INTRODUCTION

Post-traumatic stress disorder (PTSD) has been more frequently diagnosed in recent times. Applicable International Classification of Diseases (ICD-10), makes no difference in the diagnostic criteria for PTSD between adults and children (1). The American Psychiatric Association in its fourth edition of the Classification (2) offered the criteria for the diagnosis of PTSD in children, but the criteria had been defined before any serious follow-up studies. In order to compensate for the differences in the verification of expressed symptoms in children and adolescents, DSM-IV-TR has offered some modifications (3). The criteria focus was on re-experiencing, avoidance behaviors and elevated cortical arousal. However, even with such extended criteria, PTSD manifestations in younger children could not be adequately diagnosed. (4).

Following the publication of DSM-IV, more careful examination of the symptoms manifested in children began, as the ones exposed to acute, as well as those exposed to chronic trauma. It was clear that the criteria for the diagnosis of PTSD in children and adolescents cannot be identical to the criteria for adults (5). Different symptoms that had already been identified as markers of trauma in children, especially children younger than 6 years, were systematically brought into connection. The following were identified as the main markers: "traumatic play", then the fears that were not directly associated with the event(s) (e.g. fear of monsters, burglars, vampires), separation fears, "regressive" behaviors such as nocturnal enuresis, encopresis, thumb sucking, uncontrolled behaviors in the form of impulsiveness and attention deficit, with decline in school achievement or social withdrawal and isolation (6). It has been confirmed that the symptoms of PTSD can vary significantly in children and adolescents depending on the traumatic event(s) itself, as well as on the severity and duration of the trauma, and the child age at the time of trauma (7). It became clear that a new classification is necessary to define...
precisely the symptoms of PTSD in preschool children compared to adolescents and adults. Delineation was made for the first time in the DSM-V classification which appeared in 2013, bringing an absolute novelty in the diagnosis of PTSD - Post-Traumatic Stress Disorder for Children of 6 Years and Younger (8). In this way the criteria for the diagnosis became developmentally sensitive, and their use has led to an increase in diagnosis of PTSD in children three to eight times (9). DSM-V classification brings a great change in understanding the experience of a traumatic event(s), describing their reaction and manifestation of post-traumatic reactions. It was pointed out that children do not have to manifest extreme aversion reaction (distress) as a mandatory criterion for the diagnosis of PTSD. The logic of these changes lies in the fact that small children can not verbalize their avoiding reactions or it is too complicated for them to describe in a relevant way their complex cognitive experience of the traumatic event(s), so if there is no adult to testify, there is no way of acquiring information about the reactions (10). Therefore, it was difficult to fit preschool children in the DSM-IV criteria, and almost impossible in the ICD-10 classification adjusted to the adults.

The essential significance of these revolutionary changes in the classification should be reflected in more a precise diagnosis of the disorder and implementation of early intervention and prevention of psychosocial consequences.

Diagnostic criteria for PTSD

The DSM-5 classification criteria for clinical diagnosis of Post Traumatic Stress Disorder in preschool children are developmentally sensitive and contextually more specific in comparison to the criteria for school children and adults (8).

The first criterion brings before a diagnostician the task of determining whether an individual has been exposed to a traumatic event. DSM-V gives more potentially traumatic stressors compared to the previous classification and those are: death, death threat, real or threatening serious injury or actual or threatening sexual violence. Exposure to these risks can occur in one of four ways: (I) directly; (II) directly witnessing the incident; (III) learning that a close relative or a friend was exposed to real or threatening trauma whether it was intentional (eg. violence) or unintentional (eg. a traffic accident). In children older than six years, adolescents and adults, trauma can be a result of repeated or extreme indirect exposure to traumatic event(s) usually during the performance of professional duties (IV), (eg. emergency response (first responders), the duties of collecting human remains, professions exposed to the details concerning children abuse). The last criterion does not include indirect non-occupational exposure via electronic media, television or movies (including the Internet), to which many members of the public (including children) are exposed. The nature of traumatic experience was not specially studied before the publication of DSM-V.

The second criterion (B) describes one or more intrusion symptoms associated with the traumatic event, which did not exist before the traumatic event: (I) recurrent, involuntary, intrusive, distressing memories of the traumatic event(s), (II) recurrent nightmares with the content and/or affect of the dream related to the traumatic event(s), (III) recurrent dissociative reactions ("flashbacks") in which a person feels or reacts as if the traumatic event(s) is recurring in continuum until the extreme reaction of complete loss of awareness of the present environment; (IV) intense or prolonged psychological aversive experience (distress) at the exposure to internal or external cues that symbolize or resemble certain aspects of the traumatic event(s), and (V) marked physiological reactions to internal or external cues that symbolize or resemble certain aspects of the traumatic event(s). In children, certain aspects of the traumatic event may be exhibited through „traumatic play". In children younger than 6 years spontaneous and intrusive memories of the trauma do not even necessarily have to be disturbing for the child. Nightmares can also appear in children and they do not necessarily have to have any recognizable content, and in younger than 6 years the content of terrifying dreams may not be possible to associate reliably with the traumatic event(s).

The "C" criterion refers to one or more symptoms that reflect persistent avoidance of the stimuli associated with the traumatic event (or events) beginning after the traumatic event or growing worse after a traumatic event, such as: (I) avoidance of, or efforts to avoid distressing memories, thoughts and feelings of the traumatic event or of events closely associated with the traumatic ones, and (II) avoidance of, or efforts to avoid external reminders of the traumatic event (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts or feelings about, closely associated with the traumatic event. Reactions refer to children of all ages.

The "D" criterion examines the negative alterations in cognition and mood, highlighting the changes whose onset or worsening occurred after the traumatic event, and is being recorded with 2 or more symptoms: (I) inability to remember an important aspects of the trauma (typically due to dissociative amnesia, and not other factors such as head injury, alcohol or drugs), (II) persistent profusely negative beliefs or expectations of oneself, others or the world (eg. "I am bad!", "No one can be trusted," "I lost my soul forever!" "My whole nervous system is permanently ruined," "The world is dangerous"; (III) persistent distorted cognition about the cause or consequences of traumatic event(s) that lead to blaming themselves or others; (IV) Persistent negative emotional state (eg. fear, horror, anger, guilt or...
the following psychopathological problems associated with the traumatic event(s) can coexist: 
a) depersonalization: described as the subjective experience of "being detached from yourself" or "be as an external observer of the event(s)", "as it is not happening to me "or" like in a dream"; b) derealization: the subjective experience of changed reality (eg. "like things are not real, as if they are different, changed, as they do not exist"). The use of these subtypes implies that symptoms have not appeared as a side effect of substance abuse or other medical conditions (eg. complex partial crisis).

ICD 11 suggestions, in addition to the criteria for PTSD, introduce a new category - Complex PTSD (CPTSD). Complex PTSD primarily refers to the presentation of PTSD with predominant symptoms which are grouped into several broad domains: (I) difficulties in regulating emotions, (II) impairment of the ability to build relationships, (III) changes in the domain of attention and awareness (eg. dissociative phenomena) (IV) negative impact of the belief system, and (V) somatic complaints or disorganization (12). ICD-11 views PTSD as the result of exposure of an individual to trauma that is repeated or prolonged, and in some cases takes a form of interpersonal trauma, often occurring in circumstances where an escape is not possible due to physical, psychological, developmental, familial/environmental or social constraints. ICD-11 will include a description of the development-specific presentation of symptoms, which is primarily referred to children and adolescents, although there are already disagreements about the descriptions not being appropriate and separate from the ones referring to adults (13). Raising the diagnostic threshold for PTSD in the ICD-11 leads to a drop in the percentage of diagnosed children and adolescents by as much as 27% compared to the ICD-10, which carries a concern given that the use of different diagnostic algorithms in practice involve different treatment plans (14).

Some experts argue that people who suffer from complex PTSD should be considered as having a personality disorder (usually borderline personality disorder or personality change after a catastrophic experience) or substance-related and addictive disorders, because it represents a significantly greater therapeutic challenge (15).

Diagnosis of PTSD

There is still no "gold standard" in the diagnosis of PTSD in children and adolescents, which carries the risk for children with PTSD to remain undiagnosed or "overdiagnosed" (16). Children older than seven years usually can read and fill out self-assessment questionnaires by themselves, which creates a possibility for constructing useful, cheaper and less demanding tools to be used for screening, examination and diagnosis, especially with larger group of children and parents. The following recommendations could be extracted as a reliable guide for the diagnosis (17): (I) a
comprehensive physical examination (with a special screening for physical injury or sexual abuse, if suspected); (II) taking a detailed medical history; (III) taking data from multiple sources associated with the traumatic event(s), with special emphasis on family and family relations; (IV) a psychiatric examination and clinical diagnosis according to the criteria of classification systems ICD-10 (ICD-11) and DSM-V; (V) psychological testing; (VI) use of additional assessment instruments: Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA) (18), Child and Adolescent Trauma Survey (19), and Trauma Symptom Checklist for Children (TSCC) (20). Psychiatric comorbidities and family functioning is taken into account using semi-structured and structured assessment tools: The Schedule for Affective Disorders and Schizophrenia for School Age Children (K-SADS) (21), Childhood Family Functioning Scale (DRRI-2 Section: B) Parent Report of Child’s Reaction to Stress.

It is necessary to provide the conditions for conducting interviews with children. The child should feel safe and secure in a new environment, the space should be adequate, and the staff trained.

Comorbidity

Preschool and younger school children depend on the help from the outside world. When exposed to a trauma, they have an intense feeling of lack of control of the the event(s) that inevitably leads to a depressed cognitive style that it is impossible to avoid any "dangerous" situation. As a result, there is reduced resilience and increased vulnerability to future traumatic event(s) and PTSD may remain undiagnosed or misdiagnosed as a "pure" depression, generalized anxiety disorder, or mixed disorder of conduct and emotions (22). This would disable the provision of adequate therapeutic interventions.

School children may develop a fear of going to school (school phobia), to be concerned for the safety of their family and friends (developing separation anxiety), they can develop simple phobias, or the tendency to panic attacks. (6)

In the period of adolescence substance abuse, and alcohol and marijuana are very common in an effort to achieve self-healing and alleviation of the symptoms of PTSD (23). Repeated traumatic experience of abused children significantly increase the risk of developing borderline personality disorder (24), conduct disorder and depression in adulthood. Sexual abuse leaves some lasting effects on the child and affect its fully functioning, from the disturbances in establishing emotional relationships, all the way to dissociative-conversion disorders (25, 26).

Comorbidity at the time of diagnosis is common. The most important comorbid disorders that younger children with PTSD develop are: Reactive Attachment Disorder Syndrome and Attention Deficit Hyperactivity Disorder (ADHD) (27). It is recommended that traumatized children showing an initial clinical presentation of one of these two disorders should be included in the differential diagnostic assessment in relation to PTSD.

In adolescents and school children, the most commonly diagnosed comorbid conditions, with significant overlapping of symptoms, are depressive disorders (22).

Females are twice as likely to develop PTSD compared to males, but males frequently exhibit conduct disorder, personality disorder, antisocial behavior, criminal behavior as comorbid conditions, especially after a significant physical trauma (28).

Studies that have compared the groups of male subjects with and without PTSD have shown that men who suffer from this disorder are seven times more likely to develop depression, six times more often they develop generalized anxiety disorder, and are three times more likely to abuse drugs and the risk of alcohol abuse is doubled (29).

Treatment

PTSD therapy includes a package of various interventions directed towards the child, parents or guardians with the support of a school expert team (30). Before engaging in any form of therapy, the termination of all forms of trauma is necessary. This often requires the involvement of social services, police and courts (31).

As a first-line treatment of PTSD in children and adolescents, psychoeducation and psychotherapy for children and parents are recommended. Psychopharmacotherapy belongs to the multimodal approach, especially in complex and comorbid conditions (32).

The introduction of early psychological interventions in pre-school and school children, contrary to the original statements, did not show any significant effectiveness in a group of children under six years of age (33). Because of the limitations of research and a scarce data base, there is still no evidence-based data that would give us any clear guidelines and recommendations about the future treatment of children of this age. It is suggested that premature disclosure of the event(s) in traumatized children (especially if sexually abused), can cause complications, and that there is a risk of the child sensitization if reminded of the traumatic event(s) (traumatizing), without allowing sufficient time to influence the creation of experience (32, 34). However, a brief consultation with the parents in terms of psychoeducation and training in the field of dealing with stress should still be available from clinicians, and in a population of school children intervention can be used gradually with children who are at risk of developing long-term inability to integrate into the environment (33).

Psychotherapy

Psychotherapeutic intervention with a child typically includes the following components:
psychoeducation, direct exploration of the trauma, techniques of controlling and managing the symptoms, examination and modification of the wrong cognitive attitude in connection with the trauma.

Numerous studies point to new evidence to support the efficacy of cognitive behavior therapy (CBT) focused on trauma (Trauma Focused Cognitive Behavior Therapy - TF-CBT) in terms of symptom relief, mitigation of depression, behavior disorders and general functioning in children with PTSD (35).

Desensitization therapy with quick movements of the eyeballs - Eye Movement Desensitization and Reprocessing (EMDR), is a treatment that has found wide use in many European countries, and therefore there is very popular belief that it is more effective in the treatment of PTSD than the others. In a comparison of its effectiveness in children aged 8-19 years, there was not any significant difference in efficacy between different treatments. However, the children included into TF-CBT have shown significant improvement of comorbid conditions, including depression and symptoms of hyperactivity, compared to the children in the EMDR program (36).

There are also significant research results regarding the success in risk reduction through the forms of family therapy (Risk Reduction through Family Therapy - RRFT), compared to a modified TF-CBT for adolescents who have problems with substance abuse. In this population, RRFT has shown more significant efficacy in the treatment of PTSD and comorbid conditions, depression, substance abuse and internalized symptoms compared to the control group (37).

A general impression is that parents should be involved in psychotherapeutic intervention designed for the children with PTSD (38, 34). It is suggested that the treatment should start with the psychoeducation of parents, including the "normalization" and explanation of posttraumatic reactions, as well as adequate information about the way parents can help the child in the home environment. If there is evidence that the parents also show a significant emotional stress (as a result of traumatic experiences), the intervention should be directed towards exploration and resolution of the (parental) experience. This kind of approach offers the possibility that parents could later respond better to the emotional needs of their child. The school system, teachers, should be trained so that they can understand and adequately respond to the emotional needs of the child (33).

An increasing number of web-based treatments offer a wide range of useful interventions. An Internet-based application that offers an adjusted TF-CBT, "Triangle of Life", is also available as a version for children (39).

Pharmacotherapy

There is still little information about the functioning of psychopharmacological drugs in children with PTSD, because of the lack of a sufficient number of empirical studies (31). Certain drugs may show rather good results in the treatment of primary symptoms of PTSD in children. Effective pharmacological agents would be the ones that: a) are directed to cut-off the symptoms; b) improve the quality of life of the child/adolescent, allowing normal growth and development in the long term; c) allow the psychotherapeutic intervention to facilitate the processing of emotionally disturbing material by the traumatized children themselves, with a professional guidance in the process.

Selective serotonin reuptake inhibitors (SSRIs) have a wide range of application in the treatment of PTSD in adults, with very few side effects. Therefore, they are seen as the first line of psychopharmacological drugs to combat the symptoms of PTSD, which still has not been confirmed when it comes to children. In the treatment of children, they have been approved for the treatment of depression and obsessive-compulsive disorder (sertraline, fluoxetine). There still have not been sufficient controlled trials of SSRIs in the treatment of PTSD in children, but there are open-label data related to citalopram and its effectiveness in all clusters of symptoms in adolescents (40). A caution when giving SSRIs is related to the possibility of excessive activation and onset of irritability, insomnia, attention deficit, and there is a warning of an increased risk of suicidality. It is therefore advisable to consider an alternative medication or mandatory inclusion of psychotherapy along with the use of SSRIs in the treatment of children with PTSD (41). Other serotonergic agents, such as trazadone (serotonin antagonist), and cyproheptadine (serotonin and histamine antagonist) were studied in a group of children, with limited effectiveness in sleep regulation and the reduction of the nightmares, but the available data is of low validity (42).

Adrenergics drugs reduce sympathetic arousal and have proven to be effective in the treatment of irritability, symptoms of re-experiencing, impulsive reactions, sleep disturbances and nightmares that are found in PTSD (31). Clonidine (a2-adrenoceptor antagonist) administered orally (0.05 to 0.2 mg/day) lowers the level of anxiety, excitement, insomnia, impulsivity and aggressive behavior (43). In one study, data were obtained that guanfacine is effectively similar to clonidine, especially in reducing nightmares, but it was most useful if administered soon after the onset of symptoms of PTSD (44). Clonidine and guanfacine are considered especially effective in the treatment of PTSD in children with ADHD (31). It is believed that propranolol (beta-adrenergic blocker) significantly reduces neural activity in the amygdala, cognitive arousal and symptoms of imposing thoughts (intrusive, obsessive thoughts), and therefore a post-traumatic stress reaction itself (45). However, the efficacy of propranolol has not been consistently confirmed in the studies (46).
Although randomized clinical trials have demonstrated the effectiveness of tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) in the adult population with PTSD, there are still no adequate controlled studies that would evaluate them in children and adolescents, primarily due to cardiac and anticholinergic side effects. One randomized study indicates the effectiveness of low-dose imipramine (1mg/day) in the treatment of an acute outbreak of stress symptoms and their complete remission (42).

In several studies, level “E” and level “F” atypical antipsychotics risperidone, olanzapine, and quetiapine have been described as effective in controlling a wide range of symptoms of PTSD in children: dissociation, anxiety, depression, anger, and are sometimes recommended for patients with refractory PTSD symptoms and mixed clinical presentation of PTSD and comorbid psychopathological manifestations (paranoid, pseudohallucinations, intense flashbacks, parasuicidal behavior, explosive and overwhelming rage and psychosis) (31).

Antiepileptics and psychostabilizers regulate excitatory neurotransmitter glutamate and inhibitory neurotransmitter GABA. Carbamazepine has been proven to be effective in reducing re-experiencing symptoms in small, open trials with children and adolescents (300-1200 mg/day, level in the serum of 10 to 11.5 mg) (47). The administration of carbamazepine requires laboratory monitoring, while the use of lamotrigine and topiramate requires slow titration due to serious side effects in case of a rapid introduction.

The usefulness of benzodiazepines for PTSD in children and adolescents has still been under examination. The combination of a large number of side effects, and the lack of evidence of its efficacy in traumatized adults, make them a poor choice for young patients (42).

Conclusion

Changes in the diagnostic consideration of PTSD, especially in children of an early age, brought a revolutionary change in the perception of an accurate diagnosis and adequate therapy. The essential significance of the changes lies in the prevention of serious psychosocial consequences. As a first-line treatment of PTSD in children and adolescents, psychoeducation and psychotherapy for children and parents are the recommended approaches. Psychopharmacotherapy still represents a part of the multimodal approach, especially in complex and comorbid conditions, and is not yet a well-explored field, but instead requires further research in well-controlled studies.

References

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POSTTRAUMATSKI STRESNI POREMEĆAJ KOD DECE I ADOLESCNATA – KLINIČKA PREZENTACIJA, DIJAGNOZA I TERAPIJA

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