Original article:

Juvenile depression treatment with antidepressants from the selective serotonin reuptake inhibitors group

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Abstract:

Objective. The article presents the juvenile depression treatment effectiveness with antidepressants of the selective serotonin reuptake inhibitors group (SSRIs). ***Materials and methods.*** 182 patients were examined, including 114 men (62.6%) and 68 women (37.4%), age range 16 to 25 years, on treatment in a psycho-neurological dispensary in the city of Korolev (Russia, Moscow region) from 2014 to 2018. ***Results and Discussion.*** Main characteristics comparison of SSRIs antidepressants therapeutic effect in young men and adults of mature age revealed statistically significant age differences concerning the onset rate and these drugs antidepressant effect characteristics, as well as the adverse events nature. ***Conclusion***. The SSRIs antidepressants clinical action regularities for depression treatment in adolescence, their therapeutic effect features and dynamics allow us to state adequate indications for the these drugs administration in adolescence, considering their age specificity.

Keywords: juvenile depression; therapy; selective serotonin reuptake inhibitors; Paroxetine; Citalopram; Fluoxetine; Sertralin; Fluvoxamine.

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Introduction

The problem of determining the occurrence conditions and clinical manifestations patterns for depressions that manifest in adolescence is among the most pressing and complex clinical psychiatry tasks. The present necessity to address these issues is of paramount importance due to the sharp increase in this pathology prevalence among young people and adolescents.

According to a number of authors, depressive disorders various forms can be observed among 15–40% of young men and adolescents, making up more than 50% of the total psychiatric morbidity in this age group[1-7]. In addition, the extremely high suicidal attempts frequency, that reaches 40–55% for depressions at this age, as well as the completed suicides threatening level, makes these states more dangerous and requires urgent professional intervention[8-11].

One of the common depression causes in adolescence is the body hormonal changes[12, 13]. Young people in maturation period can be characterized with especially categorical expressions and views, as well as egocentrism and youthful maximalism. As it often seems to them, they are neither listened to, nor seen or noticed, and the needs get simply ignored, which often leads to family conflicts, communication problems among their peers, inability to build ties with teachers and, in case these conflicts remain unresolved, they result in depression[14]. Probable

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causes of depression include inability to follow ideal standards, breaking with friends and moving to another place of residence, loneliness, excessive workloads, problematic relations of parents such as divorce, lack of attention to the needs of growing up child, illness or death of any family member. Young people may suffer from depression due to the fact of living in families with small incomes so that they cannot afford much of what their peers own. As it often happens, teenage depressions are associated with personal achievements, especially if they neither meet the expectations of other adults nor of the young man or girl himself[12, 15]. In recent years, teenage depression is often closely linked to World Wide Web. Young people headlong into the virtual reality world and at the same time lose touch with the reality[16,17,18].

Thus, the particular complexity of juvenile depressions treatment is related to a number of reasons, which include, on the one hand, atypical clinical picture, and, on the other hand, adolescent period psychobiological features due to the lack of basic personality structures development such as emotional (timic) and intellectual (cognitive), as well as the ontogenetic development incompleteness, morpho-functional maturation of nervous, endocrine and immune systems among young men. All this leads to a greater side effects frequency and their certain manifestations during psychopharmacotherapy[12, 15, 19].

Selective serotonin reuptake inhibitors (SSRIs) antidepressants, which are close to tricyclic antidepressants and sometimes even surpass them with their clinical efficacy, but are deprived of numerous limitations inherent in tricyclic antidepressants[20-22.]

At the present time, there is data of successful experience with serotonergic antidepressants use for adolescent and juvenile depressions treatment[12, 15]. However, no special clinical study on the SSRIs effectiveness in adolescent depression was performed with a detailed relationship analysis with such important parameters as the depressive state nosological identity, severity, typological picture, depressive syndrome dominant affect (including anxiety, apathy and hypothymia), as well as the action comparison of the drugs that fall into this category. Date absence hinders the adequate criteria development for the SSRIs therapy effectiveness in juvenile depressions, that are extremely relevant in modern practical psychiatry. Therefore, such a study requires standardized conditions for the SSRIs use and the drugs use as monotherapy, which somewhat limits the patient group with juvenile depression.

The study aim was to determine the response characteristics of patients with adolescent depressions to SSRIs antidepressants, relationship between psychopathological depression variant, dominant affect nature, depression nosological nature and SSRIs therapeutic efficacy in general and for each drug separately.

Materials and study methods

The study was conducted in the period from 2014 to 2018 in the Psychoneurological specialized clinic in Korolyov (Russia, Moscow region). A group of patients for this study was formed according to the following criteria:

a) inclusion criteria: depression manifestation in adolescence, that includespatients (age range 16-25) in accordance with the common modern scale; moderate and severe depression (score on the Hamilton Rating Scale for Depression (HDRS) at the time of inclusion in the study should be at least 17); Clinical Global Impression scale (CGI) severity level from “moderate” to “significant”.
b) exclusion criteria: Presence of psychotic disturbances in the aspect of depression (i.e. first grade symptoms after Schneider); information about abuse of psychoactive substances; significant CNS organic damage; chronic somatic decompensated diseases.
c) Clinical, psychopathological, psychometric, and clinical and statistical methods were selected as the main ones in work implementation.
d) During the clinical and psychopathological examination of patients, detailed information was collected about the disease previous course, depressive state development characteristics, its psychopathological structure and dynamics.
e) In psychometric method, Hamilton Rating Scale for Depression was used to assess the depressive symptoms severity and the drugs therapeutic effect[23, 24].
f) The depressive symptoms severity was assessed before the treatment initiation with antidepressants from the Selective serotonin reuptake inhibitors (SSRIs) group — the first visit was considered the day zero, then at 7, 14, 28 and 42 days of therapy. In addition, the dynamics assessment of patients depressive state and its severity was carried out using CGI scale and was carried out on the same days. In order to note the side effects that occurred during therapy, UKU side effect rating scale was implemented, which consists of four subscales, allowing to divide side effects into mental (UKU-1), neurological (UKU-2), autonomous (UKU-3) and others (UKU-4).

g) Using the clinical and statistical method, we analyzed the obtained data in the Statistica 6.0 for Windows using non-parametric methods (Wilcoxon's paired test, Mann-Whitney U test). The drug greatest impact interval as determined by cluster analysis method (for the overall effect and for the each of its components).

h) The studied sample group consisted of 182 patients, including 114 men (62.6%) and 68 women (37.4%), age range 16-25, average age 20.15 years. Average number of postponed depressive phases was 2.6 (from 1 to 6 phases at the time of the study). The disease duration ranged from 4 months to 6 years (mean value 3.6 years). Current depressive episode lasted from 3 weeks to 18 months (mean value 9.23 months).

i) According to the nosological assessment, patients were distributed as follows: 93 (51.1%) of them were diagnosed with affective disease (manic-depressive psychosis, adolescence cyclothymia), 52 (28.6%) had low-progressive schizophrenia with affective disorders, 37 (20.3%) - psychopathy pubertal dynamics of schizoid, mosaic or psychasthenic circle.

j) According to the categories of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), the distribution of patients was as follows: bipolar affective disorder (F31.3; F31.4) - 43 people (23.6%); recurrent affective disorder (F33.1; F33.2) - 54 people (29.7%); schizotypal disorder (F21.2; F21.3) - 49 people (27.0%) and personality disorder of schizoid, obsessive–compulsive, anxious, dependent and mixed type (F 60.1; F 60.5; F 60.6, F 60.7; F 61.0) - 36 people (19.7%).

k) In the study the need to select only those patients with juvenile depression was taken into account, to whom it was possible to apply the monotherapy method with antidepressants without antipsychotics. Due to this, only the following typological varieties were included in the present study, as follows: "adolescent insolvency" depression type - 40 observations (22.0%); depersonalization depressions - 36 (19.8%); psychasthenic depressions - 38 (20.9%); depression with obsessive-phobic disorders - 47 (25.7%); senesto-hypochondriac depression - 21 (11.6%).

l) According to the dominant affect type, in accordance with the general depressions typology [25], the depressions studied could be divided into alarming - 73 observations (40.1%), apatho-dynamic - 66. (36.3%) and dreary - 43 (23.6%).

m) For a more accurate depressions selection of different severity, Hamilton Rating Scale was used. Cases with total score in the range between 17 and 27 points were regarded as moderate depression (110 patients - 60.4%), depressions with total score over 27 (72 patients - 39.6%) were classified as severe.

n) On General Clinical Impression scale (CGI), depression severity was rated as "moderate" (64 people — 35.2%), "marked" (88 patients — 48.3%) and "severe" (30 patients -16.5 %).

o) Depending on the therapy carried out by random selection, following five therapeutic patients groups were obtained: paroxetine - 43 people (23.6%); Citalopram - 42 (23.1%); fluoxetine - 34 (18.7%); sertraline - 33 (18.1%); fluvoxamine - 30 (16.5%). These groups turned out to be comparable in their main clinical and demographic characteristics. The only exception was the therapeutic group who received fluoxetine. Since this drug has a pronounced stimulating effect and ability to provoke phase inversion[26], for therapeutic and ethical reasons, we did not prescribe it to patients with anxious depression and this disease bipolar type.

p) The doses of each of the antidepressants prescribed during the study were selected individually, changing depending on the patient's tolerance, mental state and corresponded to the recommendations of the manufacturers.

q) In order to determine the clinical action age-related features and SSRIs antidepressants side effects in adolescent patients, a comparison was made of similar indicators of the depression treatment in patients of mature age, conducted according to the same standardized regimens. For this purpose, the results of studies were used, that were conducted in the time range 2014-2018 in the neuropsychiatric dispensary in the city of Korolev (Russia, Moscow region). This control group consisted of 144 patients (average age - 35.7 years) who received monotherapy with one of the serotonergic antidepressants: paroxetine, 39 patients, citalopram - 23 patients, fluoxetine - 30 patients, serotralin - 24 patients and fluvoxamine - 28 patients. The depressions severity according to Hamilton depressions scale was in the range of 18.9 - 29.1 points. The duration of the study was 42 days with the patients assessment on 0, 7, 14, 28 and 42 days of therapy. Thus, both age groups were fully comparable.

Study results and discussion

Antidepressant action main aspects detailed analysis of the SSRIs antidepressants on study primarily revealed their high therapeutic efficacy in juvenile depressions, which, undoubtedly, is due to the fact that they all share the same action mechanism (serotonin reuptake selective blocking). At the same time, along with the antidepressant effect general features of SSRIs group drugs, a number of significant differences were established between them, concerning both the antidepressant effect strength, the therapeutic effect onset and the clinical action and tolerability profile spectrum.

It was revealed that, according to Hamilton Rating Scale, on the treatment day 42, the drugs showed significant difference in terms of reduction degree of total depression rating score, in the following order (as it decreases): paroxetine - 77.1%; Citalopram - 76.2%; fluoxetine - 74.8%; fluvoxamine - 66.9% and sertraline - 65.1%.

When assessing onset rate of antidepressant effect, a statistically significant decrease in the overall depressive symptoms assessment according to the Hamilton Rating Scale was observed when Citalopram was administered by day 7, and when Paroxetine, fluoxetine, sertraline and fluvoxamine were applied - by day 14 ($p < 0.001$). In the group of citalopram-treated patients, by the 7th day, Hamilton Rating Scale score reduction was 38.8%, and by the day 14 this figure reached 51.3%. Subsequently, the reduction rate slowed down and by the end of day 42 was comparable in other therapeutic groups with these indicators. Paroxetine, fluvoxamine and sertraline-treated patients at the initial therapy stages (first and second week of the study) were noted with a different, but similar dynamics. These groups of patients showed slower depressive symptoms reduction and marked improvement in condition occurred closer to the day 28 and later. Sertraline-treated patients group showed even slower reduction rate. Moreover, in fluoxetine-treated patients group, a slight increase in depressive symptoms by day 7 (increased anxiety, agitation, sleep disturbance) was detected. This fact, apparently, is associated with a pronounced stimulating drug effect at the therapy initial stage. As a rule, these phenomena were reduced later on and the patient's condition improved fairly quickly: the average Hamilton Rating Scale total score reduction rate was also statistically significant by day 14 ($p < 0.001$).

SSRIs antidepressant effect (thymoleptic, stimulant and anxiolytic) characteristics study results in adolescent depressions showed, that the drugs studied differ in the average Hamilton Rating Scale reduction degree on day 42 (Table 1).

Table 1. SSRIs drugs antidepressant action spectrum

Drugs	Average total score reduction degree (% , from day 0)		
	Thymoleptic	Stimulating	Anxiolytic
Paroxetine	81,1	72,9	71,2
Citalopram	85,4	71,3	76,3
Fluoxetine	82,6	82,9	73,8
Sertralin	74,1	66,2	68,7
Fluvoxamine	75,9	66,5	61,2
Total effect	71,8	73,8	73,4

As can be noted from the table, although all therapeutic antidepressants groups showed clearly pronounced thymoleptic effect, the reduction rate on the first three Hamilton Rating Scale points was different. Therapy with citalopram shoed most pronounced and rapid reduction of depressive triad proper thymic component. These patients noted improvement of mood, disappearance of guilt feelings by day 7 of therapy.

Somewhat less pronounced, but quite distinct results were obtained in paroxetine-, sertraline- and fluvoxamine-treated patients. In this case, the thymoleptic effect increased with a slower rate, reaching a statistically significant value ($p < 0.05$) by day 14. Fluoxetine antidepressant effect peculiarities also manifested in the its thymoleptic action evaluation. Here, anxiety and agitation arising shortly after therapy initiation led to an increase in the self-accusation ideas and a deterioration subjective feeling. Only by day 14 these side effects were terminated, following patient's condition improved quickly.

SSRIs antidepressants stimulating effect evaluation, determined by paragraphs 7 and 8 reduction of Hamilton Rating Scale (cluster of adynamia), revealed clear differences between the drugs. In the group of fluoxetine-treated patients with the most pronounced stimulating properties a inhibition decrease manifested already from the day 7 of therapy and was very intense until the study end. However, this fact should be considered when prescribing this drug for patients with anxious depression, as well as for patients who have hidden or obvious suicidal tendencies, due to the their activation possibility. A mild but fairly rapid stimulating effect was observed in the group taking paroxetine- and citalopram-treated

patients. Sertraline and fluvoxamine stimulating effect was less pronounced.

Considering juvenile depressions clinical features, characterized by a high anxiety proportion, it was especially important to determine the features of the SSRIs antidepressants anxiolytic action, as assessed by points 9,10 reduction of Hamilton Rating Scale (anxiety cluster). It was found that, SSRIs antidepressants anxiolytic effect in general was less pronounced, unlike the thymoleptic and cumulating effects. In this case, only citalopram showed not only the highest anxiety disorders reduction degree, but also the most significant anxiolytic effect realization rate. Similar results within paroxetine-, fluoxetine-, sertraline- and fluvoxamine-treated patients could be achieved only by day 28 of therapy.

Thus, as established on the basis of SSRIs drugs action features, studied among adolescent patients, allowed to conditionally divide them into three groups. Paroxetine and citalopram were classified as antidepressants with a balanced clinical effect. Fluoxetine was considered an antidepressant with a pronounced stimulating effect. When fluvoxamine and sertraline are used, characterized by a lower anti-depressive effect level, anxiolytic effect prevails, thymoleptic effect follows, mild stimulating effect manifests only by the study end.

Another important feature of SSRIs antidepressants effectiveness in juvenile depression treatment was found in the statistically significant differences absence analysis in patients treatment with severe depression and moderate depression, which distinguishes them from depression in patients of mature age (except of fluoxetine, which showed a statistically significant difference in Hamilton Rating Scale scores on day 42 of therapy between patients with severe depression and moderate depression ($p < 0.01$).

In order to determine the relationship between the juvenile depression clinical type and therapy effectiveness, patients were divided into groups depending on juvenile depression type. When analyzing the relationship nature between SSRIs antidepressants effectiveness and juvenile depressions psychopathological type, it was found that psychiatric-like depressions depressive symptoms are most fully reduced (89.1%). In senesto-hypochondriac depression patients, the average total score reduction for Hamilton Rating Scale was 72.9%, and in adolescent depressions dominated by obsessive-phobic disorders - 70.1%. SSRIs antidepressants treatment effectiveness in depressions patients with "juvenile asthenic failure" picture and juvenile depersonalization depression reached 66.7% and 65.2% respectively.

In addition, comparable juvenile depressions typological groups differed in anti-depressive affect onset pace. The depressive disorders reduction rate in patients with juvenile psychasthenoid-like depression was smooth and harmonious. By the beginning of the second week of therapy, patients noted a significant reduction in anxiety, internal discomfort, improved mood, significantly reduced communication fear and self-doubt. They became more sociable, spent less time in the ward, and converged with patients of their own age. Painful self-analysis, characteristic of these patients, was reduced to light reflection level. Significant ideas of relationships, which arose in psycho-traumatic situations, underwent significant reduction. Communication fear, anxiety and self-doubt diminished. By the therapy course end, only slight affect fluctuations, increased vulnerability and slightly pronounced diffuse anxiety, associated with thoughts about the upcoming return to school, could be noted from residual symptoms.

Depressive disorders reduction rate in patients with juvenile senesto-hypochondriac depression was quite intense in the first two weeks of therapy. During this period they noted a significant reduction in anxiety and internal discomfort, their fixation on their somatic state decreased, and cenesthopathy faded. Their activity increased, the interests center shifted to a more "pragmatic" side - to continue studying at the institute or to look for work. Residual depressive symptoms were represented by a slightly increased anxiety level, and a tendency of more attentive attitude towards the administration and body functions remained.

In juvenile depressions patients with a obsessive-phobic disorders predominance in clinical picture, depressive symptoms reduction rate was also quite distinct and rapid. Subjectively, the patients' condition improved significantly, obsessions and phobias became less painful, their relevance decreased. Positive patients attitude towards further long-term therapy was rather quickly formed. However, it should be noted, that these changes concerned actual depressive manifestations on the first place and, to a lesser extent, the obsessive-phobic disorders themselves, which were only partially reduced by day 42.

Depressive disorders reduction dynamics in patients with depression, the "youthful asthenic insolvency" type was distinguished by low therapeutic effect

development rate. First of all, depressive triad vital component was reduced here: in the morning, patients felt themselves more vigorously, their appetite was normalized, falling asleep process was facilitated, and sleep quality was improved. In the middle of the study (after 14 days of therapy), patients noted mood improvement, became more active, interest in various types of activity, a desire to do something aroused, many of patients had a regular daily rhythm. Patients' distinctive feature of this typological group was that the cognitive functions, concentration processes and educational material understanding improvement occurred much later than the actual thymic component reduction. For quite a long time, patients reported preserving increased distractibility, fatigue, a feeling of "turbidity" in the head, and not fully restored health.

As shown in the clinical analysis, depressive symptoms dynamics among juvenile depersonalization depressions, reflected in Hamilton Rating Scale indicators, primarily concerned the depressive triad actual and motor component. Patients noted a decrease in anxiety, night sleep normalization, they decreased motor inhibition severity. Reflection level decreased, thoughts about their "change", "loss of emotions", ability to empathize and rejoice were not so painful any more. Patients also noted appearance of "bright spaces", when a feeling of one's own self returned for a short time, the surroundings acquired bright colors again, and there were glimpses of emotions. The depersonalization phenomena sensation was reduced from the level of "intolerable" to "light". It should be noted that the remission state was observed only in those patients whose initial depersonalization disorders level proper was relatively low. In general, at the time of study end (day 42), there were still quite distinct residual depressive manifestations, represented mainly by reduced depersonalization disorders and impaired performance signs, which resulted in a fairly high Hamilton Rating Scale score on day 42 of therapy.

In addition, there were also identified differences between each of the SSRIs antidepressants effectiveness and the juvenile depression type (Table 2).

Table 2. SSRIs antidepressants effectiveness ratio and juvenile depression typological picture

Drugs	Average total score reduction degree in patients (in % from day 0)				
	adolescent asthenic failure	Psychiatric-like depression	Obsessive-phobic disorders	Depersonalization depressions	Senesto-hypochondriac depression
Paroxetine	76,2	74,8	70,9	84,4	79,2
Citalopram	84,8	82,9	82,7	58,3	72,3
Fluoxetine	73,4	80,9	70,6	74,7	85,8
Sertraline	61,3	80,8	80,6	45,3	65,8
Fluvoxamine	76,3	80,6	61,4	34,3	80,3
Overall effect	66,8	89,2	70,4	62,4	72,1

Differences were also found in therapeutic response magnitude to SSRIs drugs in different nosological patients' groups with juvenile depressions in general and in using each of the drugs in particular (Table 3).

Table 3. SSRIs antidepressants effectiveness ratio and juvenile depression nosological nature

Drugs	Average total score reduction degree in patients (in % from day 0)				
	Affective disease	Low-progreduced schizophrenia	Psychopathic pubertal dynamics		
Paroxetine	77,2	74,8	81,2		
Citalopram	78,8	62,8	95,8		
Fluoxetine	79,2	66,8	91,2		
Sertraline	68,5	56,7	77,4		
Fluvoxamine	51,2	64,7	87,8		
Overall effect	73,6	64,8	83,4		

As noted from the table, serotonergic drugs antidepressant effect in patients with psychopathic pubertal dynamics was the highest. The reduction of depressive disorders was the most rapid and harmonious.

Antidepressant therapy effectiveness overall indicator in group of patients with affective disease was slightly lower, but the pronounced reduction in the average Hamilton Rating Scale score was already on the 7th day of therapy and was statistically significant ($p < 0.01$).

Serotonergic drugs effectiveness overall indicator, as assessed by average Hamilton Rating Scale total score reduction, was at its lowest in the group of patients with depressions that developed in the framework of low-professorial schizophrenia. When using SSRIs antidepressants, depressive symptoms reduction occurred more slowly in patients from this nosological group, reaching a statistically significant value ($p<0.01$) only by the end of the second week of therapy.

In the study course, adverse events accompanying SSRIs antidepressant therapy were recorded in detail. The their occurrence frequency in patients with juvenile depressions was 57.4% (104 people), of which 45.1% (76 people) had isolated side effects, and 15.4% (28 people) had a combined nature. In general, their severity level was low and only 4 patients (2.2%) were excluded from the study because of them.

In general, mental adverse events dominated with juvenile depressions when using SSRIs antidepressants. Anxiety was characteristic for all drugs as a side effect, occurred in the first week of therapy as a rule and was quickly reduced. Paroxetine, citalopram and fluoxetine were characterized by a higher severity degree for this side effect, which led to the need for tranquilizers use. Sedation also occurred during treatment with all antidepressants except fluoxetine, but its severity was maximum in fluvoxamine- and sertraline-treated patients, and minimal in paroxetine- and citalopram-treated ones. Sedation developed gradually, between days 14 and 28, gradually reducing to the study period end. Such a neurological side effect as a tremor was inextricably linked with anxiety and completely disappeared after its reduction.

Anticholinergic side effects severity, represented mainly by dry mouth and difficulty urinating, was minimal for sertraline- and fluoxetine-treated and maximum for paroxetine-treated patients. Citalopram and fluvoxamine were noted as intermediate. Cardiovascular system disturbances were mainly presented by tachycardia and hypotension, but these phenomena practically did not undergo positive dynamics until the study end. Abdominal distress (diarrhea, nausea and constipation) was rare and was slightly pronounced, but extremely painful for patients and could lead to an attempt to refuse further treatment.

The so-called "other" side effects were represented mainly by rare cases of headache and pruritus, but the causal connection of these phenomena with the studied drugs seems doubtful for us.

Thus, SSRIs antidepressants tolerability profile in adolescent depressions can be assessed as quite favorable in general, although having its own age-related side effects, that are characteristic of each of these drugs. There's surely a need to consider this for their prescription for patients with various somatic comorbidity.

One of the main study objectives was to clarify the therapy age specificity with juvenile depression samples. In order to clarify this issue, a detailed comparison of their effectiveness, SSRIs antidepressant effect features as well as side effects frequency and profile in young and mature patients, which made it possible to identify the following patterns.

Antidepressant efficacy overall level of these drugs in both age groups is quite high and does not have a statistically significant difference, but at the same time, its characteristic feature in adolescent patients is the stimulating and delayed anxiolytic effect rapid implementation. This fact must be taken into account when prescribing SSRIs group drugs to patients with active or latent suicidal tendencies, as well as with severe anxiety.

Differences between age groups on the therapeutic effect onset rate with the specific drugs use were also established: earlier with citalopram and fluoxetine and later with the paroxetine use in adolescent patients when compared with patients of mature age. At the same time, no differences in the therapeutic effect onset rate between adolescent and adult sertraline- and fluvoxamine-treated patients have been established.

Serotonergic antidepressants overall tolerance in the two age groups was comparable (63.18% of adverse events in patients of mature age and 63.45% in adolescent patients), but differences in side effects spectrum were identified. For adolescent patients, mental adverse events were most characteristic, such as anxiety, anxiety, and sleep disturbance. This was

particularly pronounced on the paroxetine, citalopram and fluoxetine treatment. SSRIs antidepressants anticholinergic manifestations in young men differed by a relatively low severity degree and a lighter nature. The exception was urinary retention in boys, which was much more common and was recorded when using each of the drugs of the group of SSRIs. Thus, the age factor, namely the psychobiological adolescence characteristics, plays a significant role in SSRIs antidepressant therapy tolerability, side effect profile and therapeutic effect rate of each of these drugs.

Conclusion

In general, drugs from SSRIs group have shown high efficacy in juvenile depressions treatment, which can legitimately be associated with "serotonin dependence" of this pathogenesis. Drug response has specific age characteristics for patients with adolescent depressions to psychopharmacological SSRIs drugs, revealing a clear relationship between adolescent depression therapeutic effect and typological types, their nosological affiliation and depressive affect component that dominates in their picture.

Despite belonging to the same series of chemical compounds, drugs of this group reveal significant differences in the characteristics of their clinical action and therapeutic efficacy in the treatment of juvenile depression. Serotonergic antidepressants therapeutic effect depth were assessed by the average total score reduction degree on the Hamilton Rating Scale on day 42 of the treatment course. This allows to rank the studied drugs by the improvement degree, achieved in the following order: paroxetine, citalopram, fluoxetine, fluvoxamine and sertralin.

In contrast to the patients of mature age, no serotonergic antidepressants therapeutic effect severity dependence on the juvenile depressive states different severity in young people was noted (with an exception of fluoxetine).

Three antidepressant effect (thymoleptic, anxiolytic and stimulating) components of SSRIs drugs psychotropic action in different ratios and with different implementation rates, determining the clinical affiliation of each of the serotonergic antidepressants and, to a greater extent, correspond to the each of the serotonergic antidepressants peculiarities, their therapeutic effects. Paroxetine and citalopram have a balanced clinical effect: when in use, thymoleptic effect itself is primarily manifested, and fluoxetine is an antidepressant with a pronounced stimulating effect. Anxiolytic effect is predominant in the fluvoxamine and sertraline antidepressant effect spectrum.

Main characteristics comparison of SSRIs antidepressants therapeutic action for young men and those of mature age revealed statistically significant age differences related to the onset rate and these drugs' antidepressant effect features, as well as the adverse events nature, which made it possible to consider this phenomenon as an age factor effect on the drug response characteristics with juvenile depression pharmacotherapy. Compared to the mature patients, the young men had a faster SSRIs antidepressants stimulating effect realization with some delay in their anxiolytic action. This fact must be considered when prescribing these drugs to patients with active or potential suicidal tendencies, often characteristic of patients with juvenile depression.

Tendencies of SSRIs antidepressants clinical action in the depression treatment in adolescence, their therapeutic effect features and dynamics allow us to formulate adequate indications for prescribing these drugs in adolescence, consider their age specificity and contribute to the implementation of a their therapeutic efficacy scientifically based prediction and condition prevention exacerbations at the initial treatment stages, as well as leveling high suicidal risk characteristic of patients with juvenile depression.

Ethical clearance: This study got approval from the Research and Ethics Committee of *Kazan Innovative University named after V.G. Timiryasov*.

Conflict of interest: None declared

Authors' Contributions:

Authors' Contributions:

Ramil F. Suleymanovconceived the idea of the study, design of the study, participated in the field work, analysis and manuscript writing, and submitting manuscript

Roman V. Gorenkov participated data analysis and reportwriting.

Natalya P. Chernusparticipated in field work, datacollation, and manuscript writing.

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Irina F. Kalininaparticipated in study design, dataanalysis and manuscript writing.

Editing and approval of final draft: all authors

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