LETTER TO THE EDITOR
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Ten years of consumption of anti-glaucoma medicaments in Serbia

Deset godina potrošnje lekova u terapiji glaukoma u Srbiji

To the Editor:

Glaucoma is a chronic disease with irreversible damage of optic nerve [1]. It is the second leading cause of blindness worldwide, and is one of leading causes of preventable blindness [2]. It is estimated that by 2020, about 79.6 million people in world will have glaucoma, and more than 11 million will be consequently bilaterally blind. Prevalence of blindness in all types of disease has been estimated at 5.2 million with 3 million cases with open-angle primary glaucoma [3]. This is predicted to increase substantially as a result of an ageing population and better detection in the community. The recommendations of good clinical practice guidelines for the treatment of glaucoma in the UK are that all cognitive and physical disorders, as well as the existence of relevant comorbidities or potential drug interactions should be taken into account before commencing treatment [4]. Glaucoma disease is a complex, significant public health and socio-medical problem [5, 6]. Glaucoma screening/diagnostics requires a detailed clinical examination of optic nerve and functional analysis/evaluation of patients' field of vision [7, 8]. Early treatment of glaucoma reduces risk of progressive damage to the vision field. Medication therapy is currently the most commonly used as an initial reduction measure for increased intraocular pressure (IOP). The recommendation of the American Academy of Ophthalmology is to consider the relationship between therapeutic effects and adverse drug reactions when selecting anti-glaucoma drugs in order to achieve the desired reduction of increased IOP for each patient [9]. The initial anti-glaucoma therapy includes medications which are individually prescribed and controlled (prostaglandin analogues, beta-blockers, adrenomimetic, parasympathomimetic, carbonic anhydrase inhibitors) [10-12].

Today, it is important to monitor the consumption of anti-glaucoma medicaments, because in this way it is possible to estimate the increase of the number of patients and the rise of their awareness that glaucoma must be treated in order to maintain a good quality of life. Thus, it is expected to have an increase in the consumption of these drugs each year.

Our analysis of the consumption of medicaments in treatment of glaucoma in Serbia during eleven-year period (2006–2016) was made based of the publication "Sale and consumption of drugs in human medicine", published annually by the Agency for Medicinal Products and Medical Devices of the Republic of Serbia (available on Agency's website). The data on drug consumption in glaucoma therapy were analyzed according to the methodology of World Health Organization (WHO) which uses the defined daily dose (DDD) method for this purpose. DDD is a statistical monitoring unit that expresses an agreed amount of a drug according to International Nonproprietary Name (INN), which is most commonly used for the most common indication and is independent of protected name of drug and manufacturer, price, pharmaceutical form and size of package. In general population, the number of DDDs per 1,000 inhabitants per day (DDD/1,000 inhabitants/day) is used. This consumption data based on DDD/1,000 inhabitants/day was obtained firstly by the total consumption of the given drug according to its INN that was expressed in weight or volume units according to the Anatomical-Therapeutic-Chemical Classification (ATC) drug code. All the drugs used in the treatment of glaucoma were then divided into five subgroups: S01EA – sympathomimetics, S01EB – parasympathomimetics, S01EC – carbonic anhydrase inhibitors, S01ED – beta blocking agents, and S01EE – prostaglandin analogues.

The consumption od the drugs used in glaucoma treatment in Serbia in the period observed is given in Table 1. The highest total consumption of drugs used in the treatment of glaucoma according to the above mentioned methodology was registered in the S01ED group (beta-blocking agents), followed by the S01EE group (prostaglandin analogues) while the other three groups had significatly lower consumption. However, the consumption of all groups had variation in the period observed. For example, consumption of beta-blocking drugs was the highest in 2007, and the smallest one in 2010, but after that an increase was evident. Unequal consumption was also recorded in the group of prostaglandin analogues - by 2011, their consumption grew from year to year, and then in 2012 there was a certain decline. In 2013, there was a rebound of the consumption that was the highest in observed period, but in 2014 a decline in consumtion of these drugs was recorded. However, from 2015, trend of an increase in the consumption of prostaglandin analogues was again recorded.

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Table 1

Medicaments in the glaucoma treatment, DDD/1,000 inhabitants/day in Serbia in the period 2006–2016

Year	ATC groups				
	S01EA (sympathomimetics)	S01EB (parasympathomimetics)	S01EC (carbonic anhydrase)	S01ED (beta- blocking agents)	S01EE (prostaglandin analogues)
2006	0.01	1.05	0.32	6.22	0.64
2007	0.05	0.35	0.30	7.89	0.93
2008	0.16	0.66	0.53	7.12	1.48
2009	0.21	0.39	0.48	5.23	2.28
2010	0.45	0.57	0.46	4.11	2.09
2011	0.49	0.36	0.46	4.50	2.61
2012	0.62	0.32	0.51	6.71	2.31
2013	0.71	0.29	0.54	6.98	3.68
2014	0.18	0.26	0.57	7.73	0.72
2015	0.28	0.34	0.60	7.14	1.41
2016	1.36	0.3	0.85	7.68	3.9
Total	4.52	4.89	5.62	71.31	22.05

DDD – defined daily dose; ATC – anatomical-therapeutic-chemical classification.

These variations in consumption can be attributed to the trend of prescribing new fixed combinations, such as travoprost/timolol, dorzolamide/timolol, timolol/brimonidine, etc, and an individual approach to the glaucoma treatment. The highest consumption of drugs in treatment of glaucoma according to DDD/1,000 inhabitants/day in all ATC groups, except for the S01EB group was registered in 2016. An individual analysis showed that the consumption of adrenomimetics and prostaglandin analogues was increasing until 2014, after which the significant fall was registered (both drugs represent an initial/effective therapy, either alone, or in the combination). At the same time, the consumption of carbonic anhydrase inhibitors had a linear rise (due to the prescriptions related to all types of glaucoma, including the secondary glaucoma), while parasympathomimetics were in linear decrease (due to the prescriptions of the medicaments mainly for the angular glaucoma).

In Slovenia, the linear increase in total consumption of forcible drugs in the period 2006–2017 was observed. An analysis of DDD/1,000 inhabitants/day indicated variations in relation to the ATC group. The highest increase in consumption was recorded in the S01EE group, while the consumption of sympthomimetics increased until 2016, after which there was a slight decline. The fall in consumption was seen in the S01EB group, while the consumption of S01EC and S01ED groups after 2011 was relatively stable [13]. In Norway, in the period 2011–2015, there was a linear decrease in the total consumption of drugs from the S01E-ATC group, observed through DDD/1,000 inhabitants/day. A more detailed analysis by groups showed that consumption of S01EA, S01EC and S01EE was growing, while consumption of S01ED decreased. At the same time, after 2013, the consumption of parasympathomimetics was relatively constant and stable [14].

The first line of treatment for glaucoma, regardless of the general rule that the therapy should be individualized taking into account the patient's comorbidity, its accompanying therapy, the existence of the contraindication for the use of some anti-glaucoma drugs, belongs to prostaglandin analogues. If glaucoma patients have an additional eye inflammation, then they should not take prostaglandin analogues, and advantage should be given to beta-blockers, or to another anti-glaucoma drugs. Our analysis indicated that the consumption of anti-glaucoma medicaments in Serbia is mainly in line with the modern recommendations on the treatment of glaucoma [15].

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