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Dynamics of Destructive Joint Changes in Juvenile Idiopathic Arthritis in Children who Received Methotrexate or Methotrexate-Tocilizumab Combination: A Cohort Study

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BACKGROUND. *Destructive joint damages in juvenile arthritis inevitably lead to persistent disability in adulthood. These consequences can be avoided by resorting to early therapy of the disease.* ***OBJECTIVE.*** *Our aim was to assess the dynamics of destructive joint changes in juvenile idiopathic arthritis (JIA) in children, depending on a basic therapy.* ***METHODS.*** *We studied the treatment results of children with systemic-onset JIA with active joint syndrome without active systemic manifestations hospitalized in the regional clinical cardiological health center. JIA activity criteria at the time of hospitalization: ≥3 joints with active arthritis; the assessment of the disease activity by a doctor ≥3 points out of 10; the assessment of wellbeing by the patient or a parent ≥3 points out of 10; the appointment of basic therapy no later than 6 months from the disease onset. Treatment results were compared in the groups of methotrexate (hospitalization from January 2008 to December 2010) and methotrexate + tocilizumab (January 2014 – September 2016). The main outcome of JIA therapy was the severity of joint destruction in 6, 12 and 24 months as determined by the modified Sharpe ratio according to radiographs obtained from patients' medical records.* ***RESULTS****. The study groups were comparable in terms of sex and age of the patients, JIA onset age, the disease activity at the time of hospitalization, and the initial assessment of joint destruction — (median) 165 (131; 187) and 162 (124; 171) (p =0.116). Under pressure of therapy, the modified Sharpe score in the group of methotrexate monotherapy was higher than in the group of combined therapy: in 6 months — 142 (126; 163) and 87 (72; 112) (p <0.001); in 12 months — 166 (121; 210) and 75 (29; 89) (p <0.001); in 24 months — 165 (113; 198) and 52 (26; 73) (p <0.001). At the first administration of tocilizumab, 4 children had nausea and abdominal pain, and 3 children had headache.* ***CONCLUSION.*** *Basic therapy with methotrexate and tocilizumab inhibits the destruction of joints in patients with systemic-onset JIA with active joint syndrome without active systemic manifestations.*
KEY WORDS*: children, juvenile idiopathic arthritis, methotrexate, tocilizumab, joint destruction, the modified Sharpe ratio.*
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RESULTS

Table 1. General characteristics of patients with JIA who received methotrexate or methotrexate-tocilizumab combination (at the time of hospitalization)

Parameters	**Methotrexate, *n* =22**	**Methotrexate + Tocilizumab, *n* =16**	***p***
Girls, abs. (%)	17 (77)	10 (63)	0.471

Age, years	7.9 (6.1; 9.2)	9.3 (7.8; 13.9)	0.064
JIA onset age, years	6.3 (4.1; 8.6)	6.1 (4.9; 8.0)	0.964
The degree of JIA activity, abs. (%) • II • II–III • III	 7 (32) 11 (50) 4 (18)	 4 (25) 10 (63) 2 (13)	 0.729 0.520 0.688

Table 2. Characteristics of therapy for children with JIA who received methotrexate and methotrexate-tocilizumab combination (at the time of hospitalization)

Medication	**Methotrexate, *n* =22**	**Methotrexate + Tocilizumab, *n* =16**	***p***
Methotrexate, mg/m^2 • Intramuscular, abs. (%) • Initial dose of 15 mg/m^2**, abs. (%) • Titration ≥20 mg/m^2, abs. (%)	16 (13; 19) 22 (100) 14 (64) 6 (27)	14 (12; 17) 14 (88)* 9 (56) 10 (63)	0.018 0.171 0.743 0.047
Tocilizumab, mg/kg	-	8.5 (8; 12)	-
Nimesulide, mg/kg	6.9 (3.5; 11.3)	4.0 (3.2; 6.7)	0.043

Note. * 2/16 patients received methotrexate subcutaneously. ** The other patients received methotrexate in a dose of 10 mg/m^2.

Table 3. Changes in the evaluation of radiographic progression of JIA within 24 months of monotherapy (methotrexate) and combined therapy (methotrexate + tocilizumab)

Groups	**Initially**	**Treatment duration, months**		
		6	**12**	**24**
Methotrexate, *n* =22	165 (131; 187)	142 (126; 163)	166 (121; 210)	165 (113; 198)
Methotrexate + Tocilizumab, *n* =16	162 (124; 171)	87 (72; 112)	75 (29; 89)	52 (26; 73)
p	0.166	0.001	0.001	0.001

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Conflict of Interests
Not declared.

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