONSEQUENCES

Gábor Takács¹, László Horváth², Lajos Botz¹

¹Pécs University Medical School, Department of Pharmaceutics and Central Clinical Pharmacy, Pécs, Hungary

²University of Debrecen, Medical Centre, Central Pharmacy, Debrecen, Hungary

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BACKGROUND

The incidence of hip fracture is constantly growing worldwide. Pharmacoepidemiological studies have demonstrated an excess risk of hip fractures attributable to the use of antidepressants. In a recent systematic review and meta-analysis a pooled estimate of relative risk (RR) of hip fracture was 1.70 (95% CI, 1.47-1.98) for antidepressant users, compared to non-users¹. The excess risk associated with selective serotonin reuptake inhibitor (SSRI) use was higher than that for tricyclic antidepressant (TCA) use.

Although the potential mechanisms in the background of antidepressant use and related fracture risk are still unclear, several hypotheses have been reported. Antidepressants may affect bone metabolism by inhibiting the serotonin transporter. Some antidepressants may increase the propensity to fall, particularly in elder patients, possibly through their anticholinergic and cardiovascular adverse effects.

On average, there is 343 hip fractures/100000 inhabitants/year in Hungary.² The relevant social burden is enormous, as the quality of life and the mortality is severely affected.

¹D. Prieto-Alhambra et al: Excess risk of hip fractures attributable to the use of antidepressants in five European countries and the USA.

Osteoporos Int (2014) 25:847–855

²M. Péntek et al.: Epidemiology of osteoporosis related fractures in Hungary from the nationwide health insurance database, 1999-2003. Osteoporos Int, 2008. 19:243-249

PURPOSE

The potential impact of the use of antidepressants on the rate of hip fracture in Hungary have not been studied before. Our aim was to quantify the possible relationship between antidepressant consumption and the excess risk of hip fracture in Hungary, based on the results of published studies and national drug utilization data in 2012. The population attributable risk (PAR) of hip fracture associated with the use of antidepressants was evaluated. We also estimated the yearly cost of the operations after hip fractures related to antidepressant use.

MATERIALS AND METHODS

For most countries, the prevalence rate (Pe) of antidepressant use can only be estimated if Intercontinental Medical Statistics (IMS) and freely available public databases (Denmark, the Netherlands, Norway) are used for data extraction. Pe in Hungary can be estimated using the following formula:

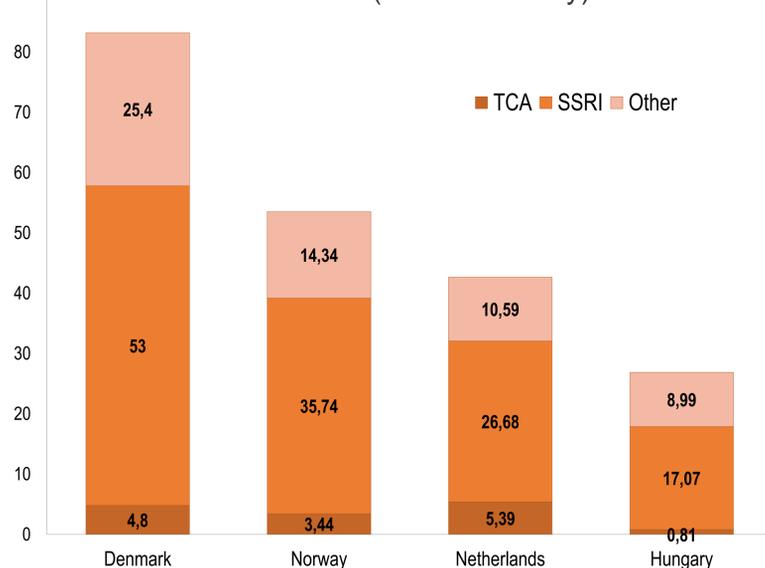
Estimated $Pe_{\text{Hungary}} = \left[\frac{\text{Antidepressants DDDs}/1000 \text{ persons/day}_{\text{Hungary}}}{\text{Antidepressants DDDs}/1000 \text{ persons/day}_{\text{Public databases}}} \right] \times Pe_{\text{Public databases}}$

Pe and the pooled RR from the systematic review of published studies¹ were combined with the following formula to calculate country-specific PAR%:

$PAR\% = \left[\frac{Pe(RR-1)}{1+Pe(RR-1)} \right] \times 100$.

Cost of the operations after hip fractures were estimated using national data.

COUNTRY-SPECIFIC ANTIDEPRESSANT USE IN 2012 (DDD/1000/day)



ESTIMATED PREVALENCE RATE OF ANTIDEPRESSANT USE (%) IN 2012

Category	Country	Prevalence Rate (%)
All antidepressants	Denmark	8.21
	Norway	6.21
	Netherlands	6.25
	Hungary	3.10
SSRI	Denmark	5.25
	Norway	3.73
	Netherlands	3.18
	Hungary	1.80
TCA	Denmark	1.06
	Norway	1.30
	Netherlands	1.55
	Hungary	0.23

ESTIMATED PAR OF ANTIDEPRESSANTS ON HIP FRACTURE RATES WITH 95% CONFIDENCE INTERVAL

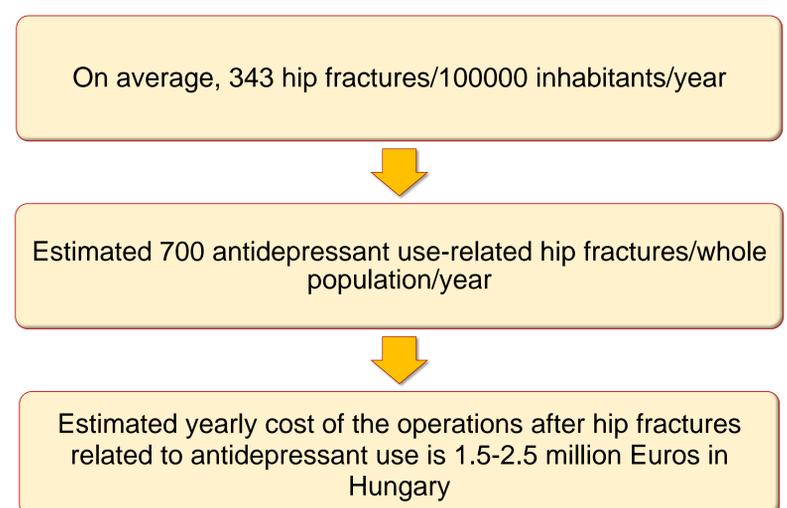
Country	PAR % All antidepressants	PAR % SSRI	PAR % TCA
Denmark	5.44% [3.72-7.45]	4.32% [2.56-6.44]	0.62% [0.34-0.98]
Norway	4.17% [2.84-5.74]	3.11% [1.83-4.66]	0.76% [0.41-1.19]
Netherlands	4.19% [2.86-5.77]	2.66% [1.56-4.00]	0.91% [0.49-1.42]
Hungary	2.12% [1.44-2.95]	1.52% [0.89-2.30]	0.14% [0.07-0.22]

SENSITIVITY ANALYSIS TO ESTIMATE THE IMPACT OF ANTIDEPRESSANT USE ON PAR IN THE ELDERLY

Denmark	Age>65
Number of users	146842
Total population	5580516
Rate of >65	17.3
Population >65	965429
Pe Age>65	0.15
Pe% Age>65	15.21
PAR%	9.62 [6.67-12.97]

Hungary	Age>65
Pe% Age>65 Denmark	15.21
Pe% overall Hungary	3.10
Pe% overall Denmark	8.22
Pe% estimated Hungary	5.74
Pe estimated Hungary	0.0574
PAR%	3.86 [2.63-5.32]

ESTIMATED COST CONSEQUENCES (HUNGARY)



CONCLUSION

We revealed a wide heterogeneity in the consumption of antidepressants among the four countries. PAR is a useful tool to express the attributable impact of antidepressant use on the rate of hip fractures at a population level. Our findings suggest that the potential contribution of antidepressant use to the population rate of hip fractures is 2.12% in Hungary. This attributable risk is higher for SSRIs. Limitations of our study are the extrapolation of the number of antidepressant users from Hungarian drug consumption data and other European prevalence rates. Furthermore, the pooled RR in the systematic review was calculated from observational studies.