

Time Trends in Prescribing Habits of Anxiolytics and Antidepressants in Slovenian Family Practices (with Emphasis on Elderly Patients)

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ABSTRACT

The aim of the study was to investigate prescription of anxiolytics and antidepressants among Slovenian family physicians regarding drug class with an emphasis on the elderly population and possible time-trends. Exploratory survey and register-based analysis of anxiolytic and antidepressant prescriptions of one hundred family physicians in Slovenia was performed in 2005 and 2008. Drugs included in the study were classified according to the Anatomical-Therapeutic-Chemical (ATC) drug classification system, and ATC data were used to calculate defined daily doses (DDD) per 1,000 practice population per day. The most often prescribed anxiolytics and antidepressants were identified and anxiolytic/antidepressant ratio was estimation by patient age-group for the two studied years. Benzodiazepines showed highest share in the overall utilization of psychotropic drugs. The ratio between short- and long-acting benzodiazepines decreased by about one tenth during the observed period. Long-acting benzodiazepines were prescribed more often to the older patients. The decrease in anxiolytic/antidepressant ratio from 2005 to 2008 was the smallest in the elderly population. Further research is needed to ascertain the prescribers' attitudes in order to devise strategies to further improve prescribing performance in elderly patients.

Key words: family physicians, drug prescriptions, anxiolytics, antidepressants, ATC/DDD methodology, elderly, Slovenia

Introduction

In Slovenia, about one third of patients in general practice suffer from mental disorder and receive psychotropic drug prescription¹. A large majority of mental health consultations is for elderly patients². The most prevalent mental disorders in this group of patients are depression and anxiety. The estimated prevalence of depression in the elderly visiting family physicians is 15%. This proportion is even larger in the elderly with somatic diseases³. The elderly population with somatic and mental health needs is cared for in the primary care settings with the possibility of referral to the secondary level. Due to severe shortage of psychiatrists working in gerontopsychiatry in Slovenia, these referrals are very rare. If

they nevertheless happen, the patients are subsequently re-allocated to primary care for further follow-up⁴.

Family physicians, being the exclusive primary treatment providers in Slovenia, are allowed to prescribe almost every psychotropic drug. They often prescribe antidepressants and anxiolytics; among the latter, they mainly prescribe benzodiazepines⁵. Therapeutic indications for benzodiazepines include treatment of insomnia, generalized anxiety disorder, panic disorder, and social phobia. They are used for acute agitation and as supplementary treatment for mania. Further uses include skeletal muscle relaxation and adjunctive treatment for seizure disorder.

ders. Generally, benzodiazepines are indicated for acute symptom relief and have considerable potential efficacy when used in this manner⁶. Problems associated with benzodiazepine use include daytime sedation and consecutively increased risk for motor vehicle accidents, falls and hip fractures⁷. Longer-term benzodiazepine use induces physical and psychological addiction, withdrawal symptoms when discontinuing the treatment and cognitive impairment⁸. It is generally recognized that long-acting benzodiazepines are less safe than short-acting agents, since they increase risk of daytime psychomotor impairment and sedation⁹. The drug use patterns with regard to patients' age and gender in Slovenia are consistent with findings from other countries^{5,10–12}. Benzodiazepines are more often prescribed to the older, female and less educated patients, and the user rates for both genders increase with patients' age. This population is prone to fractures due to osteoporosis, often suffer severe and multifaceted problems, receive multiple drugs, and is less aware of the potential side-effects of the drugs⁵.

Moreover, benzodiazepines can erroneously be used to treat symptoms of depression rather than depression itself, because anxiety commonly coexists with depression in older people¹³. There is growing awareness about the therapeutic effect of the new generation of antidepressants for these complex disorders¹⁴. In spite of lack of addiction problem, new generation of antidepressants (e.g. selective serotonin reuptake inhibitors, SSRIs, and serotonin-norepinephrine reuptake inhibitors, SNRIs) show other drug-related problems, such as sexual dysfunction, risk of bleeding, hyponatremia, discontinuation symptoms, increased body weight and increased risk of diabetes mellitus¹⁵. Guidelines defining the appropriate use of benzodiazepines in the elderly recommend that prescriptions be intermittent, brief, and limited to the acute treatments during the first several weeks. It has been a clinical routine to treat depression first and then taper off the benzodiazepine while antidepressive treatment is continued¹⁶. Despite the concerns, benzodiazepine use in older adults remains high, with a prevalence of 10% to 12% in older adults residing in the community¹⁷, and likely reflects unnecessary or suboptimal treatment¹⁸.

The anxiolytic/antidepressant ratio is one of the indicators of quality of prescribing, whereby antidepressants as etiological therapy should prevail¹⁹. In 2003, the ratio of anxiolytics/antidepressants was 2.1 for Slovenia¹⁹, 0.3 for Sweden, 0.5 for Norway, 0.7 for Denmark and 4.66 for Croatia²⁰. Appropriate anxiolytic/antidepressant ratio is yet to be defined. There may be a threshold for reduction of benzodiazepine utilization beyond which a further decrease may be difficult unless additional alternative treatments are successfully implemented²¹.

Even though Slovenia is a country with one of the highest suicide rates in elderly population²², no study has been conducted regarding prescribing of benzodiazepines in the elderly patient population. Recent research only estimated annual benzodiazepine consumption in a general population²³. Therefore, the objectives of this study were to estimate the prescription of different types of

anxiolytics and antidepressants among Slovenian family physicians, to compare the utilization of anxiolytics and antidepressants according to age of the patient population using the World Health Organization Anatomical-Therapeutic-Chemical classification system (ATC)/Defined Daily Doses (DDD) methodology, to examine changes between 2005 and 2008, and to propose appropriate interventions on the basis of the obtained results.

Materials and Methods

Physician sampling and surveying

Data were obtained from the national database of all prescriptions, which is maintained by the Slovenian Institute of Public Health (SIPH). A representative sample of 160 family physicians was selected by means of stratified random sampling. The sample was well-matched to the total population in terms of regional representation, age distribution, gender ratio and percentage of public and private practitioners. The study did not include physicians who worked part time, who were absent from work for over 3 months during the studied year, and/or those who were retired or worked at emergency departments. In order to ensure the physicians' collaboration, a letter explaining the aims and procedures of the survey was attached. A coding system was used to facilitate follow-up with two reminders in order to increase response rate while keeping the family physician's identity confidential. The positive response was obtained by 100 family physicians, yielding a 62.5% response rate. Further analyses were performed on the respondent sample because the non-respondents did not consent to the use of their data from the SIPH prescription database.

Prescribing data

From the national database, data on the prescribed medications were obtained for the year 2005 and 2008. In total, 121,638 prescriptions for anxiolytic and antidepressant drugs were analysed: 52,935 from 2005 and 68,703 from 2008. Data on the size and number of packages were obtained for each individual drug. Drugs were coded according to the ATC classification system.

Data analysis

The number of DDD, and DDD per 1000 practice population per day (DDD/1000/day) were calculated for anxiolytics and antidepressants using ATC indexes for 2005 and 2008. The required population data were obtained as publicly available from the Statistical Office of the Republic of Slovenia (<http://www.stat.si>). The anxiolytics/antidepressants ratio was calculated as the ratio of the estimated standardised prescribing amount in DDD per 1000 practice population per day between anxiolytics and antidepressants, and used as a criterion of prescribing quality¹⁹. Descriptive comparisons of the calculated quantities regarding age and gender of the patient population were performed within and between the two studied years.

Results

Prescription data for the whole patient population for individual drugs are presented in Table 1. In both observed years, short-acting alprazolam was the most often prescribed benzodiazepine (6.5 and 5.8 DDD per 1000 practice population per day in 2005 and 2008, respectively), followed by bromazepam (intermediate-acting; 4.4 and 3.7 DDD/1000/day), diazepam (long-acting; 4.3 and 3.4 DDD/1000/day) and lorazepam (intermediate-acting; 3.4 and 3.2 DDD/1000/day in 2005 and 2008, respectively), while the other three anxiolytics were prescribed rarely. Among antidepressants, SSRIs were clearly dominant, with sertraline being the most often prescribed in both studied years (5.8 and 8.2 DDD/1000/day in 2005 and 2008, respectively).

The ratio between short- and long-acting benzodiazepines in 2005 and 2008 is presented in Table 2. For the purpose of this comparison, intermediate-acting benzo-

TABLE 2
ESTIMATED STANDARDISED PRESCRIBING AMOUNT OF SHORT- AND LONG-ACTING BENZODIAZEPINES FOR THE WHOLE PATIENT POPULATION

Benzodiazepine type	DDD/1000/day	
	2005	2008
Short-acting	13.22	14.98
Long-acting	3.80	4.74
Ratio (short- vs. long-acting)	3.48	3.16
Ratio relative to 2005	100%	90.8%

DDD/1000/day – defined daily dose *per* 1,000 practice population *per* day

diazepines were included in the short-acting group. Short-acting BZD were used more often (13.2 and 15.0 DDD/1000/day in 2005 and 2008, respectively). The ratio decreased from 2005 to 2008 by about one tenth.

TABLE 1
ESTIMATED STANDARDISED PRESCRIBING AMOUNT OF INDIVIDUAL DRUGS (SORTED BY DECREASING AMOUNT WITHIN DRUG CLASS) FOR THE WHOLE PATIENT POPULATION

Drug class	Drug	ATC	2005		2008	
			DDD/1000/day	Rank	DDD/1000/day	Rank
Anxiolytics	Alprazolam (short-acting)	N05BA12	6.51	1	5.82	1
	Bromazepam (intermediate-acting)	N05BA08	4.41	2	3.73	2
	Diazepam (long-acting)	N05BA01	4.28	3	3.39	3
	Lorazepam (intermediate-acting)	N05BA06	3.40	4	3.18	4
	Oxazepam (intermediate-acting)	N05BA04	0.66	5	0.49	5
	Medazepam (long-acting)	N05BA03	0.32	6	0.25	6
	Clobazam (long-acting)	N05BA09	0.13	7	0.16	7
	Sertraline (SSRI)	N06AB06	5.84	1	8.23	2
	Escitalopram (SSRI)	N06AB10	4.45	2	8.40	1
	Citalopram (SSRI)	N06AB04	2.99	3	2.76	4
	Paroxetine (SSRI)	N06AB05	2.69	4	4.47	3
	Fluoxetine (SSRI)	N06AB03	1.58	5	1.24	5
	Tianeptine (SSRE)	N06AX14	0.68	6	0.99	7
	Venlafaxine (SNRI)	N06AX16	0.63	7	1.14	6
Antidepressants	Amitriptyline (TCA)	N06AA09	0.61	8	0.59	10
	Moclobemide (MAOI)	N06AG02	0.43	9	0.24	11
	Maprotiline (TeCa)	N06AA21	0.33	10	0.22	12
	Mirtazapine (TeCA)	N06AX11	0.24	11	0.73	9
	Mianserin (TeCA)	N06AX03	0.08	12	0.08	13
	Clomipramine (TCA)	N06AA04	0.05	13	0.05	14
	Reboxetine (NRI)	N06AX18	0.04	14	0.02	16
	Doxepin (TCA)	N06AA12	0.04	15	0.02	15
	Fluvoxamine (SSRI)	N06AB08	0.02	16		18
	Duloxetine (SNRI)	N06AX21	0.01	17	0.79	8
	Herbion Hypericum	N06AW01		18	0.00	17

DDD/1000/day – defined daily dose *per* 1,000 practice population *per* day; SSRI – selective serotonin reuptake inhibitors; SSRE – selective serotonin reuptake enhancers; SNRI – serotonin norepinephrine reuptake inhibitor; NRI – norepinephrine reuptake inhibitor; TCA – tricyclic antidepressants; TeCA – tetracyclic antidepressants

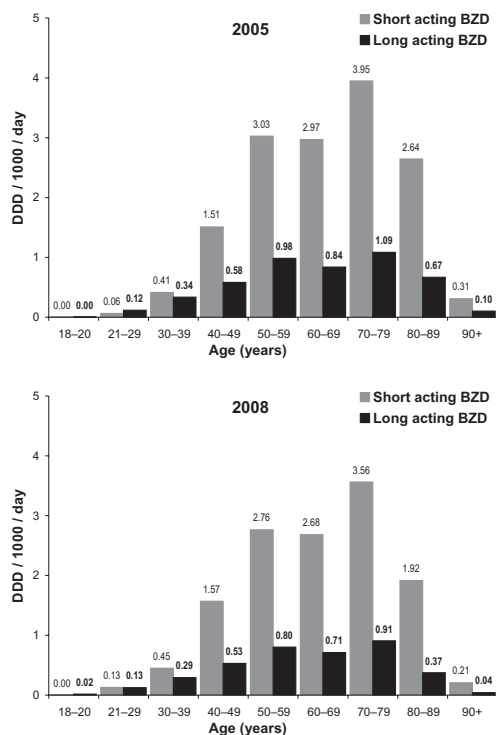


Fig. 1. Estimated distribution of standardised prescribing (in DDD/1000/day – defined daily dose per 1,000 practice population per day) of short- and long-acting benzodiazepines (BZD) across age groups in 2005 and 2008.

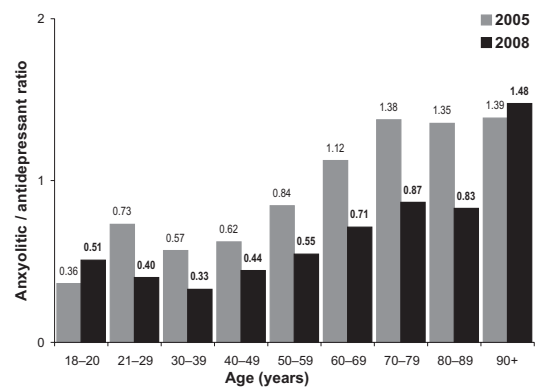


Fig. 3. Distribution of anxiolytic/antidepressant ratio across age groups in 2005 in 2008.

The distribution of short- and long-acting benzodiazepines among age groups is presented in Figure 1 (like in Table 2, intermediate-acting benzodiazepines are included in the short-acting group). Long-acting benzodiazepines were prescribed more often to patients aged 50 years or more than to the younger ones, with particularly pronounced prescribing in the 70–79 years category (1.1 and 0.9 DDD/1000/day in 2005 and 2008, respectively).

The use of different antidepressant drugs in different age groups is presented in Figure 2. SSRIs were prescribed to the large majority of the patients (note the base-2 logarithmic horizontal axis used as a consequence). There was little difference between the age groups, i.e., the distribution of each antidepressant type across age groups was similar to the combined distribution across age groups.

Figure 3 shows the anxiolytic/antidepressant ratio in different age groups. In general, the ratio increases with age, which is probably attributable to comorbidity and case-mix of diagnoses that leads to higher use of benzodiazepines with growing patient age. It decreased over the observed time-period in all age groups (by about one third, more precisely ranging from 28% to 45%) except in the youngest (aged 18–20) and the oldest patients (aged 90+), where it increased (by 40% and 6%, respectively). However, due to the very small numbers of patients in the two extreme age groups, this finding is less reliable and hence less worrying.

Discussion

This study was conducted to obtain better knowledge about prescribing patterns of anxiolytics and antidepressants in Slovenia, especially in the elderly patient population. It has previously been established that the amount of prescribed anxiolytics in Slovenia, whether estimated in absolute terms or as DDD per 1000 practice population per day, decreased by about 14%, and the amount of prescribed antidepressants increased by about 45% during the observed 4-year period, leading to the anxiolytic/antidepressant ratio reduction from almost 1 to about 0.5²⁴. This reduction of anxiolytic/antidepressant

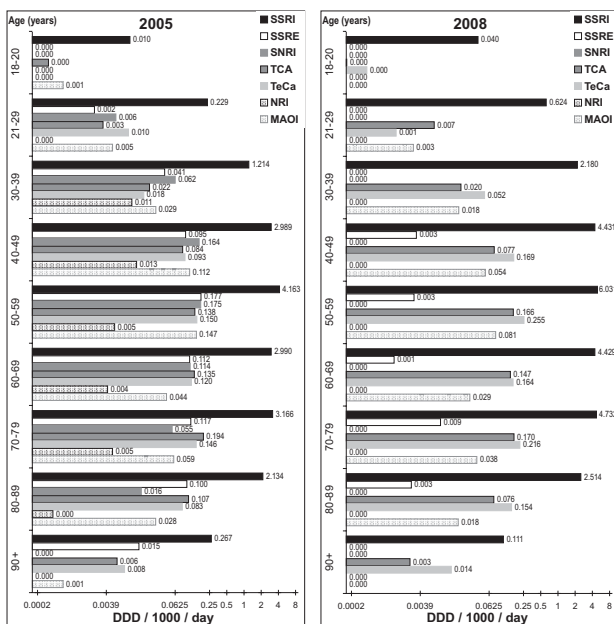


Fig. 2. Estimated standardised prescribing (in DDD/1000/day – defined daily dose per 1,000 practice population per day) of different antidepressant drugs by age group in 2005 in 2008 (SSRI – selective serotonin reuptake inhibitors; SSRE – selective serotonin reuptake enhancers; SNRI – serotonin norepinephrine reuptake inhibitor; NRI – norepinephrine reuptake inhibitor; TCA – tricyclic antidepressants; TeCa – tetracyclic antidepressants).

sant ratio indicates significant improvement in prescribing practice of Slovenian family physicians.

However, in both observed years, benzodiazepines showed highest share in the overall utilisation of psychotropic drugs, with short-acting alprazolam being the most often prescribed anxiolytic. As new generation hypnotics, benzodiazepine related drugs are currently recommended to use in treatment of insomnia²⁵, so the consumption of these drugs in Slovenia is surprisingly low. Short-acting benzodiazepines are thus introduced as drugs of choice for sedation and anxiolysis in Slovene family practice. A similar trend of decreased prescribing of long-acting benzodiazepines has been observed in studies in Canada²¹, in Holland²⁶, and in Nova Scotia²⁷. In the group of antidepressants, SSRIs accounted for the highest share of utilisation and showed a rising trend in the observed period.

Increasing age is related to increased incidence of physical illness, mental deterioration or loss of functional independence. Depression and anxiety disorders are often difficult to diagnose because of the variety of clinical presentations and the common occurrence of comorbid medical or other psychiatric conditions²⁸. Discontinuation of anxiolytic treatment is also difficult for the elderly who were prescribed anxiolytics for long periods before the anxiolytic effects of new generation of antidepressants was known. Physicians in Slovenia and other countries have difficulties with refusing the prescription of an anxiolytic, especially if the patient had positive experiences with these drugs before^{24,29}.

Additional difficulty is posed by the high workload of Slovenian family physicians, which is higher than in many of their European colleagues³⁰, leaving the physicians little time for counselling, prevention and referral to psychiatric service, which obviously generates the need to discriminate among perspective and less-perspective (i.e., older) patients. This inevitably leads to reductions in counselling, support and treatment options in the latter group. Another problem is insufficient communication with psychiatrists and psychologists because of their low number and extremely uneven distribution. Namely, almost half of Slovenian psychiatrists work in the central region and the access to psychiatric facilities in remote regions, where a large part of the older population live, is difficult³¹. There is also the problem of stigma of mental disorders, which is even stronger for the old-age population. Old people with chronic anxiety and depression and/or addicted to benzodiazepines might not be seen as candidates for treatment of addiction disorders. Physicians tend to anticipate patients' reluctance to change medication and overcome withdrawal reactions, and report about history of failed attempts to abandon the drug, especially if the patient is old³². Hence, a number of approaches could be used to implement guidelines and reverse current trends in relation to anxiolytic prescribing among the elderly. Options include delivering a clearer message related to outcomes, communicating effectively using opinion leaders and other evidenced techniques, and enabling doctors and also patients to under-

stand the true relative advantages, disadvantages, and consequences of using these drugs in this patient population⁸.

In all age groups, but particularly in the older age groups, far more women received anxiolytics than did men. This difference among recipients of anxiolytics possibly originates from the time of the initial prescription. Doctors frequently diagnose women with symptoms such as headache and general fatigue (not legitimate indications for anxiolytics) as suffering from anxiety, stress or insomnia (which are legitimate indications) and thus as candidates for anxiolytic treatment, thus more women than men are initially prescribed anxiolytics for conditions other than anxiety, stress or insomnia. However, information on patient diagnosis or on severity of symptoms would be needed to determine whether the present results reflect gender differences in medical care needs, overprescription of psychotropic drugs to females or underprescription of psychotropic drugs to males³³.

Most Slovenian family physicians are aware of prescription guidelines and recommendations (i.e., that anxiolytics are appropriate only for short-term treatment of anxiety disorders and introduction of psychopharmacological treatment in depression), but they have difficulties in refusing the prescription of anxiolytics, especially if the patient had positive experiences with these drugs²⁴. Different methods like education, feedback of quality-of-use review, and physician prescribing reminders are available to facilitate a change to more rational prescribing of benzodiazepines in elderly patients in primary care. In addition, further research is needed to investigate the prescribers' attitudes and actual prescribing, and examine how to change attitudes and behaviour to improve performance. Doctors need to be aware of and discuss these beliefs in the context of available evidence to make informed and collaborative decisions about their diagnostic and prescribing practices among older patient population, which usually require more time for diagnosis and treatment decisions³⁴.

The study showed that the total amount of prescribed antidepressant drugs notably increased during the observed time-period. The changes in antidepressant prescribing volumes are plausible because more elderly patients are on long-term medication and this group consumes the most drugs. Nevertheless, in order to better understand the rise in antidepressant prescribing, future research needs to focus on encouraging high-quality monitoring and regular review of medication³⁵. On a more general note, more clarity would be welcome over the effectiveness and appropriateness of using psychotropic drugs in the various illness, symptom and life-stress presentations seen in primary care.

Despite the obvious lack of detail on the patients' health status, evaluating a large database has its advantages. On a related note, there are other measures of good or appropriate prescribing, such as evaluating the duration of drug use, or the use of lower dosages in older people, but such questions could only have been answered through chart audits or direct patient surveys. Future studies could identify whether particular regions

or specific family physicians exhibit particularly poor prescribing habits, which could in turn lead to targeted education programs if further improvement is considered necessary beyond the current trends. We believe that the obtained data may be important for the improvement of health care and serve for evidence-based comparison of anxiolytic and antidepressant drug utilization tendencies in other countries.

Conclusions

Benzodiazepines showed highest share in the overall utilization of anxiolytics and antidepressants. The decrease in anxiolytic/antidepressant ratio from 2005 to 2008 was the smallest in the elderly population. The ratio between short- and long-acting benzodiazepines de-

creased by about one tenth during the observed period. Long-acting benzodiazepines were prescribed more often to the older patients, however their use decreased in the observed period. Further research is needed to ascertain the prescribers' attitudes in order to devise strategies to further improve prescribing performance in elderly patients.

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VREMENSKI TRENDovi NAVIKA PROPISIVANJA ANKSIOLITIKA I ANTIDEPRESIVA U SLOVENSKIM ORDINACIJAMA OBITELJSKE MEDICINE (S NAGLASKOM NA STARIJIM BOLESNICIMA)

S A Ž E T A K

Cilj studije bio je istražiti propisivanje anksiolitika i antidepresiva među slovenskim obiteljskim liječnicima u pogledu vrste lijeka s naglaskom na starijoj populaciji i mogućim vremenskim trendovima. Anketno istraživanje i analiza na temelju registra provedeni su za recepte za antidepresive i anksiolitike između sto obiteljskih liječnika u Sloveniji u 2005. i 2008. godini. Lijekovi uključeni u studiju bili su klasificirani prema anatomsko-terapijsko-kemijskom sustavu klasifikacije lijekova (ATC), a ATC podaci korišteni su za izračun definiranih dnevnih doza (DDD) na 1,000 stanovnika prakse po danu. Identificirani su najčešće propisani anksiolitici i antidepresivi i procijenjen je omjer anksiolitika i antidepresiva po dobnim skupinama pacijenata za obje proučavane godine. Najveći udio u ukupnom korištenju psihotropnih lijekova pokazali su benzodiazepini. Omjer kratko- i dugodjelujućih benzodiazepina smanjio se za oko jednu desetinu u promatranom razdoblju. Dugodjelujući benzodiazepini su propisani češće u starijih pacijenata. Smanjenje omjera anksiolitika i antidepresiva od 2005. do 2008. godine bilo je najmanje u starijoj populaciji. Potrebna su daljnja istraživanja kako bi se utvrdili stavovi liječnika i smislile strategije za dodatno poboljšanje propisivanja u starijih bolesnika.