

CREATIVE PSYCHOPHARMACOTHERAPY IN CHILD AND ADOLESCENT PSYCHIATRY AND EXPERIENCES FROM BOSNIA AND HERZEGOVINA

Nermina Kravić^{1,2}, Martina Krešić Ćorić³, Marija Burgić Radmanović⁴, Nermina Ćurčić Hadžagić⁵, Mira Spremo⁴, Zihnet Selimbašić^{1,2}, Izet Pajević^{1,2}, Vesna Horvat⁵, Sabina Kučukalić⁵, Mevludin Hasanović^{1,2} & Miro Jakovljević⁶

¹Department of Psychiatry University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina

²Faculty of Medicine, University of Tuzla, Tuzla, Bosnia and Herzegovina

³Department of Psychiatry, University Clinical Hospital of Mostar, Mostar, Bosnia and Herzegovina

⁴Department of Psychiatry, University Clinical Center of Republic of Srpska, Banja Luka, Bosnia and Herzegovina

⁵Department of Psychiatry, Clinical Center of University Sarajevo, Sarajevo, Bosnia and Herzegovina

⁶Department of Psychiatry and Psychological Medicine, University Hospital Centre Zagreb, Zagreb, Croatia

SUMMARY

Introduction: Paediatric psychopharmacology involves the application of psychotropic agents to the treatment of children and adolescents with mental disorders and gathered knowledge from child and adolescent psychiatry (CAP), neurology, paediatrics and pharmacology. Defining elements of this discipline are: the metabolism of drugs is different in children than in adults (pharmacokinetics), the developing brain reacts specifically to the drug (pharmacodynamics), and psychopathology itself is not differentiated yet. To make an overview of specifics in psychopharmacological use in CAP and emphasize some experiences from Bosnia and Herzegovina in that field.

Methods: Through insight in current literature, we presented comprehensive findings and compare it with situation in Bosnia and Herzegovina.

Results: The most common conditions in which psychopharmaceuticals are used in CAP were attention deficit hyperactivity disorders (ADHD), depressive and bipolar disorder, obsessive compulsive disorder and the treatment of early psychosis. Psychopharmaceuticals were also used to treat agitated conditions in various causes. We made an overview of psychopharmaceuticals use in Bosnia and Herzegovina CAP and emphasized the fact that psychostimulants are not approved for the use yet, although they are mostly prescribed medication in CAP over the world. That limits us in the effectiveness of the treatment in ADHD and put us in the situations to use other medications instead (anxiolytics, antipsychotics, mood stabilizers) which are not approved for that condition.

Conclusion: The use of psychopharmacotherapy in CAP is justified in cases where it is necessary to reduce the suffering of children and to improve their functionality at the time when cognitive, social and emotional advancement is most pronounced. Further research and clinical monitoring of efficacy and safety in the use of psychopharmaceuticals in youngsters are necessary.

Key words: psychopharmacotherapy - child and adolescent psychiatry - Bosnia and Herzegovina

* * * * *

INTRODUCTION

Children and adolescents constitute about one-third of the world's population. They are a particularly vulnerable group for the onset of mental disorders. Approximately one-half of all mental disorders emerge before 14 years of age and 75% by 25 years. Furthermore, globally, one-quarter of disability-adjusted life years (DALYs) for mental and substance use disorder occurs in youth (Skokauskas et al. 2019).

To make an overview of specifics in psychopharmacological use in CAP and emphasize some experiences from Bosnia and Herzegovina in that field.

CHILD AND ADOLESCENTS' PSYCHOPHARMACOLOGY

Medications to treat mental conditions have become increasingly used in child and adolescent psychiatry around the world. Pediatric psychopharmacology involves

the application of psychotropic agents to the treatment of children and adolescents with mental disorders and gathered knowledge from child and adolescent psychiatry, neurology, pediatrics and pharmacology. The defining elements of this discipline are the developing organism, the metabolism of drugs is different than in an adult person (pharmacokinetics), the developing brain reacts specifically to the drug (pharmacodynamics), and psychopathology itself is not well differentiated yet. Although children are smaller in body size than adults, they have a greater proportion of liver and kidney parenchyma after adjustment for body weight, so they have faster metabolism and elimination of drugs. The phase I oxidative processes are mediated by cytochrome 450 (CYP450) microsomal enzymes, which are concentrated primarily in the liver. The CYP450 system is immature at birth, but its metabolizing capacity increases rapidly, so that by one month of age it is already about 20% of the mature level, which is achieved by three years of age. Because children have

proportionally more liver parenchyma than adults, they have greater weight-adjusted metabolic capacity (Lorberg et al. 2019, Zohar et al. 2018, Kocijan Hercigonja 2002).

Diagnostically statistical manual 5th revision (DSM 5) and International classification of diseases 11th (ICD-11) provide further evidence that categorical diagnosis, while robust and important, also has distinct limits. As the field tries to more fully describe the dimensions of all aspects of developmental psychopathology, the development of new models and tools for phenotyping will be necessary. Further studies will be necessary to validate these tools and translate them for use as a part of standard clinical practice. Studies using evolving brain imaging technology (e.g., fMRI, MEG, fNIR, and EEG) will provide insights into the systems biology of the brain in health and disease and will create new opportunities for defining functional elements in the brain and their role in developmental psychopathology. Further studies of the genetics (including studies on coding and non-coding regions and on epigenetics and gene expression) of psychopathology will be necessary to elucidate the etiologic understanding of disorders and phenotypes. Of note is growing evidence for the impact of stress and inflammatory processes on the developing brain and emergence of developmental psychopathology, both directly and through an impact on glial and other brain functions (Skokauskas et al. 2019)

A developmental perspective should be a key underpinning of prevention research, providing insights into the pathways, continuities, and changes in normal and pathological processes over the life span (Costello 2016). It will move research away from the notion of a single causal agent and will attempt to examine different and sometimes interacting causal factors as well as identify optimal points for intervention. Given this complexity, it is expected that child and adolescent psychiatry and multiple other disciplines will work together to succeed in comprehensive preventive research trials.

Advocacy around the prevention of psychological trauma is a particularly important focus given that early childhood exposure is likely to affect formative developmental processes in a manner that impairs the foundation of future growth and that may have inter-generational consequences (Hasanović 2021).

The development of the brain in adolescents moves from caudal to the rostral parts of the brain. During late adolescence and early adulthood, neurobiological systems responsible for self-regulation and control undergo a complex maturation. This maturation involves a decrease in prefrontal gray matter related to synaptic pruning, an increase in myelination within the prefrontal cortex, and a proliferation of white matter tracts between cortical and subcortical areas, especially

including the prefrontal regions, amygdala, nucleus accumbens, and hippocampus. This normal maturation of neurobiological systems may underlie the decrease in antipsychotic treatment prevalence during late adolescence among youth who do not have enduring cognitive impairments and long-term severe behavioral disorders (Steinberg 2008).

Cerebellum and amygdala are involved in maturation process during adolescence before prefrontal cortex, what increased impulsivity and decrease thoughtfulness in certain age (before the age of 20). It could influence increased risk for suicidal behavior in adolescents treated with antidepressants.

Researches in child and adolescent psychopharmacology are in greater delicacy for clinical application because low regulations are stricter than in adult psychopharmacology, sample size are small, age groups are heterogenous, children are more often placebo reactors, and they have restricted verbal description of their inner state.

A comprehensive diagnostic evaluation and psychosocial formulation is the necessary first step (Figure 1). Patients with psychotic disorders often require pharmacological treatment as a first step to control symptoms and restore functioning. Patients with non-psychotic disorders may often be successfully treated with non-pharmacological interventions first. In child and

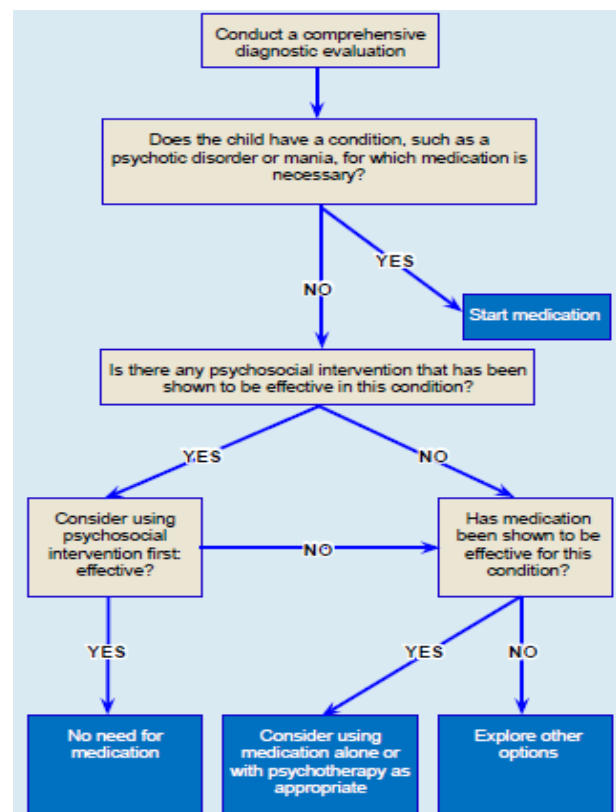


Figure 1. General approach to psychopharmacotherapy in children and adolescents

adolescent psycho pharmaceutical treatment we should start with lower doses. Dosage for older than 17 is same as for an adult (Lorberg et al. 2019, Zohar et al. 2018, Kocijan Hercigonja 2002).

Approaching to a child with mental health problems we should always consider detailed medical anamnesis and psychological evaluation, as well as laboratory diagnostics, neuro radiological and neuro physiological examination (Figure 2).

Diagnosics in child and adolescent psychiatry

Whole blood tests, C-reactive protein, sedimentation, creatinine, urea, transaminases, bilirubin, ceruloplasmin, CPK (creatine phosphor kinases), urine tests, level of thyroid gland hormones, prolactin, EEG, Mg, Ca, Fe, phosphates, Bit B12 level, folate acid, tests for psychoactive substances use. Additional tests: HIV, hepatitis B and C, pregnancy tests, syphilis. Neuro-radiological and neuro-physiological diagnostics (Figure 2).

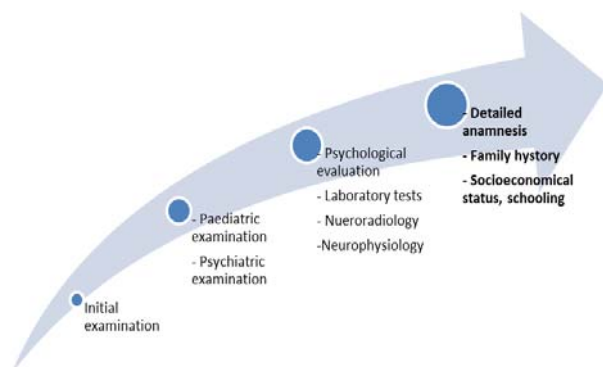


Figure 2. Psychiatric approach to a child and adolescent with mental health problems

PSYCHOTROPIC MEDICATION IN CHILD AND ADOLESCENT PSYCHIATRY

Indication for antipsychotic use in child and adolescent psychiatry:

- Psychosis (manic, bipolar, SCH),
- Tick (Sy de la Tourett)
- Psychomotor agitation (ASD, ID)
- Difficult behavioural problems

Side effects antipsychotic use in child and adolescent psychiatry:

- Iatrogenic Extra Pyramidal Sy
- Sedation, hypotension
- Metabolic sy
- Weight gain
- Hyperprolactinaemia

- Granulocitopaenia
- Epileptic seizures.

Indications for anxiolytic use in child and adolescent psychiatry:

- Acute agitation in adolescence,
- Panic attacks,
- Epileptic seizure
- Mio-relaxation.

Indications:

- Major depression
- Obsessive compulsive disorder
- Social anxiety
- Generalised anxiety
- Panic disorder
- Posttraumatic stress disorder
- Eating disorder
- Elective mutism
- Enuresis
- Attention Deficit Hyperactivity Disorder (third line)

Side effects:

- Increased suicidal ideation and suicidal risk
- Gastro intestinal symptoms
- Sexual dysfunctions
- Prolonged QT interval
- Sedation
- Weight gain

Indications for use of medicines for hyperactivity and attention deficit:

- Attention deficit Hyperactivity Disorder

Side effects:

- Decrease of appetite and weight loss
- Insomnia
- Irritability and aggression
- Worsening of tick disorder and psychosis
- Headache
- Palpitations
- Those medicines are not registered in Bosnia and Herzegovina

Indications:

- manic, BAP,
- aggression in behavior,
- Encopresis,
- Intellectual deficit with affective and behavioral.

Side effects:

- Liver problems,
- agranulocytosis,
- aplastic anemia,
- Polycystic ovaria problems.

Table 1. Antipsychotic use in child and adolescent psychiatry. First generation antipsychotics (conventional)

Medicament	Age	Dosage	Maximal daily dose
Low potent			
Chlorpromazine	6 month	2.5 mg/kg/day divided in two or three dosage, <5 year – not more than 40 mg/day	40-50 mg
Levomepromazine	12 years	12.5-50 mg/day, 75-150 mg/day	300 mg
Promazine	12 years	12.5-100 mg/day, 1 mg/kg	
Tioridazine	2 years		30 mg/day
Sulpiride	14 years	50-100 mg, tbl; 25 mg/5 mg, syrup (3 mg/kg)	100 mg/day

Table 2. First generation antipsychotics (conventional) in CAP

Medicament	Age	Dosage	Maximal daily dose
High potency			
Haloperidol	3 years	3-12 y. 0.25-0.5 mg in 2-3 dose PO 6-12 g. 1-3 mg/dozina 4-8 h IM	5 mg
Pimozide	12 years	0.05-0.2 mg/kg evening (1-2 mg/day)	10 mg/day
Fluphenazine	16 years	0.5-1.5 mg/day	10 mg/day

Table 3. Second and third generation antipsychotics (atypical) in CAP

Medicament	Age	Dosage	Maximal daily dose
Clozapine	16 years	12.5-100 mg	450 mg divided in 2-3 dose/day
Olanzapin	10 (13) years	2.5-5 mg initial dose 10 mg/day	20 mg/day
Aripiprazol	6 (10) years	2.5-5 mg initial, 20 mg recommended	30 mg/day
Amisulprid	(16) 18 years	50 mg-initial, Recommended 400-800 mg/day	1200 mg/day (adults)
Asenapin	10 years	2.5-5 mg 2x/day SL	10 mg/day
Risperidon	5 (10) years	<50 kg 0.25-0.5 mg/day >50 kg 0.5-2 mg	2 mg/day 8 mg/dayadol
Quetiapine	10 (13) years	25 mg once a day, 400 mg/12 h	600 mg/day
Ziprasidone	10 years	Initial 20 mg/day, 80-160 mg/day	160 mg/day

Table 4. The use of anxiolytics in child and adolescent psychiatry

Medicament	Age	Comment	Maximal daily dose
Diazepam	6 months	0.1-0.3 mg/kg	10-15 mg for children 20-30 mg for adolescents
Lorazepam	12 y Epi status	0.25-6 mg 2-4x day PO or IM	
Clonazepam		Initial dose 0.125 mg for children For adolescents 0.5-0.75 mg (minimal age is not determined)	0.2 mg/kg for children 4 mg for adolescents

Table 5. The use of antidepressant in child and adolescent psychiatry

Medicament	Age	Dosage	Maximal daily dose
Fluoxetine	8 years	10 mg younger than 12, 20 mg older than 12	60 mg
Fluoxamin	8 years	25 mg	250 mg/day
Sertralin	6 years	12.5-50 mg	200 mg/day
Escitalopram	12 years	5 mg younger than 12, 10 mg adolescents.	20 mg/day
Citalopram	*	10 mg/day increase every 2 weeks 5-10 mg	40 mg/day
Paroxetin	18 years	10 mg/day	60 mg/day
Venlafaxin	8 (17) years	18.75 mg-300 mg	300 mg/day
Mirtazapin	*	7.5-15 mg	45 mg/day
Bupropion	*	100-150 mg/day in 2 dose	450 mg/day
Duloxetine	*	30-60 mg/day	60 mg/day

SSRI, +NA, +DA *- risk for higher suicidal ideation in younger than 25

Table 6. Tricyclic antidepressants

Medicament	Age	Dosage	Maximal daily dose
Highly potent			
Clomipramin	10 years	25 mg initial, 75-250 mg/day in 2 dose	250 mg/day
Desipramin	12 years	25 mg, 75-150 mg/day in 2-3 dose	300 mg/day
Imipramin	6 years	6-12 years 25-50 mg/day, 12-18 years 25-75 mg/day	2.5 mg/kg/day
Doxepin	12 years	25 mg/day, 75-300 mg/day in 2-3dose	300 mg/day
Amitriptilin	12 years	25-50 mg/day	75-150 mg/day

Table 7. Medicament treatment in ADHD

Medicament	Age	Dosage	Maximal dose
Metilphenidat and dexmetilphenidat	6 years	0.3-2.0 mg/kg/day Initial 2.5-5 mg	72 mg/day
Amphetamin and dextroamphetamin	3 years	0.1-1.5 mg/kg/day 5-10 mg/day in 2 dose	30 mg/day
Atomoxetin	6 years	0.5-1.2 mg/kg/day 40 mg	80 mg/day in the morning
Clonidin	6 years	0.05 mg/day less than 40.5 kg 0.1 mg/day more than 40.5 kg	0.2 mg/day 3x 0.4 mg/day
Guanfancin	6 god	0.5 mg/day less than 40.5 kg 0.5 mg/day more than 40.5 kg	2 mg/day 4 mg/day

Table 8. Mood stabilizers in child and adolescent psychiatry

Medicament	Age	Dosage	Plasma level
Lithijum carbonat	7 years	10 mg/kg/day initial 300-1800 mg/day	0.6-1.2 mmol/l
Valproat acid	2 years	7.5 mg/kg in 2x younger 12 y (60-120 mg) 300mg/day older than 12 y	50-100 µg/l
Carbamazepin	4 years	0.5-10 mg/kg (4-10 years) 2x10 0mg, max. 1200 mg/day	4-12 mg/l
Lamotrigin	2 (12) years	0.15-0.6 mg/kg/d initial 200 mg 1.2-5 mg/kg/d maintaining 400 mg	
Gabapentin	3 years	10-15 mg/kg/day for <12 24-50 mg/kg/day Adolescents 300-2400 mg	
Pregabalin		25-400 mg/day	

Table 9. Medicaments for sedation / tranquilizers

Medicament	Dosage (mg/kg)	Way of use	Max effect	Duration
Midazolam	0.1-0.2 0.3-0.5	i.v., i.m. p.o.	10-35 min	45 min
Diazepam	0.1-0.2	p.o., i.v., i.m.	60-90 min	45 min-18 h
Chloral-hydrate	20-100	p.o.,	60-90 min	4-6 h
Phenobarbital	5-10	p.o., i.m.	60-90 min	4-6 h

The use of supplements in child and adolescent psychiatry

Vitamin D

Plays a dual role as hormone and fat-soluble vitamin, regulating the expression of more than 900 genes. It is important in calcium and phosphorus homeostasis, bone health and various cellular and neuromuscular

functions. The vitamin D receptor and vitamin D metabolizing enzymes are expressed in the brain (Eyles et al. 2013). Due to its pleiotropic function vitamin D is also involved in signaling cascades and neurobiological pathways, which may affect mental health. The active metabolite 1.25(OH)₂D₃ is thought to modulate the differentiation and maturation of dopaminergic neurons and to affect brain serotonin concentrations. Low

vitamin D status is associated with a range of adverse neuropsychiatric outcome. In particular, population based epidemiological and clinical studies showed an association of low 25(OH)-vitamin D serum levels (25(OH)D) with depressed mood, attention Deficit Hyperactivity Disorder (ADHD) or Autism Spectrum Disorders (ASD). The Institute of Medicine (IoM) defines 25(OH)D levels >50 nmol/l (equals 20 ng/ml) as sufficient, whereas levels of 30–50 nmol/l or < 30 nmol/l are classified as at risk for inadequacy or as at risk for deficiency. Recommended dosage depends on age and clinical conditions, vary from 300 IJ - 500 IJ in neonatal age up to 4000 IJ for deficiencies. In treatment of depression in adolescence it is recommended to use 2600 IJ vit D3 for 28 days (Föcker et al. 2018).

Melatonin

Melatonin is used in treatment of insomnia, its activity is targeting MT1, MT2 and MT3 receptors in brain. In child and adolescent psychiatry is often use for change of circadian sleep rhythm which is often in patients with autism spectrum disorder. Dosage is 1-12mg, concerning age and weight. It should be avoided to be taken together with benzodiazepine hypnotics (zolpidem, zolpiklon, zalepton) (Jakovljević 2016).

Herbal supplements

Melissa officinalis, Humulus lupulus, Lavandula officinalis, Valerian officinalis) base the sedative effect on increasing level of inhibitory neurotransmitter GABA. Those substances are often use for anxiety and acute stress reactions in children and sometimes in adolescents, their effect is often as „transitional object“ which's duty is to remind on psychotherapeutical safety of the psychiatrist who recommended it, to comfort and reduce fearful expectations which increase during the separation of parents /caretakers before the sleeping time.

SOME SPECIFITIES AND CREATIVITY OF TREATMENT IN CHILD AND ADOLESCENT PSYCHIATRY

Parents / caregivers are always included in the treatment of the child and adolescent with mental health problems, their relationship is sometimes crucial for the development of pathology and could help in the process of the treatment and recovery. Psychotherapeutical approach to parents/caregivers, without accusation, but with understanding and explanations are necessary. Each parent expect healthy child, their positive narcissist expectations are invested in their child and if something is going unexpected and wrong way, they could feel it as their own failure, or project it in others, looking for a cause accusing themselves or others. Getting parent's /caregivers awareness that

treatment of the child with mental health problems could be long term and demand their cooperation at home, school and other children's life circumstances is very important for remission and recovery of the child. Comprehensive and sincere parent/patient – doctor relationship is important for reliable psychopharmacological treatment of children, parents are usually very concerned about side effects of medical treatment and delay its application. We should always discuss benefits and potential worries of medical treatment, as well as consider possibilities for reducing suffer and make no harm to child (Olfson et al. 2018, Angold et al. 2000, Delate et al. 2004).

Adolescents should be recognized as representing a special population. On the one hand, the community must respect their developmental rights and movement toward full autonomy; on the other, there must be recognized that their capacities may be limited in some functional areas. Adolescents therefore need a different approach in fostering healthy development and resilience. They should be protected from violence and exploitation, but approaches must take into account their emerging competencies and capacities developing during this period of life.

Adolescence is characterized by marked growth in body size and redistribution of body compartments, differences between sexes become more pronounced. In males, the percentage of total body water increases and that of body fat decreases, while the opposite occurs in females. These changes can produce gender differences in pharmacokinetics (Goodwin et al. 2001).

Early childhood interventions (including those addressing mental health and socio-emotional development) should be integrated into the systems for general healthcare with adequate funding; they can and should be provided as a core element of the larger investment in the health, economic prosperity, and safety of each nation and community (McVoy & Findling 2015).

THE USE OF ANTIPSYCHOTIC MEDICATION IN CHILD AND ADOLESCENT PSYCHIATRY IN BOSNIA AND HERZEGOVINA

The child and adolescent psychiatry in Bosnia and Herzegovina (BH) is a branch of psychiatry which is in expansion. Currently, there are 15 child and adolescent psychiatrist in Bosnia and Herzegovina, for the population of 786.461 (22.7% of the whole BH population) under 19 years old. We will give a brief overview of our multi-centric study that we did by retrospective monitoring of the prescribed psychopharmaceuticals on the outpatient and inpatient basis during one calendar year.

SAMPLE AND METHODS

In our research we did retrospective multi-centric study where we wanted to get insight in prescription of antipsychotic in child and adolescent psychiatry practice for inpatient (Sarajevo and Banja Luka) and outpatient (Tuzla and Mostar) settings in four BH Clinical Centers, for a one year period (from November 1st, 2017 to October 31st, 2018). At outpatient units in Tuzla and Mostar there were 1352 psychiatric checkups of youngsters during the observing period (Tuzla 875 and Mostar 477).

RESULTS

Antipsychotics were prescribed in 343 times (25.3%), mostly the second generation of antipsychotics: risperidon (39.6-60.5%), olanzapin (about 22%), aripiprazol (about 9.3-12.5%), quetiapine (10.4%). There were still some prescriptions of first generation antipsychotics: promazine (3.1-12.5%) and haloperidol (3.12-8.3%). Adjuvant therapy combined with antipsychotics were: diazepam (20-40%), sertraline (6.2-14.5%), lamotrigine (about 15%), Valproic acid (10-12.5%), promazine (6.2-21%), fluoxetine (6.2%), hypnotics (6.2-20%).

Antipsychotics were prescribed mostly for acute and other psychotic disorders (18-30%), for intellectual disabilities (about 30%) and autistic spectrum disorders with some specific disturbances (about 15%), and rarely for obsessive compulsive disorder (about 4%), conduct and affective disorders (less than 10%).

At Banja Luka and Sarajevo inpatient units there were hospitalised 278 patients (130 Banja Luka and 148 Sarajevo) in one year period. Antipsychotics were used in treatment of 104 patients (37.3%) – 48 (36.9%) patients in Banja Luka and 56 (37.8%) patients in Sarajevo.

The use of antipsychotics and dosage varies for inpatient treated adolescents: risperidon (1–3 mg), olanzapin (2.5–10 mg), aripiprazol (2.5–15 mg), haloperidol (0.5–4 mg), promazine tbl (12.5-100 mg), flufenazin (0.5–2 mg) and clozapin (12.5–50 mg).

For inpatient minors antipsychotics were used in further conditions: psychotic disorders, conduct disorders, intellectual disabilities with co-morbid psychotic symptoms, psychotic depression, obsessive compulsive disorder, autistic spectrum disorder with psychiatric comorbidities and anorexia nervosa.

Departments for child and adolescent psychiatry in Tuzla and Mostar do not have specific wards for inpatient treatment, so in the situation when hospitalization is necessary, and parents gave permission for that (previously offered to transport child/adolescent in some of centers where inpatient treatment is available: Sarajevo or Banja Luka), we have to hospitalize

youngsters in adult psychiatric departments, what is additionally stressful for them as well as their families. Inpatient treatment of adolescents in adult inpatient units: In Mostar there were 11 and in Tuzla 10 adolescents who were hospitalized in adult psychiatric wards in one year period, their mean age was 17.1 years and about 80% of them were treated with antipsychotics, mostly olanzapine and quetiapine.

PSYCHOTROPIC MEDICATION IN YOUTH- WAYS AND PERSPECTIVES

The use of antipsychotic medication in children and adolescents has increased immensely for a wide range of psychiatric disorders which occur in the age of <18 years. The use of psychotropic medication for children and adolescents should be provided in a holistic way and involve a commitment to the evidence based biopsychosocial perspective, trauma-informed care principles, and system-of-care values and principles. Care that is individualized, family-driven, and youth-guided, with recognition that collaborating with children and families is both an ethical and a pragmatic imperative (Anonymous 2017).

Our research shows certain strengths as well and weakness of Bosnia-Herzegovina child and adolescent psychiatry:

- Departments for child and adolescent psychiatry in Tuzla and Mostar do not have specific wards for inpatient treatment. In the case that hospitalization is necessary, children and adolescents are referred to inpatient psychiatry units in Sarajevo or Banja Luka, what could keep child far from his/her family more than 100 kilometers away.
- If parents refuse to put their child away, and gave their written permission, we have to hospitalize youngsters in adult psychiatric departments.
- Sarajevo and Banja Luka inpatient child and adolescent units do not have indoor /acute wards. Children and adolescents in acute psychiatric state (suicidal, acute psychotic, aggressive...) are often treated in adult closed wards. It is additionally stressful for them and increase a risk for harmful situations
- In Bosnia and Herzegovina there is a legislative restrictions, it means that there is no permission for prescription of psycho-stimulants for any disturbance, what force us to prescribe other medication for children with ADHD.
- Human resources of experienced child and adolescent psychiatrists are our highest strength. Most of them have additional education in group analysis, cognitive behavioral techniques, EMDR. They put a lot of effort, creativity and love in their work with children, adolescents and their families. Psychotherapy is important part of our activities work, and allied professionals are also included in team work.

- Legislative restriction for prescription of psychostimulants in Bosnia and Herzegovina put child and adolescent psychiatrist in the situation to treat minors with ADHD inadequately and to prescribe some other psychotropic medicaments off label (Anonymous 2017)
- The prescription of antipsychotics in children and adolescents treated in child and adolescent psychiatric units in Bosnia and Herzegovina were present in about 25% outpatient and about 40% inpatient treated.
- It was mostly used for psychotic disturbances, intellectual disabilities with psychotic symptoms and autistic spectrum disorder with behavioral problems.
- Mostly prescribed were second generation antipsychotics risperidone and olanzapine, first generation antipsychotics were also used occasionally.

CONCLUSION

The use of antipsychotic medication in children and adolescents has increased immensely for a wide range of psychiatric disorders which occur in the age of <18 years. The prescription of antipsychotics in children and adolescents treated in child and adolescent psychiatric units in Bosnia and Herzegovina were present in about 10% outpatient and about 40% inpatient treated.

It was mostly used for psychotic disturbances, intellectual disabilities with psychotic symptoms and autistic spectrum disorder with behavioural problems.

Mostly prescribed were second generation antipsychotics risperidone and olanzapine, occasionally first generation antipsychotics were also used.

Acknowledgements: None.

Conflict of interest: None to declare.

Contribution of individual authors:

Nermina Kravić: conception and design of the manuscript, manuscript preparation and writing the paper; and gave final approval of the version to be submitted.

Martina Krešić Ćorić: collecting data and analyses of data, participated in revising the manuscript and gave final approval of the version to be submitted.

Marija Burgić Radmanović: collecting data and analyses of data, participated in revising the manuscript and gave final approval of the version to be submitted. collecting data and literature searches, analyses and interpretation of literature,

Nermina Ćurčić Hadžagić: collecting data and analyses of data, participated in revising the manuscript and gave final approval of the version to be submitted.

Mira Spremo: collecting data and analyses of data, participated in revising the manuscript and gave final approval of the version to be submitted.

Zihnet Selimbašić: collecting data and analyses of data, participated in revising the manuscript and gave final approval of the version to be submitted.

Izet Pajević: made substantial contributions to conception and design, and interpretation of data, participated in revising the manuscript and gave final approval of the version to be submitted.

Vesna Horvat: collecting data and analyses of data, participated in revising the manuscript and gave final approval of the version to be submitted.

Sabina Kučkalić: collecting data and analyses of data, participated in revising the manuscript and gave final approval of the version to be submitted.

Mevludin Hasanović: made substantial contributions to conception and design, literature searches, participated in revising the manuscript and gave final approval of the version to be submitted.

Miro Jakovljević: made substantial contributions to conception and design, and interpretation of data, participated in revising the manuscript and gave final approval of the version to be submitted.

References

1. Angold A, Erkanli A, Egger H & Costello E: Stimulant treatment for children: A community perspective. *J Am Acad Child Adolesc Psychiatry* 2000; 39:1-9
2. Anonymous: *Appropriate Use of Psychotropic Drugs in Children and Adolescents, A Clinical Monograph: Magellan Healthcare & Magellan Rx Management, divisions of Magellan Health, Inc., 2017*
3. Costello E: *Early detection and prevention of mental health problems: developmental epidemiology and systems of support. J Clin Child Adolesc Psychol* 2016; 45:710-7
4. Delate T, Gelenberg AJ, Simmons VA, et al: Trends in the use of antidepressants in a national sample of commercially insured pediatric patients, 1998 to 2002. *Psychiatric Services* 2004; 55:387-391
5. Eyles DW, Burne TH & McGrath JJ: Vitamin D, effects on brain development, adult brain function and the links between low levels of vitamin D and neuropsychiatric disease. *Front Neuroendocrinol* 2013; 34:47-64
6. Föcker M, Antel J, Grasmann C, Führer D, Timmesfeld N, Öztürk D, Peters T, Hinney A, Hebebrand J & Libuda L: Effect of an vitamin D deficiency on depressive symptoms in child and adolescent psychiatric patients – a randomized controlled trial: study protocol. *BMC Psychiatry* 2018; 18-57
7. Goodwin R, Gould M, Blanco C, Olfson M: Prescription of psychotropic medications to youths in office-based practice. *Psychiatr Serv* 2001; 52:1081-1087
8. Hasanović M: "A good/beautiful word like a good/beautiful tree..." from the perspective of creative psychopharmacotherapy. *Psychiatr Danub* 2021; 33(Suppl 4):S1065-1080
9. Jakovljević M: *Kreativna psihofarmakoterapija. Pro-Mented.o.o., Zagreb, 2016*

10. Kocijan Hercigonja D, Kozarić Kovačić D & Hercigonja V: Psychopharmacotherapy in children and adolescents. *MEDICUS* 2002; 11:259-262
11. Lorberg B, Davico C, Martsenkovskiy D, Vitiello B: Principles in using psychotropic medication in children and adolescents. In Rey JM, Martin A (eds): *IACAPAP e-Textbook of Child and Adolescent Mental Health*. Geneva: International Association for Child and Adolescent Psychiatry and Allied Professions, 2019; Chapter A.7.:1-25
12. Martin A & Leslie D: Psychiatric inpatient, outpatient, and medication utilization and costs among privately insured youths, 1997-2000. *Am J Psychiatry* 2003; 160:757-764
13. McVoy M & Findling R: *Clinical Manual for Child and Adolescent Psychiatry*. Arlington USA: APA Publishing, 2015
14. Morris J & Stone G: Children and Psychotropic Medication: A Cautionary Note. *Journal of Marital and Family Therapy* 2011; 37:299-306
15. Olfson M, King M & Schoenbaum M: Treatment of Young People With Antipsychotic Medications in the United States. *JAMA Psychiatry* 2018; 72:867-874
16. Pidano AE & Honigfeld L: Pediatric psychopharmacology: context, model programs, and considerations for care. *Psychiatr Serv* 2012; 63:929-34. doi: 10.1176/appi.ps.201100318. PMID: 22810116
17. Rosenthal MB, Berndt ER, Donohue JM, et al.: Promotion of prescription drugs to consumers. *N E J Med* 2002; 346:116-118
18. Skokauskas N, Fung D, Flaherty LT, von Klitzing K, Pūras D, Servili C, Dua T, Falissard B, Vostanis P, Beatriz Moyano M, Feldman I, Clark C, Boričević V, Patton G, Leventhal B & Guerrero A: Shaping the future of child and adolescent psychiatry. *Child Adolesc Psychiatry Ment Health* 2019; 13-19 <https://doi.org/10.1186/s13034-019-0279-y>
19. Steinberg L: A social neuroscience perspective on adolescent risk-taking. *Dev Rev* 2008; 28:78-106
20. Thomas C, Conrad P, Casler M & Goodman E: Trends in the use of psychotropic medications among adolescents, 1994 to 2001. *Psychiatric Services* 2006; 57:63-69
21. Walkup JT: Increasing use of psychotropic medications in children and adolescents: what does it mean? *J Child Adolesc Psychopharmacol* 2003; 13:1-3. doi: 10.1089/104454603321666126. PMID: 12812148
22. Walkup J: Increasing use of psychotropic medications in children and adolescents: What does it mean? *J Child Adolesc Psychopharmacol* 2003; 13:1-
23. Zohar J, Arango C, Veenestra-Vanderweele J, Stahl S, Blier P, Nutt D, Kupfer D, Uchida H, Drago F, Zuddas A, Zalsman G & Correl C: Neuroscience based Nomenclature Child and Adolescent (NbNC&A). Utrecht: European College of Neuropsychopharmacology, 2018. www.ecnp.eu
24. Zito JM, Safer DJ, Valluri S, Gardner J, Korelitz J & Mattison RE: Psychotherapeutic medication prevalence in Medicaid in-insured preschoolers. *J Child Adolesc Psychopharmacol* 2007; 17:195-203

Correspondence:

Nermina Kravić, MD, PhD
Department of Psychiatry, University Clinical Center Tuzla
Ul. Rate Dugonjića, 75 000 Tuzla, Bosnia and Herzegovina
E-mail: kravic.nermina@gmail.com