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Pharmacotherapy of ADHD in Slovenia: realities and perspectives

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common mental disorders in children and adolescents, with the worldwide-pooled prevalence of 5.3 % [1]. Although seen as a problem that takes place predominantly in childhood and adolescence, clinical and epidemiological research has shown that ADHD persists into adulthood in 30–50 % of the patients [2]. ADHD is treated with pharmacotherapy and behavioral interventions. Although the behavioral interventions are often used to treat children and adolescents with ADHD, pharmacotherapy is more effective because of its medium-to-high effect size and because it allows a stepwise approach, which can be tailored to the patient's current condition. If pharmacological treatment is prescribed, it should be in conjunction with behavioral interventions. Individual circumstances, such as academic or employment demands, and the patients' medical history should be taken into account and appropriate evidence-based treatments for comorbidities should also be initiated [3, 4]. ADHD can result in economic costs, family stress, academic and vocational impairments, and has a negative effect on the patients' self-esteem [3]. Because of the high disease burden of ADHD, the data about ADHD epidemiology and pharmacoepidemiology are necessary to plan appropriate national interventions within this field.

Until 2015, the MEDLINE/PubMed Database did not contain articles on the incidence and prevalence of ADHD in Ex-Yugoslavian countries (e.g. Croatia, Slovenia, Serbia, Bosnia and Herzegovina). In the most recent paper on this topic, by Stuhec et al. in April 2015, the mean prevalence rate of child and adolescent ADHD patients in 2012 was estimated to be 750 per 100,000 children and adolescents (about 0.75 %). It was also estimated that the prevalence rate in Slovenia in 2020 would be 1 %, which is 6.3-fold higher than in 1997. The data clearly show that ADHD is a common mental health disorder among Slovenian children and adolescents, and ADHD, while diagnosed, is still under diagnosed in comparison to Western countries (e.g. Germany and Spain) [5]. These results indicate a need for improved interventions in Slovenia, not only in child and adolescent psychiatry but also in primary settings and adult psychiatry, where ADHD should be recognized more efficiently and the time it takes before patients visit a specialist should be shortened.

Stimulants are the first-line treatment for ADHD in children, adolescents and adults, with medium to high effect sizes. According to the ADHD treatment guidelines; non stimulant atomoxetine (ATX) is often the second-line treatment after stimulants. As such, ATX prescribing should be closely monitored to prevent inappropriate prescribing, which has additional costs [3]. In most European countries, there are no drug consumption studies for ADHD. The list of approved ADHD drugs in Slovenia is limited to immediate-release methylphenidate (IR-MPH), methylphenidate-osmotic release oral delivery system (OROS-MPH) and ATX. The situation is similar in most Central European countries. Amphetamines and other methylphenidate forms were not available in Slovenia until now. ADHD drug consumption in Slovenia increased from

0.0537 defined daily dose (DDD)/1000 inhabitants/day in 2001 to 0.3076 DDD/1000 inhabitants/day in 2012. The increase was largely due to an increase in the consumption of OROS-MPH and ATX consumption, while the consumption of IR-MPH decreased rapidly. During the same period, the total cost of the medicines increased 31-fold. From 2007 to 2010, the total cost of ADHD medicines increased 14-fold and from 2010 to 2012 the cost only increased by 11.4 % [6]. The changes in the prescription patterns are evident in Slovenia, primarily in the increase of OROS-MPH and ATX prescriptions and in the rapid decrease of IR-MPH prescriptions. This pattern (very high ATX and low IR-MPH consumptions) has not been seen in Germany, where prescribing of ATX is still stable [6, 7]. From these results, it can be concluded that when new medicines are available, their prescription rates increase rapidly. It is interesting how availability and marketing may have changed and increased prescribing. From 2006 to 2012, the total consumption increased almost fivefold, while the marketing of these medications was nonexistent prior to 2006. The result is an observed time shift in the total consumption in Slovenia in comparison with Western countries [6].In Slovenia, the ATX consumption increased rapidly, while IR-MPH consumption became almost insignificant (IR-MPH is not the first-line drug in most cases). This suggests it is urgent to introduce the European treatment guidelines into clinical practice and to tighten the cooperation with the European Society for Child and Adolescent Psychiatry (ESCAP) [3, 8].

The most effective treatment strategies should be available for all patients with ADHD in all developed countries including Slovenia. In Slovenia, amphetamines and other methylphenidate forms than IR-MPH and OROS-MPH are not available on the Slovenian market [8]. Lisdexamfetaminedimesylate (LDX) was shown to have a high effect size and to be the most effective treatment strategy [9, 10]. According to the 2014 guidelines of the British Association for Psychopharmacology, stimulants should be the first-line treatment and non-stimulants the second-line treatment, the latter used when the treatment with stimulants fails, which happens in approximately a third of all treatments [3]. Guanfacine extended release (GXR) is also not available in Slovenia, although it would be an additional treatment strategy (along IR-MPH, OROS-MPH and ATX), because of its different mechanism of action as a selective alpha-2 receptor agonist. GRX could be of great use in patients with almost selective hypoactivity of the adrenergic system, especially when an alternative mechanism of action is needed, and when treatment with stimulants or ATX fails [11].

Most adult patients with ADHD need pharmacotherapy; therefore, the medications for adult ADHD should be approved and available. In most countries in Central Europe, including Slovenia, ATX is the only new drug approved for adult ADHD in the period between 2013 and 2015. The most effective treatment strategies (e.g. stimulants with medium-to-high effect sizes) have not been approved [8]. Late pharmacotherapy availability also means that almost no new adult patients have been diagnosed with ADHD in these countries (in Slovenia less than 0.1 % in 2012). As a result, ADHD in adults remains underdiagnosed and patients are not treated with pharmacotherapy [5].

In conclusion, ADHD is diagnosed and treated in Slovenia, although the gap in comparison with Western countries is evident. The rates of incidence and prevalence of children and adolescents with ADHD in Slovenia are increasing, but at a rate 2–10 times is slower than in some comparable countries. However, the pattern of ADHD medication use in Slovenia is not comparable with that of other countries. These data also present an opportunity for possible restrictions from the payers (national insurance companies) on ATX prescribing, which could also reduce the price of ATX. As of 2015, the countries do not have national guidelines for ADHD treatment and diagnosis, or any published data on the prevalence of ADHD (except in Slovenia). Intensive management of ADHD is needed to translate the European guidelines into clinical practice, which is currently inadequate in Slovenia.

National guidelines for treatment should be established by a multitude of different specialists (e.g. child and adolescent psychiatrists, adult psychiatrists, clinical pharmacists, psychologists, general practitioners, etc.) to improve stimulant use in most patients and control high ATX use. Afterward, the patients and specialists should contact the national insurance companies and pharmaceutical companies to bring new drugs on the market as soon as possible (e.g. GXR, LDX, other forms of MPH), with an approved indication for adult ADHD. Last, the cooperation between specialists (child and adolescent psychiatrists, adult psychiatrists, clinical pharmacists, psychologists, general practitioners) and associations such as the ESCAP and European Psychiatric Association should be strengthened to diagnose and ensure the patients an early treatment.

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