



Benzodiazepines Consumptions - - Influence on Traffic Accidents

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SUMMARY

Introduction: Benzodiazepines belong to the group of anxiolytic sedatives and the most prescribed drugs in the world. Since these drugs have a potential for rapid anxiolytic effect and sedation, as well as driver capability impairment, there is a lack data of safety of benzodiazepines in traffic accidents.

The aim: To make an assessment of the interconnection of time series of traffic accidents outcomes with time series of benzodiazepine anxiolytic consumption in the Republic of Serbia.

Methods: This paper is a part of IV phase academic study regarding the factors potentially affecting benzodiazepine consumption and effects. We conducted a pharmaco-epidemiological time series analysis study of monthly sold benzodiazepine anxiolytics in pharmacies and indicators of the crush road outcome on a monthly basis in the Republic of Serbia. The research was performed from January 2014 to December 2018.

Results: Applying ARIMAX modeling we found a significantly link between DID of alprazolam with monthly total traffic accident, a high stochastic regression positive association of DID of diazepam with the dependent variable monthly total traffic accident, the prediction of monthly fatalities of traffic accident or traffic accident with severe or slight injuries per total traffic accident we have demonstrated positive influence of DID of alprazolam in second-order autoregressive and moving average model with constant. In prediction of monthly fatalities traffic accident, a significant positive influence of DID of benzodiazepines (all together) in auto-regression model without constant was demonstrated.

Conclusion: Consumption of both long-acting (over 12 h) and short-acting benzodiazepines together with all other causes highly determined the total number of traffic accidents on a monthly basis in 2014-2018 in the Republic of Serbia.

An assessment of the interconnection of time series of traffic accidents outcomes with time series of benzodiazepine anxiolytic consumption in the Republic of Serbia we found a significant positive influence of DID of benzodiazepines on traffic accidents outcomes. In total, all used benzodiazepines increase the number of fatal traffic accidents by 8.5 fold per month.

Alprazolam additionally contributed with about ten percent (9.7%) to the frequency of traffic accidents on a monthly basis.

Measures to prevent traffic accidents at all levels should be effective immediately in order to achieve positive results timely. The authors suggest that the great responsibility is rais-

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ing awareness of compliance with traffic regulations with doctors who prescribe benzodiazepines.

Keywords: Benzodiazepines, Consumptions, Traffic, Accidents

INTRODUCTION

Benzodiazepines belong to the group of anxiolytic sedatives and the most prescribed drugs in the world [1, 2].

Research and monitoring of benzodiazepine consumption / use is usually done in relation to the economic parameters that determine the stability and efficiency of the health system of countries. An academic investigator initiated, pharmaco-epidemiological difference-in-difference time series analysis of population exposure to benzodiazepines between the three, geographically close Balkans countries (Slovenia, Serbia, Croatia) with varying degrees of socioeconomic development has been carried out annually, during the study period from January 2014 to December 2018, compared to Slovenia, Serbia and Croatia had higher DIDs, from 5 fold (Croatia) to 6 fold (Serbia), for all benzodiazepines in total [2]. In mentioned study authors gave critical analysis for liberal prescribing policy of benzodiazepines in the Republic of Serbia, which resulted in both enormous consumption of benzodiazepines and a positive trend of growth of their consumption during this period [2].

Since these drugs have a potential for rapid anxiolytic effect and sedation, as well as driver capability impairment, there is a lack data of safety of benzodiazepines in traffic accidents [3].

AIM

To make an assessment of the interconnection of time series of traffic accidents outcomes with time series of benzodiazepine anxiolytic consumption in the Republic of Serbia.

MATERIAL AND METHODS

This paper is a part of IV phase academic study regarding the factors potentially affecting benzodiazepine consumption and effects. We conducted a pharmaco-epidemiological time series analysis study of monthly sold benzodiazepine anxiolytics in pharmacies

and indicators of the crush road outcome on a monthly basis in the Republic of Serbia. The research was performed from January 2014 to December 2018. Data on sold anxiolytics were obtained from the IQIA Institute for Human Data Science [4] while data on traffic accidents outcomes were taken from the annual reports, publicly announced on the website of the National Agency for Traffic Safety of the Republic of Serbia [5,6,7,8,9]. Each country has its own way of monitoring consumption at the state level. The authors used the IQIA international database for further multicenter comparison [4].

Variables

On a monthly basis, data on sold anxiolytics included: the type of active ingredient, the amount of active ingredient, unit (packs/bottles), the number of pharmaceutical forms per pack unit. Publicly available data on the population of the Republic of Serbia were taken from the Statistical Office of the Republic of Serbia. Consumption of all medicines by their generic ingredients is transposed as a defined daily dose per 1000 inhabitants per day (DID) according to the following formula:

$$DID = (U \times PF \times Q \times 1000) / (DDD \times \text{inhabitants} \times \text{number of days in each month})$$

where are U – units (packs / bottles), PF – number of pharmaceutical forms per unit, Q – amount of active ingredient in each pharmaceutical form. DID is used to measure the daily exposure of the population to a particular drug.

At the monthly level, the following variables regarding traffic accident indicators have been analyzed: the total traffic accident (fatalities, severe or slight injuries or material damage), fatalities traffic accident, traffic accident with severe or slight injuries and fatalities traffic accident or traffic accident with severe or slight injuries.

Statistical methods

The data for continuous variables are described by the arithmetic mean as a measure of the central tendency and standard deviation as a measure of variation of the data set.

For a review of trends and autocorrelation of variables over time, we analyzed time series data using autoregressive integrated moving average modeling with explanatory variable (ARIMAX), employing the Boxe-Jenkins method that finds an adequate stochastic dependence of consecutive data. Itch of ARIMAX models were constructed to determine the significance of the impact of the benzodiazepines anxiolytics consumption on traffic accident indicators. According to the Boxe-Jenkins criteria, for each dependent variable the model fit was evaluated. It involves the following steps: (1) the first stationarity (a constant mean and variance) is checked (graphically – by visual assessment and testing with Augmented Dickey-Fuller method) and testing of the normality of the distribution of noise residuals in each individual model after identification of possible significant trends (outliers) and elimination of their influences on the observed time series, (2) the form of the model (p, d, q) with autocorrelation parameters (ACF) and partial autocorrelation (PACF) is identified, (3) further regression model parameters and their statistical significance is estimated, and (4) the most adequate model is chosen. Among the various models that have adequate fit, the model containing the smallest number of parameters („most parsimonious”) is chosen. In each individual model, presence of autocorrelation of the dependent time series, as well as the estimation and predictors multicollinearity was estimated using Ljung-Box Q(18). Additionally, with stationary R-squared and normalized BIC, the overall fit of itch of ARIMAX models is measured. The accepted level of significance was set at 0.05. The statistical analysis was conducted using IBM SPSS 20 (NY), while Augmented Dickey-Fuller critical values were calculated using the Real Statistics Resource Pack for Excel 2010/2013/2016/2019/2021/365.

RESULTS

Descriptive statistics for the consumption of benzodiazepine anxiolytics are presented in Table 1, while traffic accident indicators are

Variables	Year	Mean	SD
diazepam (total DID)	2014	19.14	2.35
	2015	22.08	4.08
	2016	23.16	4.70
	2017	31.29	15.90
	2018	22.80	9.24
prazepam (total DID)	2014	0.73	0.16
	2015	0.65	0.09
	2016	0.65	0.13
	2017	0.42	0.43
	2018	0.43	0.06
bromazepam (total DID)	2014	30.87	2.66
	2015	32.15	5.51
	2016	31.98	6.45
	2017	33.82	3.89
	2018	33.35	3.82
lorazepam (total DID)	2014	21.58	2.12
	2015	23.18	3.42
	2016	23.21	3.99
	2017	25.46	3.35
	2018	25.80	2.94
alprazolam (total DID)	2014	9.99	1.85
	2015	12.74	2.05
	2016	14.22	3.54
	2017	20.86	7.58
	2018	22.14	6.55
all benzodiazepines (total DID)	2014	82.31	6.75
	2015	90.82	10.17
	2016	93.22	16.04
	2017	111.85	28.56
	2018	104.54	17.44

Table 1. Descriptive statistics for the total DID of benzodiazepine anxiolytics, sold in pharmacies by years in Republic Serbia from January 2014 to December 2018. Adapted from Markovic SZ et al 2019. Table 1 [2]

DID - defined daily dose per 1000 inhabitants per day
SD - standard deviation

described in Table 2. All time series had a stationary trend with a constant, ie all obtained t values were less than Augmented Dickey-Fuller critical value = -3.477 for the critical level alpha = 0.05. Applying ARIMAX modeling we have constructed four non-seasonal stochastic ARIMAX models with very good characteristics of adequacy (Table 3). The construction of the mentioned models followed the identification of significant trends (outliers) and the elimination of their influences on the observed dependent variables (time series) – Table 4. In Model 1, a high stochastic regression positive association of DID of diazepam with the dependent variable monthly total traffic accident have been demonstrated. In first-order autoregressive (AR) model (Model 2 in Table 3), we

Table 2. Descriptive statistics for the traffic accident consequences by years in Republic Serbia (January 2014 - December 2018)

SD - standard deviation

Variables	Year	Mean/Monthly	SD	SUM
The total traffic accident (fatalities, severe or slight injuries or material damage)	2014	2917.75	274.27	35013
	2015	2847.58	321.51	34171
	2016	2997.58	309.66	35971
	2017	3039.75	340.62	36477
	2018	2984.58	215.88	35815
Traffic accidents fatalities	2014	39.67	8.15	476
	2015	45.67	11.02	548
	2016	45.92	9.04	551
	2017	43.75	9.81	525
	2018	40.75	10.54	489
Traffic accident with severe or slight injuries	2014	1047.33	154.92	12568
	2015	1092.25	195.31	13106
	2016	1154.17	188.56	13850
	2017	1185.92	201.65	14231
	2018	1144.50	129.16	13734
Traffic accidents fatalities because of or traffic accident with severe or slight injuries	2014	1087.00	160.19	13044
	2015	1137.92	203.17	13654
	2016	1200.08	194.95	14401
	2017	1229.67	210.01	14756
	2018	1185.25	136.83	14223

found a significantly link between DID of alprazolam with monthly total traffic accident. In the prediction of monthly fatalities of traffic accident or traffic accident with severe or slight injuries per total traffic accident (Model 3 in Table 3), we have demonstrated positive influence of DID of alprazolam in second-order autoregressive and MA (1) model – ARIMAX (2, 0, 1) with constant. In prediction of monthly fatalities traffic accident, a significant positive influence of DID of benzodiazepines (all together) in AR (2) model without constant was demonstrated (Model 4 in Table 3). All mentioned time series of dependent variables (January 2014 - December 2017) are shown in Figure 1.

DISCUSSION

We found that there was a highly significant non-seasonal positive correlation of total traffic accidents (fatal with or without injuries) depending on diazepam consumption (Table 3, Model 1), where it is seen that the total number of traffic accidents increases 5.9 fold depending on the total DID for diazepam on a monthly basis. This model is equivalent to a linear regression model with a constant, which

tells us that with the growth of DID for diazepam the total number of traffic accidents in Serbia in the observed period from January 2014 to December 2018 increased 5.9 fold. In Norway, a study assessing benzodiazepines in drivers suspected of driving under the influence of drugs reported only the percentage of samples that were positive for diazepam [10, 11]. The identified outliers in the mentioned, but also in other constructed ARIMAX models (Table 4) coincide with the previous intensification of driver control and vehicle correctness control in order to implement new regulations related to traffic safety, reduction of maximum speed in populated areas, tightening of penalties in case of exceeding speeding, violent driving or using a mobile phone while driving, etc.) [12].

In our previous studies, we showed that the monthly exposure of the population to long-acting benzodiazepines, including exposure to diazepam, increases with a decrease in the total number of hours of insolation per month in the Republic of Serbia in the same period. in such months, regardless of other causes, such as ice, reduced visibility on the roads, etc. [13]. In Model 2 (Table 3), we see that the total number of accidents monthly

Model 1 - ARIMAX (0,0,0) (0,0,0) model parameters in prediction of monthly total traffic accident								
Ljung-Box Q(18) = 12.198, p = 0.837 Stationary R-squared = 0.866, Normalized BIC = 10.029			Estimate	SE	t	P		
Constant			2781.008	48.476	57.369	0.000		
Total DID - diazepam			Lag 0	5.903	1.684	3.506	0.001	
Model 2 - ARIMAX (1,0,0) (0,0,0) model parameters in prediction of monthly total traffic accident								
Ljung-Box Q(18) = 21.437, p = 0.207 Stationary R-squared = 0.817, Normalized BIC = 10.252			Estimate	SE	t	P		
Constant			2849.896	68.738	45.460	0.000		
			AR	Lag 1	0.491	0.130	3.789	0.000
Total DID - alprazolam			Lag 0	9.525	3.320	2.869	0.006	
Model 3 - ARIMAX (2,0,1) (0,0,0) model parameters in prediction of monthly fatalities traffic accident or traffic accident with severe or slight injuries per the total traffic accident								
Ljung-Box Q(18) = 10.504, p = 0.787 Stationary R-squared = 0.887, Normalized BIC = 9.325			Estimate	SE	t	P		
Constant			(Natural log)	6.763	0.069	97.454	0.000	
Traffic accident fatalities or traffic accident with severe or slight injuries			AR	Lag 1	1.620	0.063	25.687	0.000
				Lag 2	-0.809	0.057	-14.107	0.000
			MA	Lag 1	0.983	0.108	9.087	0.000
Total DID - alprazolam			(Natural log)	Lag 0	0.097	0.27	3.643	0.001
Model 4 - ARIMAX (2,0,0) (0,0,0) model parameters in prediction of monthly fatalities traffic accident								
Ljung-Box Q(18) = 20.893, p = 0.183 Stationary R-squared = 0.790, Normalized BIC = 3.759			Estimate	SE	t	P		
Fatalities traffic accident			AR	Lag 1	0.784	0.099	7.889	0.000
				Lag 2	-0.274	0.099	-2.765	0.008
Total DID - all benzodiazepine (Natural log)			Lag 0	8.541	0.369	23.162	0.000	

Table 3. ARIMAX models parameters in prediction of total traffic accident and its consequences on monthly basis in the Republic of Serbia (January 2014 - December 2018)

DID - defined daily dose per 1000 inhabitants per day
SE - standard error
MA - moving average
AR - auto-regression
Lag - lag time

increases non-seasonally 9.5 times in proportion to the total DID for alprazolam. Model 2 is an AR (1) model with a constant, which tells us that there was a constant monthly number of accidents that occurred independently of the DID for alprazolam, just as it increased by about 0.5 (0.491) from month to month due to other causes related to road safety (quality and/or correctness of roads), weather conditions during road traffic, the correctness of vehicles, compliance with traffic regulations and other factors originating from the participants in traffic, etc.) [14]. In our study we found a significantly link between DID of alprazolam with monthly total traffic accident, with severe or slight injuries per total traffic accident. A placebo-controlled study conducted in the Netherlands showed that alprazolam significantly impairs the functioning and psychomotor performance of drivers, with the recommendation not to drive vehicles and other dangerous machines under the influence of alprazolam [15]. As a consequence general

physicians are urged to warn patients taking alprazolam not to drive a car or operate potentially dangerous machinery [14].

On the other hand, in meta-analyzes, it was estimated that all benzodiazepines administered in single or multiple doses, regardless of their elimination half-life and length of anxiolytic action, disrupt driver performance on the day they were administered [3]. In our study, we see high adequacy ratios in both models (insignificant Ljung-Box Q(18) statistic with Stationary R-squared greater than 0.8), suggesting that the consumption of both long-acting (over 12 h) and short-acting benzodiazepines along with to all other causes, highly determined the total number of traffic accidents on a monthly basis in the observed period in the Republic of Serbia.

When it comes to the monthly rate of fatal traffic accidents with severe or minor body injuries to the total number of traffic accidents, we see that it was best determined by non-seasonal ARIMAX Model 3 (Table 3),

Table 4. Identified and eliminated trends (outliers) in ARIMAX analysis of time series of road crush and its consequences on a monthly basis in the Republic of Serbia (January 2014 - December 2018)

	Month	Trend type	Estimate	SE	t	p
Model 1 - Outliers parameters in prediction of monthly total road crush	Jan 2014	Seasonal Additive	-398.186	55.328	-7.197	0.000
	Feb 2014	Seasonal Additive	-653.286	54.676	-11.948	0.000
	Mar 2014	Seasonal Additive	-200.862	55.397	-3.626	0.001
	Oct 2014	Seasonal Additive	348.401	55.216	6.310	0.000
	Dec 2014	Additive	429.299	118.790	3.614	0.001
Model 2 - Outliers parameters in prediction of monthly total road crush	Jul 2015	Level Shift	149.606	34.043	4.395	0.000
	Jan 2014	Seasonal Additive	-382.633	72.043	-5.311	0.000
	Feb 2014	Seasonal Additive	-553.861	62.456	-8.868	0.000
	Oct 2014	Seasonal Additive	327.672	55.926	5.859	0.000
Model 3 - Outliers parameters in predictions of monthly fatalities road crush or road crush with severe or slight injuries per the total road crush	Dec 2014	Additive	481.715	124.562	3.867	0.000
	Feb 2014	Seasonal Additive	-0.120	0.023	-5.320	0.000
	Oct 2014	Seasonal Additive	0.089	0.022	4.036	0.000
	Jan 2015	Innovational	-0.298	0.059	-5.024	0.000
	Apr 2016	Transient Decay factor	0.889	0.048	18.438	0.000
Model 4 - Outliers parameters in prediction of monthly fatalities road crush	Jan 2017	Innovational	-0.333	0.065	-5.085	0.000
	May 2018	Additive	0.184	0.050	3.660	0.001
	Oct 2014	Additive	23.371	3.714	6.292	0.000
	Jul 2015	Transient Decay factor	0.858	0.082	10.446	0.000
	Jul 2016	Innovational	25.373	4.959	5.117	0.000
	Oct 2017	Additive	14.199	3.734	3.802	0.000
	Aug 2018	Innovational	20.261	4.928	4.111	0.000

depending on the naturally logarithmically transformed value of total DID for alprazolam (Stationary R-squared = 0.887). It is observed that for all other causes of a monthly increase in the rate of fatal traffic accidents with severe or minor bodily injuries, the naturally logarithmically transformed total DID for alprazolam additionally contributed about ten (9.7) percent monthly (Table 3, Model 3). In a slightly less determined non-seasonal ARIMAX model (Table 3, Model 4) than the above, we showed that monthly fatal traffic accidents, naturally transformed total DID for all benzodiazepines additionally contribute 8.5 times. In an interesting study controlling cognitive and psychomotor abilities, a standardized driving test was performed 4 hours after dosing, cognitive and psychomotor tests were performed 2.5 and 5.5 hours after dosing and memory function was assessed 1 hour after administration. Contrary to expectations, the acute impairing effects of alprazolam XR 1mg on driving and psychomotor functions were generally less, as compared to its immediate-release equivalent, but still of sufficient magnitude to increase the risk of becoming involved in traffic accidents [15].

The last mentioned model (there is

no constant, but all other causes of fatal traffic accidents are expressed by a positive autoregressive coefficient with a latent delay time of one month and a negative autoregressive coefficient with a latent delay time of two months. Model 2 and Model 3 indicate that in the study period in the Republic of Serbia, especially tightened and strengthened preventive control measures with exclusion from traffic of drivers in all months in which in the previous month there was an increase in the rate of fatal accidents or traffic accidents with serious or minor injuries in relation to the total number of traffic accidents.

Also, similarly in the study period, only in the following month, there was increased intervention after the increase in the absolute number of fatal traffic accidents in the previous month. Such measures led to a reduction in the mentioned outcomes in the following month.

Since the growth of the population's exposure to benzodiazepines has shown a permanent monthly positive impact, both on the total number of traffic accidents and on the number of fatal traffic accidents, in order to reduce traffic accidents it is necessary to implement additional measures to control and

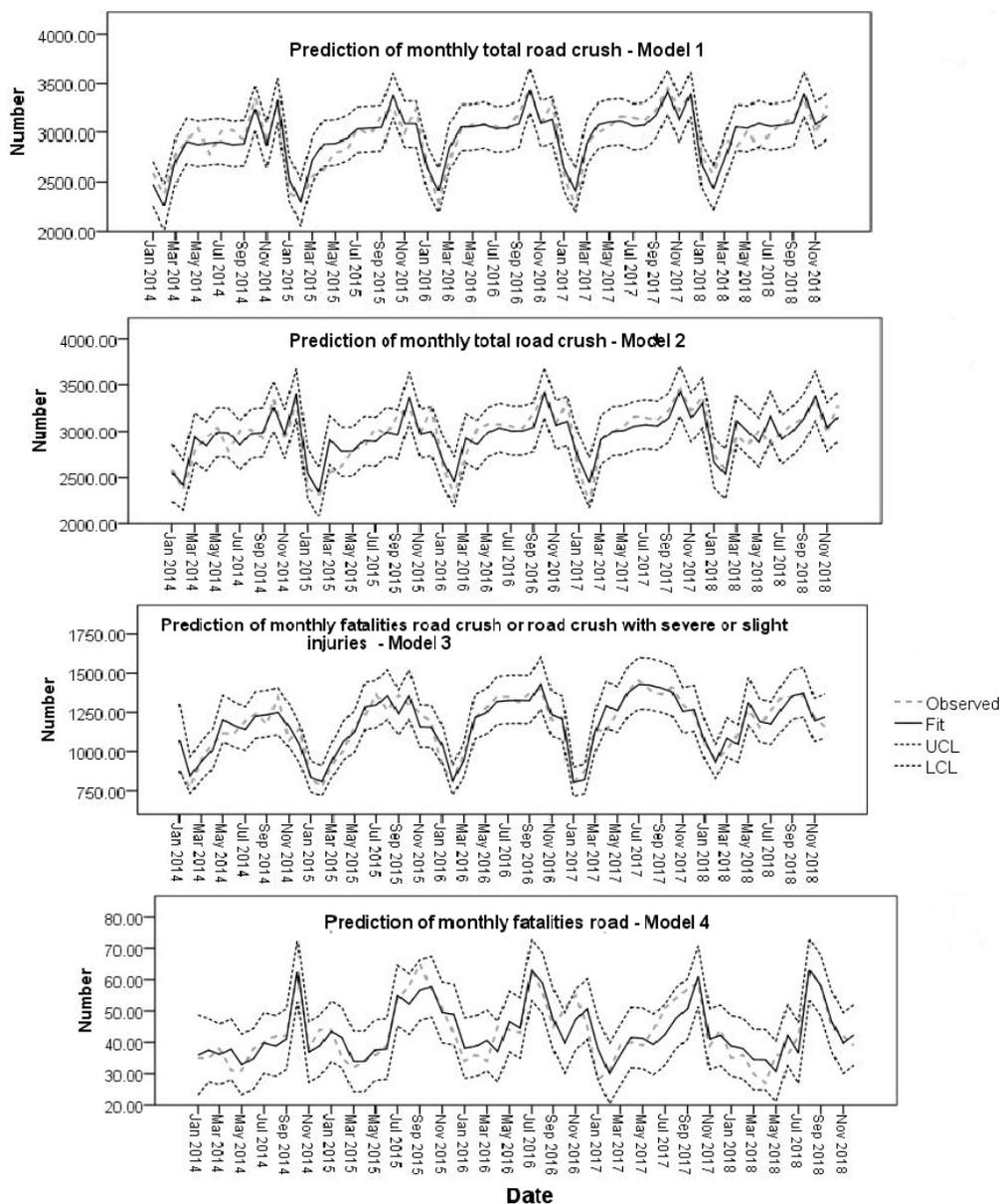


Figure 1. Time series of traffic accident consequences variables of on monthly basis in Republic Serbia (January 2014 - December) - observed, predicted, UCL and LCL 2018)

UCL - Upper Control Limit
LCL - Lower Control Limit

exclusions from traffic of all drivers consuming benzodiazepines permanently [14,16,17].

The implementation of such measures began in mid-2019, when in addition to controlling and excluding drivers due to alcohol consumption, control of the consumption of numerous psychoactive controlled substances, including benzodiazepines, also began. In order to avoid confusion and slowness due to the use of benzodiazepines, both by pedestrians and drivers, it is necessary to make the health system more practical with more mobile medical teams and call centers so that traffic participants can quickly solve their health problem. Clinicians should be aware of the increased risk of impaired driving with

specific populations and classes of medications when prescribing these agents, educate their patients, and/or consider safer alternatives [18, 19, 20]. We believe that frequent control of the concentration of psychoactive substances in the framework of routine traffic controls together with the media campaign would give good results [11].

On the other hand, in Serbia, based on recent research, in 2011, road crashes represented a total social cost of approximately EUR 640 million, equivalent to 2% of GDP [21]. Also, it is estimated that around 5% – 7% of fatal crashes were attributed to drink driving [22]. There are numerous published results of studies on the influence of antidepressants,

opiates, alcohol, psychoactive substances and various diseases on the number and outcome of traffic accidents [16, 17, 23, 19]. Benzodiazepines are considered „light psychoactive drugs” which do not produce much effect. However, this is not the case in practice. In a case-control study (Ravera et al 2011) it was estimated that there is a significant association between traffic accident risk and exposure to anxiolytics, concluding that these risks should be known to physicians who prescribe them, as well as patients who use these drugs [24]. Therefore, knowing the pharmacodynamics of this group of drugs, we try to rationalize the application through evidence-based medicine. In order to find an efficient model for rationalizing the use of benzodiazepines in Serbia, we estimated that the consumption of benzodiazepines increases with population economic poverty [2], but also with unfavorable climatic factors such as reduced isolation on a monthly basis [13].

Study limitations. The limitations of this study relate to the study design, as this is a time series study that cannot answer the question of whether a driver's anxiety condition in itself contributes to reduced traffic safety or whether the consumption of benzodiazepines is an independent contributing factor in causing accidents. Ravera et al 2011, showed that the use of other drugs that are the first line in the treatment of anxiety (SSRIs), even more than benzodiazepines significantly increase the risk of accidents [24]. In contrast, Verster et al 2005, found that driving a car is safe for drivers on buspirone, venflaxin or SSRIs therapy, while driving under the influence of benzodiazepines requires special caution [25]. Also, the study did not enable the analysis of the connection between the consumption of other psychoactive drugs (hypnotics, tranquilizers, antiepileptics) and road traffic accidents.

CONCLUSION

Consumption of both long-acting (over 12 h) and short-acting benzodiazepines together with all other causes highly determined the total number of traffic accidents on a monthly basis in the observed period in the Republic of Serbia.

An assessment of the interconnection of time series of traffic accidents outcomes with time series of benzodiazepine anxiolytic consumption in the Republic of Serbia found a

significant positive influence of DID of benzodiazepines on traffic accidents outcomes.

In total, all used benzodiazepines increase the number of fatal traffic accidents by 8.5 fold per month.

Alprazolam additionally contributed with about ten percent (9.7%) to the frequency of traffic accidents on a monthly basis.

Measures to prevent traffic accidents of all degrees should work immediately and now because it is impossible to achieve the timeliness of the applied measures and positive results. The authors suggest raising awareness of compliance with traffic regulations, with doctors who prescribe benzodiazepines also bearing a great responsibility for this cause.

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CONFLICT OF INTEREST

All authors declare no conflict of interest.

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Potrošnja benzodiazepina - uticaj na saobraćajne nesreće

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KRATAK SADRŽAJ

Uvod: Benzodijazepini pripadaju grupi anksiolitičkih sedativa koji su najčešće propisivani lekovi na svetu. S obzirom da, ovi lekovi daju brzi anksiolitički efekat i sedaciju, te uticaj na sposobnosti vozača, značajno je dopuniti postojeći nedostatak podataka o sigurnosti primene ovih lekova u odnosu na saobraćajne nesreće.

Cilj: Cilj rada bio je da se uradi procena povezanosti vremenskih serija ishoda saobraćajnih nezgoda sa vremenskim serijama potrošnje benzodiazepinskih anksiolitika u Republici Srbiji.

Metodologija: Ovaj rad je deo akademske studije IV faze koja se bavi analizom potrošnje benzodiazepina u odnosu na saobraćajne nesreće. Sproveli smo studiju odnosa između vremenskih serija na mesečnom nivou prodatih anksiolitika u zdravstvenom sistemu Republike Srbije i indikatora za broj i ishode saobraćajnih nesreća na mesečnom nivou u periodu januar 2014 - decembar 2018 u RS.

Rezultati: Primenom ARIMAKS modela, utvrdili smo značajnu vezu između DID alprazolama sa brojem saobraćajnih nesreća na mesečnom nivou, visoku stohastičku regresionu pozitivnu povezanost DID diazepama sa mesečnim ukupnim brojem saobraćajnih nesreća kao zavisnom varijablom; predviđanjem mesečnih poginulih u saobraćajnoj nezgodi ili saobraćajnoj nezgodi sa teškim ili lakšim povredama u odnosu na ukupan broj saobraćajnih nesreća pokazali smo pozitivan uticaj DID alprazolama. U predikciji ukupnog broja saobraćajnih nesreća sa fatalnim ishodom postoji značajan uticaj upotrebe svih benzodijazepina ukupno, dokazano autoregresionim modelom bez konstante.

Zaključak: Upotreba dugo- (preko 12 sati) i kratkodelujućih benzodiazepina sa svim ostalim mogućim razlozima, visoko determiniše ukupan broj saobraćajnih nesreća na mesečnom nivou u period od 2014 - 2018 u Republici Srbiji.

Primenom interkonekcije time series ishoda ozbiljnih saobraćajnih nesreća sa time series upotrebe benzodiazepinskih anksiolitika u RS pronašli smo značajan pozitivan uticaj DID benzodijazepina na ishode saobraćajnih nesreća. Ukupno, svi korišćeni benzodiazepini povećavaju broj fatalnih saobraćajnih nesreća na mesečnom nivou 8.5 puta.

Alprazolam je dodatno doprineo za oko deset posto (9.7%) učestalosti saobraćajnih nesreća na mesečnom nivou.

Mere prevencije od saobraćajnih nesreća na svim nivoima bi morale da stupe na snagu odmah i sad, kako bi se pozitivni rezultati postigli sto pre. Autori sugerišu podizanje svesti o poštovanju saobraćajnih propisa, u čijoj uspešnosti veliki značaj imaju i lekari koji ordiniraju benzodiazepine.

Ključne reči: benzodiazepini, potrošnja, saobraćaj, nesreće

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