

The Treatment of Autistic Children with Risperidone

Katarina Dodig-Ćurković¹, Mario Ćurković², Josipa Radić³ and Mislav Radić³

¹ »J. J. Strossmayer« University, Osijek University Hospital Center, Department of Child and Adolescent Psychiatry, Osijek, Croatia

² Family Medicine Office, Health Center Osijek

³ University of Split, Split University Hospital Center, Department of Internal Medicine, Croatia

ABSTRACT

Autism is a pervasive developmental disorder characterised by impairment in social interaction and communication, with unusual behavior. In some cases the pharmacotherapy is prescribed and the most studied antipsychotic drugs include haloperidol and risperidone. In this paper we displayed the treatment of two cases of autism in boy and girl with risperidone. With the use of risperidone in girl, we have achieved reduction of psychomotor symptoms and reduction of hetero-aggressive and self-destructive behavior, and in boy we have also achieved reduction of psychomotoric symptoms, with improvement in contact with his surrounding, he had less learning problems and he has felt familiar not only with his mother, but with other persons. Research on the use of risperidone in the treatment of autistic disorders among children in Croatia are rare, given the limited use of risperidone in children younger than 15 years, the question arises about the need to expand the scope of application of risperidone in younger age groups.

Key words: autism, risperidone, self-injurious behavior, social isolation

Introduction

Autism is a pervasive developmental disorder characterised by impairment in social interaction and communication, with unusual behaviour¹.

Autistic disorder is believed to occur at a rate of about five cases *per* 10 000 children (0.05 percent). The onset of autistic disorder is before the age of 3 years and is four to five times more frequent in boys than in girls. Girls with autism are more likely to have more severe mental retardation. The causes of autism spectrum disorders are unknown, although genetic and environmental influence have been implicated. There is increasing evidence that people with autism spectrum disorder have abnormalities in the serotonergic system^{2,3}.

There are limited options for pharmacological therapeutic interventions in children with autism disorders and some studies showed that risperidone as an atypical antipsychotic may be effective for the treatment of people with autism and intellectual disabilities⁴.

The most studied antipsychotic drugs include haloperidol and risperidone⁵. In low dosages, they have been

shown to reduce repetitive behaviors (stereotypes) and social withdrawal, as well as a number of related symptoms, such as a hyperactivity, aggression, self-abuse behavior, liability of mood and irritability. All the listed symptoms have appeared in adult patients with schizophrenia, where also with the application of atypical antipsychotics may affect on described clinical picture⁶.

70% of children have mild to moderate learning disability, the remaining 30 % with normal IQ are classified as either *high-functioning autism* (with language difficulties) or Asperger's syndrome (with normal language). 1–2 % of those with autism have a normal life; 5 to 20 % of those with autism have a borderline prognosis; but 70 % are totally dependent upon support⁷.

In this paper we displayed two cases of autism in boy and girl with confirmed diagnosis of autism according to DSM-IV (Diagnostic and Statistical Manual of Mental Disorders), ICD-10 (International Statistical Classification of Diseases and Related Health Problems) classification criteria.

Case Reports

Example number 1

NN is a girl born in complete family as the youngest child of four children. The oldest sister was treated by psychiatrist because of enuresis and encopresis.

Pregnancy and childbirth have passed without any problems. Body weight after birth was 3450 grams and body height was 50 centimeters. Girl regularly received all necessary vaccines, she did not have any of pediatric infectious diseases. She started walking with ten months, she began to speak with twelve months of age, but before she came to the first psychiatric examination (at the age of five years) she did not establish control of sphincters.

First review by the psychiatrist was in 1997 year at the age of five years. The mother brought her child because she was seemed that the girl was »hyperactive«. Mother described that the girl was not sleeping during the night, frequently was awoken, she was restless, constantly had the need to touch things and people, was afraid to stay alone and sought the light. She often cried at night, if something was not according to her gnawed at her hands, struck the head of the table, two months before the review she has rejected to communicate, and people in surrounding area have found that she was less communicative in relation to other children of her age. She was disturbed by sounds, covered her ears with hands, screamed, struck the head of the wall, swung and swayed like pendulum, refused to play with peers. We have found that the all listed symptoms started at the age of less than three years. She has also reacted to changes at home, such as changes in the position of furniture with frequent patterns of self-destructive behavior.

The only words pronounced by her were »mom« and »dad« and only in communication with toddlers, with the others she did not communicate. Every night she was enuretic and when she was angry struck the head of the floor. We have also noticed an increase in body weight, the mother alleged that the girl had a stronger appetite. She often gnawed her hands while being wounded, so we had to wrap her hands that they can not easily hurt.

At the age of 5 years treatment started with haloperidol (1/mg in the morning and 1/mg at the evening) with lower doses of anxiolytics and then we noticed that the girl was calm, but still uninterested in the environment and play with peers. Haloperidol dose was increased to 2 mg three times a day when the girl was five and a half. After examining the medical records, it was evident that the girl regularly had outpatient treatment at child's psychiatrist during following three years, with minimum correction therapy (haloperidol, diazepam, oxazepam). From the described behavior it was evident that the girl was a bit calmer, but still liked throwing things around the house, could not stay alone without parental supervision, enjoyed watching her mother cooking, watched just commercials on tv, she was less aggressive, she did not trash her head anymore and sometimes she stayed alone in the bedroom.

At that time she was taking the recommended therapy of haloperidol 2,5 mg two times a day with lower doses of anxiolytics. At the age of eight, 3 mg dose of risperidone was introduced in place of haloperidol in the evening.

The reason for the change in therapy was the occurrence of tics and stereotypes (possible adverse effects of haloperidol). The family said that the phenomenon of tics increases aggressive behavior in girl, during the night constantly wet the bed, tend to frequent night awakening. Evaluation is done by psychologist and the IQ level was 33. The finding was noted that there are serious intellectual damage and that the person is totally incapable of independent life and requires continuous care from other persons.

After the introduction of risperidone, girl was psychomotorically more tranquil, rarely behaved self-destructive, better sleep, but still indifferent for surrounding and daily events, more time was carried out in the room, usually near her mother and sister and still was needed to wrap her hands. In the therapy was introduced meprobamate in the dosage of three times a day.

At the age of nine years, mother said that the girl during the day was more tranquil, but still did intentional self-injury (was observed bruises by the body, continually held hands in the mouth, was less aggressive towards family members, except when they hindering her to make self-inflicted injury (therapy: risperidone, biperidin, meprobamate).

At the age between nine and ten years was continued outpatient psychiatric treatment, but due to enhanced autodestructivity, in the therapy was re-introduced haloperidol with promazin and diazepam. On several occasions was made the laboratory control of lipids and liver enzymes: the values were within the reference ranges. With regard to the increasing fear and avoidance of the outside world, the family became increasingly difficult to bring a girl on the reviews. At the age of 13 years was noticed that the girl has increased whole body tremor, not went outside and one year after, family has managed to bring the girl to the control examination. In the therapy was re-introduced risperidone in dosage of four mg daily, divided in two doses, with lower levels of anxiolytics.

At the age between 14 and 15 years according to the existing outpatient documentation it was shown, that the girl during this period of time was psychomotorically more tranquil, had better sleep, but she was completely dysfunctional when it comes to her social and working life, she was dependent on others and their continuing care. Diagnosis was autism with a very high risk from self-inflicted injury.

Chronological review of therapeutic interventions in girl is shown in Table 1.

Example number 2

MM is a boy and the only child in primary family.

First psychiatric examination was at the age of 6 years.

TABLE 1
PSYCHIATRIC INTERVENTIONS IN GIRL DEPENDING ON
AGE – EXAMPLE NUMBER 1

Age	Psychiatric interventions
<3 years	First observed symptoms of disease by parents
5 years	First review by child psychiatrist
5 years	Haloperidol – 1 mg twice daily
half past five years	Haloperidol – 2 mg three times a day
6 years	Haloperidol – 2,5 mg twice daily anxiolytics – lower doses
8 years	Risperidone – 3 mg in the evening
9 years	Risperidone meprobamate biperidin
>13 years	Risperidone – 4 mg in two divided doses

According to anamnestic findings, mother's pregnancy was burdened by constant conflicts with the husband, who was opposed to pregnancy, allegedly now accepted boy. During pregnancy the mother has taken diazepam.

By birth, boy spent some time in the incubator for difficulty breathing, after three weeks was released to home care. He started to walk with fourteen months, spoke with two years. To third year of life established sphincter control. The same year began to attend children's nursery, but with many difficulties. In the children's nursery was restless, behaved hyperactive, disobedient, often in conflicts with other children, and governess recommended them to seek help. We found out from the family that the boy at the age of two years had difficulties with sedation and his mother had to hold him by the hand and swing him. He expressed tics of the head, especially the movements of the eyes and lips. As a small child on several occasions he bit out lower lip to the blood. During his stay in children's nursery, all the time awaited his parents at the window, less communicate with peers. He did not play with toys the same way as the other children. Parents have learned him all the letters and numbers up to hundred when he was five years, easy to remember all the songs by heart, but could not distinguish colors. In a children's nursery it was noticed that he did not know draw, rejected to sit quietly in one place, for a longer time. Sometimes for no reason at all said something, spoke puzzlingly, without a motive and then can not remember what was uttered.

It was observed that the boy's mother had lower mood level, weepy, scared, and the father of the boy was extremely negativistic, he did not want to help, emotionally cold and restrained toward the boy. Additionally, mother described a number of adverse family circumstances which further affect her psychological functioning (co-existence with father-in-law, aggressive brother-in-law). Working diagnosis was hyperkinetic disorder and in the therapy was introduced sulpiride and vitamine B complex. During the following control was found irregularly taking medications, it was stated that the boy was still hyperactive, hardly held attention, protruded the tongue, bit

lower lip, touched objects in the room, had a constant need to touches certain things or people around himself and upon arrival at kindergarten, mother have allways found himself alone, without the society of children. He was included in the individualized work with psychologist and defectologist, with the control examinations by psychiatrist.

Mother was motivated to cooperate, she was constantly in touch with the latest literature, has read about disorders that were noticed in boy, she was very motivated for any kind of help. In the boy were significantly expressed stereotype actions, neologisms, hardly fits in the group of peers, they did not accept him, described him as a bizarre.

At the age of 6 years, first psychological tests were made and described uneven intellectual development in the broad limits of average, under developed graphomotoric skills. Psychological retest displayed under average global intellectual development (IQ was 70), child started first grade of primary school with an adjusted programme. In the school he displayed a number of characteristics of poor adaptation, tics and grimacing were emphasized, and pharmacotherapy was introduced.

At the age of nine years in the therapy was introduced risperidon at a dose of 0.5 ml in the evening (liquid form). During the control examinations because of psychomotoric disturbance and sleep disturbances, in the therapy was also included diazepam at a dose of 2 mg in the morning and afternoon and 5/mg in the evening. Patient became psychomotorically more tranquil, with better sleep, but still expressed tics, stereotypes, oscillations in the mood, separation fears. It was made elaboration, because of selection of adequate education forms, and was recommended individualized approach with adapted programme. Therapy for further treatment is risperidon at a dose of two ml daily and diazepam as required.

At the age of ten years, was done retest by psychologist, psychological retest displayed global intellectual functions at the level of mild mental retardation, child was moved to a school with special conditions and continuing education under special programme.

Subsequently testing continued in Zagreb at the age of eleven years and set suspected to hyperkinetic disorder.

TABLE 2
PSYCHIATRIC INTERVENTIONS IN BOY DEPENDING ON
AGE – EXAMPLE NUMBER 2

Age	Psychiatric interventions
<3 years	First symptoms
6 years	First examination by child psychiatrist IQ=70 sulpiride and B vitamins as a therapy
9 years	Risperidone liquid – 0.5 ml in the evening
10 years	Mild mental retardation
11 years	EEG – irritative changes
13 years	Diazepam – 2 mg in the morning and afternoon and 5 mg in the evening risperidone liquid – 2 ml once a day

der, Tourette syndrome and epilepsy-incomplete differential diagnosis (MRI of brain was within the limits of normal, EEG irritative changes).

In the contrary he has overcome some abstract skills such as playing chess (he also learned the alphabet between second and third years of age and many other informations), but with weaker follow-up of a story content, less understanding of social interactions.

Given results besides of disharmonic, confirmed also a slow pace of cognitive maturation, through a series of features of pervasive developmental disorder, highly functioning type of child with autism.

Chronological review of therapeutic interventions in boy is shown in Table 2.

Discussion

The both first and second-generation antipsychotics have shown safety and efficacy in short-and long-term studies in autism. Safety concerns associated with treatment include the risk of drug-related dyskinesias, which is greater with the first-generation drugs (haloperidol, flufenazin), and the risk of weight gain and associated metabolic problems (increases in glucose and lipids), which is greater with the second generation agents⁸.

Risperidone has been shown to reduce repetitive behaviors and social withdrawal, hyperactivity, aggression, self-harm behavior, temper tantrums, liability of mood and irritability⁶. It is also has been proved helpful in treating children and adolescents with autism spectrum, conduct and bipolar disorder, Tourette's syndrome and schizophrenia⁹. Risperidone is a high potency antipsychotic with combined dopamine D2 and serotonin 5-HT₂ receptor antagonist properties, has been used to subdue aggressive or self-injurious behaviors. Several reports have suggested that risperidone is effective in diminishing aggressiveness, hyperactivity and self-injurious behavior in children with autistic disorder. For children with autism, lower dosages ranging from 0.5 to 4 mg *per* day are generally used¹⁰. Treatment with atypical antipsychotic olanzapine also can be beneficial in alleviating some behavioral symptoms (irritability, hyperactivity/non-compliance, lethargy), associated with autism¹¹.

The average dose of risperidone in presented cases was between two and four mg *per* day. It is very important careful drug titration, usually start with half ($\frac{1}{2}$) or one (1) mg in the morning, and then gradually increase the dose in order to prevent adverse effects¹².

It is important to educate parents of children about possible side effects of treatment with antipsychotics. Most often side effects are feeling of stiffness, primarily in the neck and spinal muscles, sedation and weight gain. In rare cases also galactorrhoea. This approach can help parents to distinguish between symptoms of disorder and adverse drug effects, reduce their anxiety and intimidation, and simultaneously upgrade compliance and trust between parent and child.

In the section about the girl, example number 1, a combination of risperidone and lower doses of anxiolytics have been successful in reducing self-inflicted injuries, bouts of aggression and stereotypes, but still largely marked social inhibition, inability to achieve contact with the environment and any involvement in the school environment. It is hampered continuous arrival of girl at the regular psychiatric reviews, because it is observed that during his stay with other children in the waiting room the girl became very agitated, self-destructive, parents have trouble controlling her behavior and reactions. Now girl has eighteen years, remains on treatment with risperidone, with regard to the clinical picture described and marked side-effects from the typical antipsychotic haloperidol (tics, tremor, stereotypes), she has got an approval by the competent committees at the Croatian Institute for Health Insurance to continue treatment with risperidone at a dose of four mg daily. Prognosis is very uncertain.

In the section about the boy, example number 2, we have also managed to reduce hyperactivity with risperidone, partially improved his attention and concentration, and it is possible through a program tailored to his abilities, attempts to implement school training. However, it is still present social inhibition, more difficult inclusion into group of peers and making contacts with other children.

With the presented cases, we have tried to show how difficult is to treat autistic children, because there are extremely limited opportunities for intervention with medications, according to a survey of literature, in the first place are mentioned risperidone and haloperidol. These medications are usually studied in adult schizophrenic patients, and there are frequent dilemmas on the use of this group of drugs in children. It is important to always take into account the adverse effects of this group of drugs, time to inform parents about them and have continuous monitoring of children. We have noticed that is often required professional assistance to parents of such children, because of the constant confrontation with difficulties and unpredictable course of illness and fear of the uncertain future of their children.

Conclusion

Antipsychotics as drugs are intended primarily for the treatment of adult patients with psychotic disorders, but showed a favorable effects on the symptoms in autistic children, especially risperidone. Some studies indicate that the earlier use of antipsychotics in autistic children may have protective effect on IQ, which further justifies the use of these drugs in early childhood¹³. Research on the use of risperidone in the treatment of autistic disorders among children in Croatia are rare, given the limited use of risperidone in children younger than 15 years, the question arises about the need to expand the scope of application of risperidone in younger age groups.

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K. Dodig-Ćurković

*»J. J. Strossmayer« University, Osijek University Hospital Center, Department of Child and Adolescent Psychiatry, Josipa Huttlera 4, 31000 Osijek, Croatia
e-mail: kdodig@yahoo.com*

LIJEČENJE AUTISTIČNE DJECE RISPERIDONOM

SAŽETAK

Autizam je pervazivni razvojni poremećaj, obilježen oštećenom socijalnom interakcijom i komunikacijom i neobičnim ponašanjem. Pojedini slučajevi su zahtijevali farmakološko liječenje, a najistraživaniji lijekovi za liječenje autizma kod djece su antipsihotici risperidon i haloperidol. U ovom radu smo prikazali liječenje dva slučaja djece s autizmom primjenom risperidona. Kod djevojke smo smanjili psihomotoričke poteškoće, heterodestruktivno i autodestruktivno ponašanje, a kod dječaka smo smanjili psihomotorne smetnje, poboljšali smo kontakt sa okolinom, ublažili smetnje učenja i omogućili da funkcionira i u društvu ostalih osoba, a ne samo unutar obitelji. Istraživanja o uporabi risperidona u liječenju autističnih poremećaja kod djece u Hrvatskoj su rijetka, a s obzirom na ograničenost uporabe risperidona za djecu mlađu od 15 godina, postavlja se pitanje o potrebi proširenja indikacijskog područja uporabe risperidona kod mlađih dobnih skupina.