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Effect of Monotherapy with Methotrexate, Etanercept and their Combination on the Quality of Life in Children with Early and Late Juvenile Idiopathic Arthritis: A Prospective Study

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Background. An important goal of treating patients with juvenile idiopathic arthritis (JIA) is to achieve the best quality of life associated with health. **Objective.** Our aim was to assess the impact of methotrexate plus etanercept therapy on the quality of life of patients with early and late JIA. **Methods.** The study included patients with early and late JIA without systemic manifestations. The patients' quality of life was assessed with the help of questionnaires for children and parents: the Pediatric Quality of Life Inventory (PedsQL) Generic Core Scale, the Pediatric Quality of Life Inventory (PedsQL) Rheumatology Module, and the Health Utilities Index Mark 3 (HUI3). The quality of life was assessed prior to the therapy and after one, six, and 12 months of treatment. **Results.** 150 children with JIA aged 5.1 (2.0; 17.7) years; 50 children aged 4.0 (2.3–11.4) years in the group of etanercept monotherapy, 50 children aged 5.0 (3.2–9.0) years in the group of methotrexate monotherapy, and 50 children aged 9.9 (6.4–13.0) years in the group of methotrexate plus etanercept combination therapy. All groups showed low scores on all questionnaires before treatment, compared to healthy children. In the course of therapy, there was a tendency for score increase to almost 1.0 according to the HUI3 questionnaire in all groups. After one year of etanercept therapy, the parameters of the quality of life of children with early JIA did not differ from healthy children; the score increased from 56 to 90 ($p = 0.942$) according to the physical functioning scale and from 60 to 85 $p = 0.889$ according to the emotional functioning scale. In the 2nd group, there was a tendency for score increase, but a statistically significant difference was found across all scales of the questionnaire. After 12 months of etanercept plus methotrexate combination therapy in patients with late JIA, the questionnaire analysis showed that the responses of healthy children and children with JIA differed with probability $p = 0.001$ for the physical functioning scale, $p = 0.001$ for the social functioning scale, $p = 0.001$ for role functioning, and $p = 0.001$ — for the total score. The score increase from 60 to 85 ($p = 0.789$) was noted for emotional functioning scales. **Conclusion.** The use of questionnaires to assess the quality of life in children with severe chronic diseases can significantly improve the efficacy of treatment and ensure its control.

Key words: children, juvenile idiopathic arthritis, methotrexate, etanercept, quality of life, PedsQL Generic Core Scale, PedsQ Rheumatology Module, HUI3.

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RESULTS

Table 1. Characteristics of patients and previous therapy with newly diagnosed JIA without systemic manifestations who received etanercept/methotrexate monotherapy (early JIA) or combined treatment (late JIA)

Parameter	Etanercept, <i>n</i> =50	Methotrexate, <i>n</i> =50	Etanercept + methotrexate, <i>n</i> =50
Sex (girls), abs. (%)	36 (72)	26 (52)	37 (74)
Age, years min-max	4.0 (2.3; 11.4) 2.0 - 17.7	5.0 (3.2; 9.0) 2.0 - 17.0	9.9 (6.4; 13.0) 3.5 - 17.0
Age of the disease onset, years min-max	2.5 (1.7; 10.0) 0.5 - 16.0	3.5 (2.0; 9.0) 1.0 - 14	3.0 (2.0; 8.0) 1.0 - 13
Duration of the disease, years min-max	0.9 (0.4; 1.2) 0.3 - 1.9	0.9 (0.5; 1.9) 0.25 - 1.9	4.0 (3.0; 6.5) 2 - 15
Intra-articular GC injections, abs. (%)	18 (36)	21 (42)	34 (68)
NSAIDs, abs. (%)	50 (100)	50 (100)	50 (100)
Methotrexate, abs. (%) dose, mg/m ² /week	13 (26) 12.5 (7.5; 10)	0	48 (96) 15 (9.5; 20)
Sulfasalazine, abs. (%) dose, mg/m ² /week	9 (18) 35 (33; 37)	7 (14) 35 (32; 38)	2 (4) 35 (33; 38)

Note. NSAIDs — non-steroidal anti-inflammatory drugs.

Table 2. Clinical characteristics of patients with JIA without systemic manifestations included in the study

Parameter	Etanercept, <i>n</i> =50	Methotrexate, <i>n</i> =50	Etanercept + methotrexate, <i>n</i> =50
Sex (girls), abs. (%)	36 (72)	26 (52)	37 (74)
Age, years min-max	4.0 (2.3; 11.4) 2.0 - 17.7	5.0 (3.2; 9.0) 2.0 - 17.0	9.9 (6.4; 13.0) 3.5 - 17.0
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Intra-articular GC injections,	18 (36)	21 (42)	34 (68)

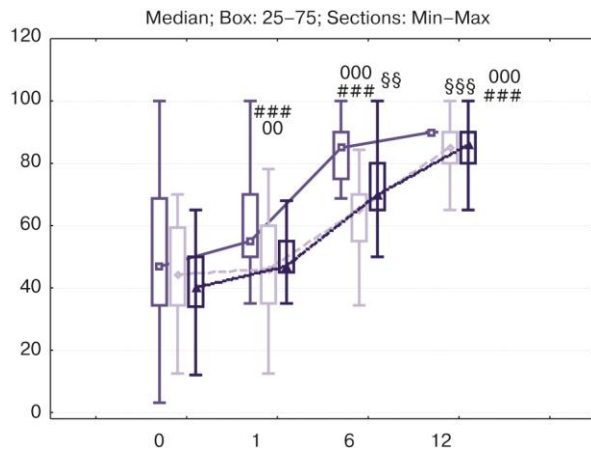
abs. (%)			
NSAIDs, abs. (%)	50 (100)	50 (100)	50 (100)
Methotrexate, abs. (%)	13 (26)	0	48 (96)
dose, mg/m2/week	12.5 (7.5; 10)		15 (9.5; 20)
Sulfasalazine, abs. (%)	9 (18)	7 (14)	2 (4)
dose, mg/m2/week	35 (33; 37)	35 (32; 38)	35 (33; 38)

Note. VAS — visual analogue scale, CHAQ — Childhood Health Assessment Questionnaire, ESR — erythrocyte sedimentation rate, CRP — C-reactive protein.

Table 3. Indicators of the quality of life of children with JIA before therapy and healthy children according to the PedsQL Generic Core Scale questionnaire

Parameter	Etanercept, n =50	Methotrexate, n =50	Etanercept + methotrexate, n =50	Comparison group (conditionally healthy children)
<i>Children's form</i>				
Physical functioning (min-max)	56 (43; 71.88) (18; 96)	40 (30.00; 60.00) (25; 71)	43 (30.00; 55.00) (3; 85)	93 (87.00; 96.00) (71; 100)
Emotional functioning (min-max)	60 (35.00; 80.00) (15; 90)	45 (40.00; 70.00) (20; 80)	60 (40.00; 80.00) (0; 90)	85 (80.00; 90.00) (55; 100)
Social functioning (min-max)	80 (60.00; 90.00) (20; 100)	60 (50.00; 65.00) (40; 75)	80 (60.00; 85.00) (20; 100)	95 (90.00; 95.00) (70; 100)
Role functioning (min-max)	45 (40.00; 60.00) (10; 85)	55 (40.00; 60.00) (25; 75)	50 (40.00; 60.00) (0; 90)	85 (75.00; 90.00) (60; 100)
Total quality of life score (min-max)	56 (44.06; 70.78) (0;89)	50 (41.25; 60.00) (33; 73)	55 (45.00; 73.25) (0; 81)	86 (83.25; 90.75) (80; 98)
<i>Parent form</i>				
Physical functioning (min-max)	46 (34.38; 68.75) (3; 100)	45 (35.00; 60.00) (12; 78)	40 (34.00; 50.00) (3; 100)	93 (87.00; 96.00) (81; 100)
Emotional functioning (min-max)	52 (40.00; 65.00) (20; 90)	50 (45.00; 60.00) (25; 75)	45 (35.00; 70.00) (0; 90)	85 (80.00; 90.00) (60; 100)
Social functioning (min-max)	67 (60.00; 80.00) (20; 100)	55 (55.00; 65.00) (35; 75)	55 (40.00; 85.00) (8; 100)	95 (95.00; 100) (70; 100)
Role functioning (min-max)	55 (40.00; 66.60) (0; 90)	50 (40.00; 55.00) (25; 70)	50 (35.00; 70.00) (0; 90)	83 (75.00; 90.00) (65; 100)
Total quality of life score (min-max)	55 (40.94; 63.91) (18; 90)	42 (39.21; 54.68) (23; 70)	51 (33.50; 62.00) (3; 90)	88 (83.75; 91.50) (80; 100)

Fig. 1. Dynamics of the quality of life indicators of children with JIA treated with etanercept (group I), methotrexate (group II), methotrexate + etanercept combination (group III), according to the physical functioning scale of the PedsQL Generic Core Scale.



Note. # — $p < 0.05$, ## — $p < 0.01$, ### — $p < 0.001$ — statistically significant differences in the indicator values as compared to the initial value between group I and group II; 0 — $p < 0.05$, 00 — $p < 0.01$, 000 — $p < 0.001$ — statistically significant differences in the indicator values as compared to the initial value between group I and group III; § — $p < 0.05$, §§ — $p < 0.01$, §§§ — $p < 0.001$ — statistically significant differences in the indicator values as compared to the initial value between group II and group III.

Fig. 2. Dynamics of the quality of life indicators of children with JIA treated with etanercept (group I), methotrexate (group II), methotrexate + etanercept combination (group III), according to the emotional functioning scale of the PedsQL Generic Core Scale.

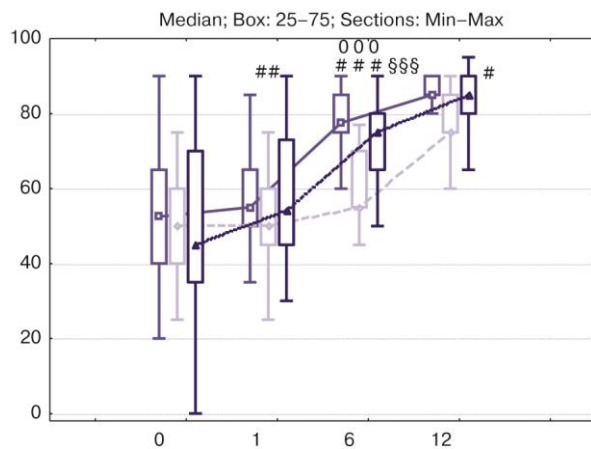


Fig. 3. Dynamics of the quality of life indicators of children with JIA treated with etanercept (group I), methotrexate (group II), methotrexate + etanercept combination (group III), according to the social functioning scale of the PedsQL Generic Core Scale.

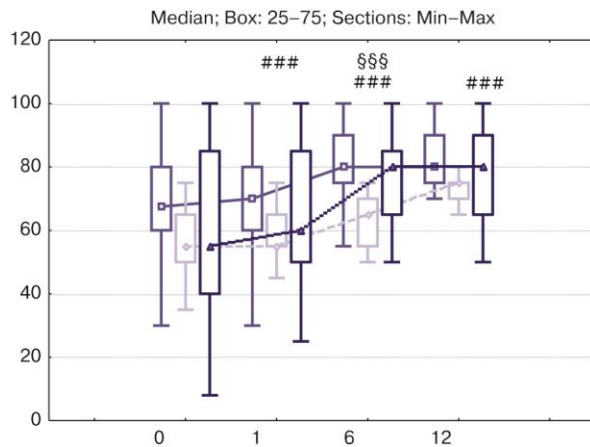
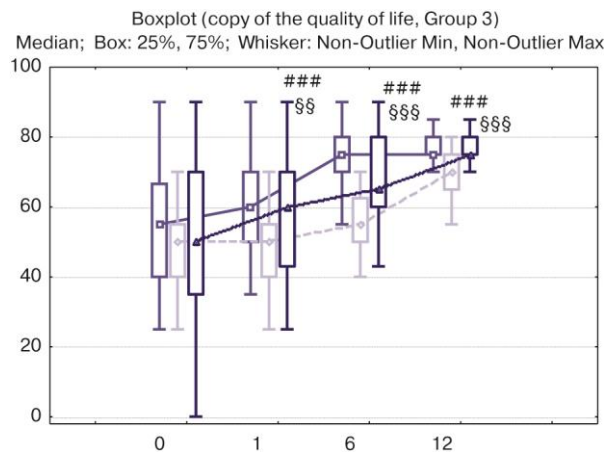


Fig. 4. Dynamics of the quality of life indicators of children with JIA treated with etanercept (group I), methotrexate (group II), methotrexate + etanercept combination (group III), according to the role functioning scale of the PedsQL Generic Core Scale.



Note. # — $p < 0.05$, ## — $p < 0.01$, ### — $p < 0.001$ — statistically significant differences in the indicator values as compared to the initial value between group I and group II; ○ — $p < 0.05$, ○ ○ — $p < 0.01$, ○ ○ ○ — $p < 0.001$ — statistically significant differences in the indicator values as compared to the initial value between group I and group III; § — $p < 0.05$, §§ — $p < 0.01$, §§§ — $p < 0.001$ — statistically significant differences in the indicator values as compared to the initial value between group II and group III.

Fig. 5. Health Utilities Index Mark 3: Dynamics of the quality of life indicators in the course of etanercept treatment in patients with early JIA by single attribute traits ($n = 20$).

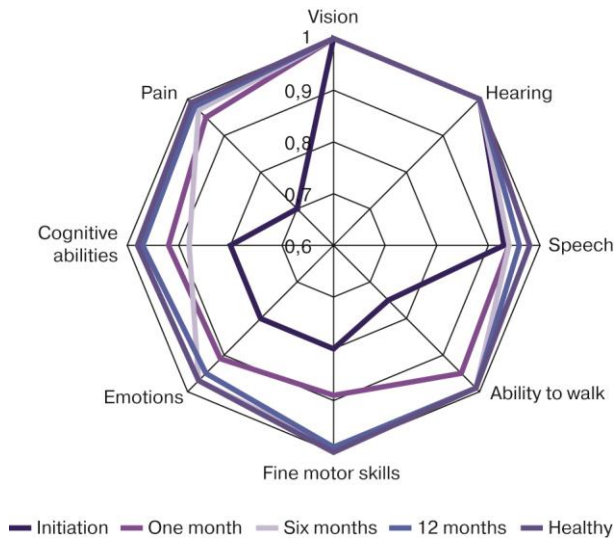


Fig. 6. Health Utilities Index Mark 3: Dynamics of the quality of life indicators in the course of methotrexate treatment in patients with early JIA by single attribute traits ($n = 26$).

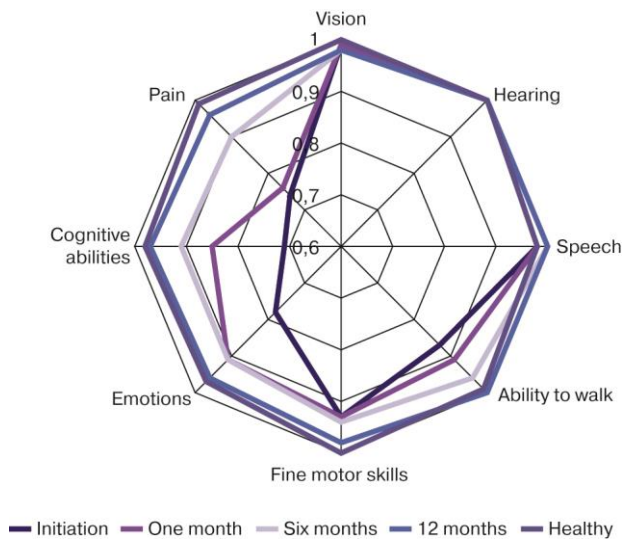
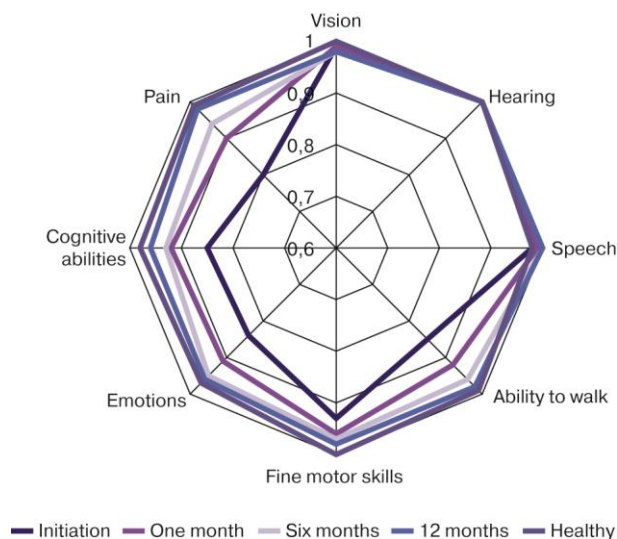


Fig. 7. Health Utilities Index Mark 3: Dynamics of the quality of life indicators in the course of methotrexate plus etanercept combination treatment in patients with late JIA by single attribute traits ($n=47$).



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Conflict of Interests

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The other contributors confirmed the absence of a reportable conflict of interests.