



Consumption of antihistamines in Serbia in the period 2011–2015 and the correlation with adverse drug reaction reports

Potrošnja antihistaminika u Srbiji u periodu 2011–2015. i povezanost sa izveštajima o neželjenim reakcijama na lekove

To the Editor:

Considering the results of the study published by Poluzzi et al.¹, that also included the results on the consumption of antihistamines in 13 European countries including Serbia for the period 2005–2009/2010, it was observed that during this period the consumption of antihistamines was high in almost all the countries. Based on the Food and Drug Administration database on spontaneous reports on adverse drug reactions, the study demonstrated a number of signals of arrhythmogenicity among the antihistamines. Five of them (cetirizine, desloratadine, diphenhydramine, fexofenadine, loratadine) were found to have high arrhythmogenic potential (medicines having so-called strong signals) and another six (cyclizine, dexchlorpheniramine, alimemazine, carbinoxamine, cyproheptadine and doxylamine) were found to be drugs with weak signals. It is interesting that most strong signals were associated with the second generation antihistamines for which previously no such adverse effects had been published¹. Among them are loratadine and desloratadine which were, at that time, the most consumed antihistamines in Serbia. Due to this the aim of our analysis was to assess anti-

histamines consumption in Serbia for the following 5-year period (2011–2015), including also the consumption of drugs for common cold treatment containing an antihistamine as one of their active substances, as well as to check if any reports on adverse drug reactions to heart rhythm had been submitted to the National Pharmacovigilance Centre (NPC) for that period.

According to the Law on Medicines and Medical Devices of Serbia ("Official Gazette", No. 30/2010), the main activities of the Medicines and Medical Devices Agency of Serbia include regulatory activities, monitoring the marketing and consumption of medicinal products as well as monitoring adverse drug reactions through the NPC within the Agency². This includes both reimbursed medicines as well as medicines that are 100% co-payment including pharmacy only dispensed medicines such as the antihistamines. Consumption was recorded as Defined Daily Doses *per* 1,000 inhabitants *per* day (DID), according to the recommended ATC/DDD methodology³.

The consumption of antihistamines for systemic use (ATC R06) in Serbia in the period 2011–2015 ranged from 7.31 DID in 2011 to 9.04 DID in 2015, with fluctuations among the years (Table 1). The most preferred medicines for

Table 1
Consumption of antihistamines (ATC code R06) in Serbia in 2011–2015, expressed as defined daily doses (DDD) *per* 1,000 inhabitants *per* day (DID)

Antihistamines	2011	2012	2013	2014	2015
dimenhydrinate	0.072	0.085	0.146	0.156	0.179
dimetindene				0.000	0.000
chlorfenamine	0.001	0.009			
pheniramine	0.537		0.076		
chloropyramine	0.057	0.137	0.129	0.125	0.136
cetirizine	0.283	0.171	0.480	0.714	1.285
levocetirizine	0.504	0.834	0.790	0.145	1.225
loratadine	4.295	6.046	3.804	4.861	3.590
ketotifen	0.192	1.842	1.165	1.399	0.309
fexofenadine		0.000	0.083	0.117	
desloratadine	1.369	1.575	1.775	2.136	2.034
bilastine				0.113	0.281
Total	7.310	10.697	8.448	9.766	9.039

treatment of various forms of allergy in Serbia in the observed 5-year period, similarly to the previous one, were the second generation antihistamines, loratadine and desloratadine, followed by cetirizine and levocetirizine, as they are relatively free from anticholinergic, antiserotonergic and alpha adrenergic activity (1,4,5).

Consumption of antihistamines (ATC codes R01, and N02) in combination with other products for the treatment of common cold, represented approximately 12–21% of the consumption of antihistamines in the ATC R06 group, ranging from 1.44 DID in 2011 to 1.91 DID in 2015 (Table 2).

professionals in reporting any suspected adverse drug reactions. In Serbia these activities are insufficient. Spontaneous reporting should be viewed through the prism of professional and ethical responsibility, and healthcare professionals should direct future efforts towards intensifying the reporting of adverse drug reactions and integration of pharmacovigilance into their professional practice as part of their routine activities. Authorities should encourage this activities through physician's societies in Serbia since spontaneous adverse reaction reporting by healthcare professionals, and also by patients and drug manufacturers, remains the main method for post-

Table 2
Antihistamines in combination with the products for common cold treatment (ATC N02 and R01) expressed as the amount of active substances in defined daily doses (DDD) per 1,000 inhabitants per day (DID)

Antihistamines	2011	2012	2013	2014	2015
pheniramine	1.336	1.257	1.024	1.207	1.459
chlorfenamine	0.046	0.060	0.238	0.326	0.430
loratadine	0.060	0.060	0.070	0.028	0.021
Total	1.442	1.377	1.332	1.562	1.910

In view of the consumption of medicines for treatment of common colds in Serbia (Table 2), and those containing antihistamines as active constituents, mainly pheniramine and chlorphenamine, we consider it necessary to monitor the utilisation of these medicines alongside any adverse effects on heart rhythm, considering that OTC medicines, such as antihistamines, are among the most advertised medicines in Serbia with sales expected to continue growing⁶. These findings should also be used to make recommendations to the Ministry of Health and the Health Insurance Fund of the Republic of Serbia if needed.

From 2011 to 2015, the NPC collected 25 reported cases of drug-induced arrhythmia. Among them was only one report of tachyarrhythmia associated by loratadine. This may be an under-estimated finding since the efficiency and success of any national program for monitoring the safety of medicines once on the market depend on the active participation of healthcare

marketing surveillance in Serbia. Also, the authorities should actively conduct monitoring of any further cases of antihistamine-induced tachyarrhythmias to provide updated guidance to healthcare professionals in Serbia if and when the need arises.

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R E F E R E N C E S

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