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Retrospective analysis of the effectiveness of local corticosteroid therapy in children with oligoarticular juvenile idiopathic arthritis

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ABSTRACT

Background. Despite the progress in diagnosis and treatment of chronic rheumatic diseases in children, the choice of anti-inflammatory drugs in case of the onset of oligoarticular juvenile idiopathic arthritis (JIA) still remains relevant. Till present, pediatric rheumatologists have not reached a consensus on this issue yet.

The aim of this study was to search for predictors of early failure of local steroid therapy and assess its feasibility in patients with oligoarticular JIA.

Materials and methods. In a retrospective study, 92 children aged 11 months–9 years with chronic oligoarticular JIA without extra-articular manifestations were monitored. The features of the clinical, instrumental, and laboratory diagnosis during the disease onset were studied, along with the dynamics of the articular syndrome and the effectiveness of intra-articular administration of corticosteroid drugs.

Results and discussion. The data on 92 children with 164 active joints who received 218 local intra-articular injections of triamcinolone acetonide at the onset of the disease were analyzed. Intra-articular injections of triamcinolone acetonide at a dose of 20–40 mg were performed with an interval of 3, 6, and 12 months, depending on the intensity of the disease. In about one third of children with oligoarticular JIA, arthritis became inactive on average after two intra-articular injections of triamcinolone acetonide. The study did not reveal the predictors of early ineffective topical corticosteroid monotherapy in children. No clinical, instrumental, and laboratory signs were identified that would directly indicate the need for early therapy with methotrexate.

Conclusion. Triamcinolone acetonide is an effective and safe drug for children with oligoarticular JIA. Despite the widespread use of biological, gene, and other innovative therapies, application of local corticosteroids as the first-line therapy in children with oligoarticular JIA should not be neglected.

Key words: oligoarticular juvenile idiopathic arthritis, local steroid therapy, triamcinolone acetonide.

Conflict of interest. The authors declare the absence of obvious or potential conflict of interest related to the publication of this article.

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Conformity with the principles of ethics. All patients (their representatives) signed an informed consent to participate in the study. The study was approved by the local Ethics Committee at H. Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery (Protocol No. 1 of 20.01.2014).

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Оценка эффективности локальной стероидной терапии у детей с олигоартикулярным вариантом ювенильного артрита: результаты ретроспективного исследования

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РЕЗЮМЕ

Актуальность. *Несмотря* на большой *прогресс* в диагностике и лечении ревматических заболеваний у детей, все еще остается актуальным вопрос выбора противовоспалительной терапии в случае дебюта хронического олигоартрита. Единого мнения на этот счет у детских ревматологов нет и по настоящий день.

Цель. Поиск предикторов ранней неэффективности и оценка целесообразности локальной стероидной монотерапии у пациентов с дебютом олигоартикулярного варианта ювенильного артрита.

Материалы и методы. Основу ретроспективного исследования составили 92 ребенка в возрасте от 11 мес до 9 лет с хроническим олигоартритом без экстраартикулярных проявлений (олиго-ЮА). Были изучены особенности клинико-инструментальной и лабораторной диагностики в дебюте заболевания, динамика суставного синдрома и эффективность внутрисуставного введения глюкокортикостероидного препарата.

Результаты и обсуждение. Проанализированы данные 92 детей со 164 «активными» суставами, которые получили 218 изолированных внутрисуставных манипуляций по введению стероидного препарата (триамцинолон ацетонид). Триамцинолон ацетонид вводился внутрисуставно в дозе 20–40 мг с интервалом 3, 6, 12 мес в зависимости от активности заболевания. Около одной трети детей с олиго-ЮА достигли неактивной стадии болезни в среднем после двукратного введения данного препарата. Исследование не позволило выявить предикторов ранней неэффективности монотерапии локальными стероидными препаратами у детей. Не выявлено достоверных клинико-инструментальных и лабораторных признаков, которые напрямую указывали бы на необходимость начала ранней терапии препаратом «Метотрексат».

Заключение. Триамцинолон ацетонид является эффективным и безопасным препаратом у детей с олигоартикулярным вариантом ювенильного артрита. Несмотря на популяризацию генно-инженерной биологической терапии, не следует пренебрегать лечением локальными стероидными препаратами как первой линией противоревматической терапии у детей.

Ключевые слова: ювенильный артрит, хронический олигоартрит, триамцинолон ацетонид.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Соответствие принципам этики. Все пациенты и их представители подписали добровольное информированное согласие на участие в исследовании. Исследование одобрено локальным этическим комитетом Научно-исследовательского детского ортопедического института им. Г.И. Турнера (протокол № 1 от 20.01.2014).

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INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a chronic childhood inflammatory musculoskeletal disease which progressive course leads to joint contractures and loss of their function. Increased incidence of JIA worldwide at the end of the 20th century, joint contractures at the early stage of the disease, and high disability rate determine the relevance of improving the methods of diagnosis and treatment of the rheumatic pathology. JIA is an autoimmune disorder characterized by chronic inflammation of the synovium in one or more joints inevitably resulting in arthrosis–arthritis [1, 2]. Therefore, rapid achievement of the inactive stage of arthritis is considered as a priority goal of drug therapy in JIA. Pediatric rheumatologists have not reached a consensus on the best method of treatment of oligoarticular JIA to this day.

JIA encompasses a group of heterogeneous forms of arthritis characterized by persistent joint inflammation of unknown origin lasting longer than 6 weeks. This heterogeneity is determined by different clinical forms of arthropathies, including the ones with extra-articular manifestations. Chronic oligoarthritis with simultaneous damage to no more than 4 joints prevails in children with JIA [3].

Oligoarticular JIA can be persistent (this type affects fewer than four joints throughout the course of the disease), extended (asymmetric arthritis that developed from oligoarthritis 6 months after the onset of the disease) or have a short-term (abortive) course. The most common manifestation of oligoarthritis is asymmetric lesion of the joints of the lower extremities (except for the hip joint).

This subtype mostly affects pre-school girls with the onset at the age of 6–8 years (peak at the age of 2–4 years). Besides the knee and ankle joints, the elbow, wrist, or one or two small joints of the hand and (or) foot can be remotely involved. More rarely, the clinical course of oligoarticular JIA may resemble symmetric arthritis or monoarthritis. Besides high risk of eye lesions, features of oligoarticular JIA include low laboratory disease activity and variability of clinical symptoms in the joint [4, 5].

Currently, the majority of pediatric rheumatologists adhere to a stepwise scheme of treatment in oligoarticular JIA. This method consists in gradual need for amplification of anti-inflammatory therapy, which is determined by the persistence of "active arthritis", progressing articular syndrome, or uveitis (the exception is systemic arthritis).

This approach to JIA treatment allows to provide fast inactivation of arthritis and control over the disease course [6, 7]. The treatment strategy for JIA without systemic manifestations can be represented by three main directions: proactive therapy, actual treatment of clinical symptoms of arthritis, and orthopedic and surgical elimination of disease consequences.

Despite the evidence of highly aggressive nature of JIA, a number of unresolved issues regarding the treatment strategy for oligoarticular JIA remain. It is well known that some children with uveitis-negative chronic oligoarthritis have experience in controlling the course of the disease without systemic disease modifying antirheumatic drugs (DMARDs). The opinions of pediatric rheumatologists about treatment of this subtype of oligoarticular JIA in most cases differ.

The aim of this study was to assess the feasibility and efficacy of local steroid therapy for the onset of oligoarticular JIA in children in the Russian Federation.

MATERIALS AND METHODS

The study included 92 children (85% were girls) with 164 active joints who were treated at the Orthopedics and Rheumatology Department No. 7 of H. Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery from 2012 to 2018. All children met Edmonton ILAR criteria for oligoarticular JIA and did not have extra-articular manifestations (ILAR 1997; 2001; the Edmonton revision 2004). All patients (their representatives) signed an informed consent to take part in the study.

As of the time of inclusion in the study, none of the patients had received therapy with DMARDs (Fig. 1). The age of the children ranged from 11 months to 9 years (average age (4.2 ± 2.6) years). Children under 2 years accounted for 32.7% of cases (30 / 92; all girls), children from 2 to 6 years accounted for 54.3% (50 / 92; 40 girls, 10 boys), and a group of older children amounted to 13% (12 / 92; all girls).

Triamcinolone acetonide at a dose of 20–40 mg / joint was administered intra-articularly without ultrasound guidance in no more than 3 joints

at a time. Extra-articular administration of the drug was prohibited. The maximum allowable number of consecutive isolated intra-articular injections (is-IAI) was 4. The interval between injections varied from 2 to 12 months.

All children were divided into two groups depending on the intensity of the disease. The first group contained children with inactive arthritis resulting from effective local corticosteroid therapy. The second group included children who were prescribed therapy with DMARDs due to low effectiveness of local steroid injections. Joining of eye lesions and (or) subsequent increase in the active joint count by 2 or more at this stage of therapy, and 3 or 4 ineffective consecutive intra-articular injections with corticosteroids in one joint were considered a reason for the start of parenteral methotrexate therapy (at the rate of 15 mg / m² / week).

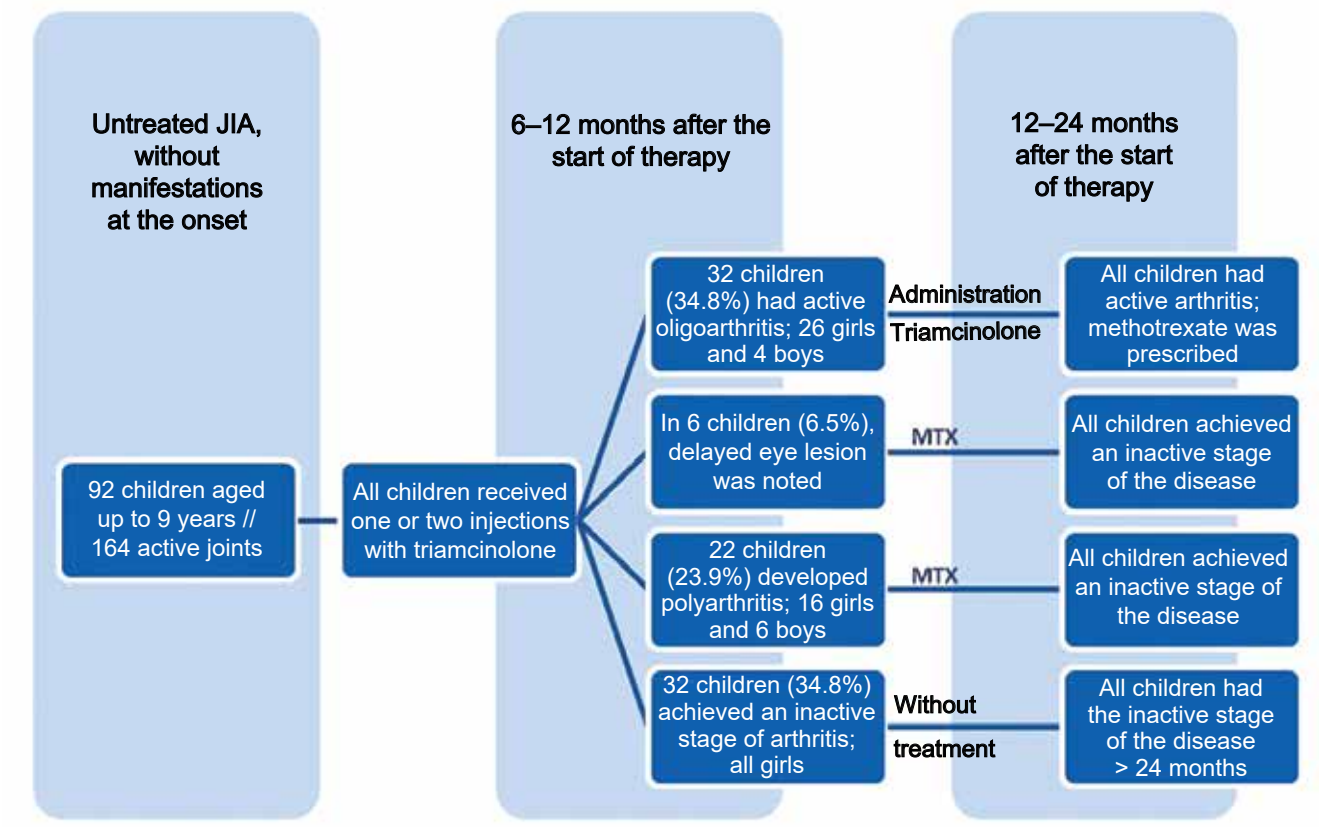

Fig. 1. Study design. MTX – treatment with methotrexate

The degree of disease intensity and the dynamics in the active joint count against the background of therapy, markers of active inflammation in the blood serum and synovial fluid, and the nature of the joint lesion according to instrumental data as of the moment of the first visit were assessed. Achievement of inactive disease and clinical remission of JIA were evaluated according to the criteria proposed by C. Wallace et al. in 2011 (the disease phase that lasted no less than 24 months was considered statistically significant). Assessment of X-ray changes in juvenile arthritis was performed using a modified Steinbrocker scoring method (2000).

The disease intensity and the effectiveness of treatment of oligoarticular JIA were evaluated by the clinical Juvenile Arthritis Disease Activity Score (cJADAS10) adapted for pediatric rheumatology practice [7]. Digital data were statistically processed using the Microsoft Excel and Statistica 6.0 software package (Microsoft, USA). A comparative analysis of empirical data was presented in tables. The results were represented as the median and the interquartile range *Me* [25; 75].

Immunological research was carried out at the laboratory of H.Turner National Medical Research Center for Children's Orthopedics and Trauma

Surgery (head – Bogdanova S.L.) and the laboratory of autoimmune diseases of Saint-Petersburg State Medical University (head – Lapin S.V.). The concentration of tumor necrosis factor alpha (TNF-α) in the serum and synovial fluid was determined using enzyme-linked immunosorbent assay (TNF-α-ELISA-BEST kit; Vector-Best, Russia). The serum and synovial fluid concentration of interleukin 6 (IL-6) was determined by the electrochemiluminescence immunoassay (ECLIA) method on the Cobas E411 analyzer (Roche, Switzerland). Antinuclear factor (ANF) in the blood serum was detected by the indirect immunofluorescence technique using HEp-2 human epithelial cells derived from a larynx carcinoma as the substrate (laboratory of Saint-Petersburg State Medical University).

RESULTS

The efficacy of therapy for oligoarticular JIA in 92 children was studied. The duration of the disease as of the moment the diagnosis of JIA was established was 4–5 [3;8] months on average. The average patient follow-up was 48 [38;62] months, the maximum follow-up period was 98 months. A total of 218 active joints were injected with triamcinolone acetonide: knees – 156 injections, ankles – 62 injections. Simultaneous administration of the corticosteroid in 2 or more joints was performed in almost one third of children (simultaneous injection in 2 or more joints is one manipulation). Single or double is-IAI of triamcinolone was performed in 65.2% (60 / 92) of children, the injection was performed three or more times in 34.8% (32 / 92) of children. Only one joint was treated in 43.5% (40 / 92) of children, in 39.1% (36 / 92) of cases – two different joints, and in 17.4% (16 / 92) of children – three or more joints were treated.

34.8% of children (32 / 92; all girls) achieved the inactive stage of the disease after the intra-articular administration of the corticosteroid; of them 21.7% (20 / 92) of children had monoarthritis, 8.7% (8 / 92) – asymmetric oligoarthritis, and 4.4% (4 / 92) – symmetric oligoarthritis of the lower extremities (Table 1). The average number of intra-articular injections in this group of children was 2 [1.75; 2], The average duration of the inactive phase of the disease between two consecutive injections was 7 [5.25; 10] months.

Table 1

Clinical manifestation of the onset of oligoarticular JIA in children, abs. (%)

Parameter	Group 1, *n* = 32	Group 2, *n* = 60	*p*
Monoarthritis	20♀ (62.5%) 0♂ (0%)	20♀ (33.3%) 4♂ (6.7%)	<0.01 >0.05
Asymmetric oligoarthritis	8♀ (25%)	16♀ (26.7%)	>0.05
Symmetric oligoarthritis	4♀(12.5%) ♂ (0%)	12♀ (20%) 4♂ (6.7%)	>0.05 >0.05
Psoriatic oligoarthritis	0♀ (0%) 0♂ (0%)	2♀ (3.3%) 2♂(3.3%)	>0.05 >0.05

Note. ♀ – girls, ♂ – boys

Table 2

Clinical and laboratory features at the onset of oligoarticular JIA in children

Parameter	Group 1, *n* = 32	Group 2, *n* = 60	*p*
Girls, abs. (%)	20 (83.3%)	50 (92.6%)	< 0.01
Age of JIA onset, years, *Me* [25;75]	2 [2; 3]	4 [3; 7]	> 0.05
Active joint count, abs., *Me* [25;75]	1 [1; 2]	1 [1; 2]	> 0.05
JADAS, *Me* [25;75]	10 [8; 12]	11 [8.5; 14]	> 0.05
ESR, mm / h, *Me* [25;75]	14 [6; 28]	17 [10; 25]	> 0.05
CRP, mg /l, *Me* [25;75]	2.7 [1.3; 4.5]	2.2 [1.8; 9.3]	> 0.05
Hemoglobin, g / l, *Me* [25;75]	114 [110; 128]	112 [108; 124]	> 0.05
Leukocytes, 10^9 / l, *Me* [25;75]	8.0 [6.8; 10.6]	7.4 [6.2; 10.8]	> 0.05
Platelets, 10^9 / l, *Me* [25;75]	442 [416; 476]	438 [408; 466]	> 0.05
Gamma globulins, %, *Me* [25;75]	21.6 [19.6; 22.3]	22.3 [20.4; 23.5]	> 0.05
IL-6, pg /ml, *Me* [25;75]	4.1 [2.5; 6.75]	5.8 [3.4; 10.5]	> 0.05
TNFα serum, pg /ml, *Me* [25;75]	0.65 [0.2; 0.85]	0.6 [0.1; 0.9]	> 0.05
ANF ≥ 1/160, abs. (%)	26 (81.25%)	45 (75%)	> 0.05
ANF ≥ 1/1,280, abs. (%)	12 (37.5%)	14 (23.3%)	> 0.05

Note. JADAS – Juvenile Arthritis Disease Activity Score; ESR – erythrocyte sedimentation rate; CRP – C-reactive protein; TNFα serum – tumor necrosis factor alpha in the serum; ANF – antinuclear factor (here and in Table 5).

The remaining 65.2% of children (60 /92) did not achieve the inactive phase of the disease after is-IAI of triamcinolone, which required application of conventional anti-rheumatic therapy. In this group, 23.9% of children (22 / 92; 16 girls and 6 boys) developed polyarthritis after two is-IAI; in 6.5% of cases (6 / 92; all girls), delayed onset of uveitis was registered, and in 34.8% of children (32 / 92; 26 girls and 4 boys), active disease persisted after more than three is-IAI. The average number of intra-articular injections in this group of children was 3 [2; 4].

The average duration of the inactive phase of the disease between the first two consecutive injections was 5.5 [4.25; 7] months and between subsequent injections – 2 [2; 3] months.

The main treatment-related complications were post-injection reversible (transient) manifestations of local atrophy and hypopigmentation of the skin. Complication rates in the knee and ankle joints did not exceed 10%. No other complications were noted. The comparative analysis of the active joint count and cJADAS-10 score in children of both groups did not reveal statistically significant differences in the disease onset.

The main laboratory inflammatory markers (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and the platelet and leukocyte levels) were the same in both groups of children with oligoarticular JIA. The concentrations of TNFα and IL-6 in the blood serum and the titer of antinuclear antibodies (ANA) were comparable (Table 2).

The average IL-6 and TNFα levels in the inflamed synovial fluid at the onset of inactive and active oligoarticular JIA did not significantly differ (Table 3). Moreover, the nature of the articular lesion and the frequency of early erosion did not differ significantly, despite different outcomes of the disease. Dry synovitis, which is considered a rare form of JIA, had almost the same incidence in both groups (Table 4).

An attempt was made to search for models of predicting the efficacy of non-systemic steroid therapy in children. It was revealed that girls with monoarthritis predominated in the group of children with inactive oligoarticular JIA (20 / 62.5% – achieved remission vs. 20 /33.3% – active JIA; $p = 0.0087$, $\chi^2 = 2.8$). However, the statistical analysis did not reveal a correlation between monoarthritis and the inactive stage against the background of local steroid therapy (R^2 (coefficient of determination) = 0.158, T = 1.23, odds radio (OR) = 4.01, 95% confidence interval (CI) 0.57–27.69, $p = 0.227$).

Table 3

Cytological analysis and immunological features of synovial fluid at the onset of oligoarticular JIA in children

Parameter	Group 1, $n = 32$	Group 2, $n = 60$
Cytosis, 10^9 / l	4.3 [3.5; 7]	4.35 [3.7; 6.35]
Lymphocytes, %	54 [31.75; 66.5]	32 [26.5; 53.5]
Neutrophils, %	18 [12.7; 37.5]	40 [6; 57.3]
Monocytes, %	16 [10; 21.75]	14 [9.2; 19.3]
Synoviocytes, %	1 [0; 7]	1 [0; 4]
Ragocytes, %	3 [2; 4]	3 [2; 7]
IL-6 synovial (sIL-6), pg /ml	2,208 [710; 4,564]	3,234 [1,265; 16,902]
TNFα synovial (sTNFα), pg /ml	3.3 [2.5; 3.8]	1.1 [0.6; 3.7]

Note. Ragocytes – cells (macrophages, neutrophils) containing large granules – phagolysosomes, including immune complexes, various immunoglobulins, and rheumatoid factor; $p > 0.05$.

A significant positive correlation was not found in the multiple linear regression analysis between the efficacy of steroid therapy and different inflammatory laboratory parameters (Table 5). The linear regression analysis revealed a direct relationship between the ESR (mm / h) and interleukin 6 in the synovial fluid ($p < 0.001$; Fig. 2).

Table 4

Clinical and instrumental features of synovitis at the onset of oligoarticular JIA in children, abs. (%)

Parameter	Group 1, $n = 32$	Group 2, $n = 60$
Exudative synovitis	16 (50%)	28 (46.7%)
Exudative and proliferative non-erosive synovitis	9 (28.125%)	18 (30.0%)
Exudative and proliferative erosive synovitis	1 (3.125%)	2 (3.3%)
Dry non-erosive synovitis	4 (12.5%)	8 (13.3%)
Dry erosive synovitis	2 (6.25%)	4 (6.7%)

Note. $p > 0.05$.

The analysis revealed a direct correlation between a short period of disease inactivity after consecutive intra-articular injections of triamcinolone acetonide and a risk of active arthritis development (with an inactive phase of arthritis lasting less than 3 months, OR = 2.09, $p < 0.001$; with an inactive phase lasting less than 2 months – OR = 8.9, $p < 0.001$; Table 6).

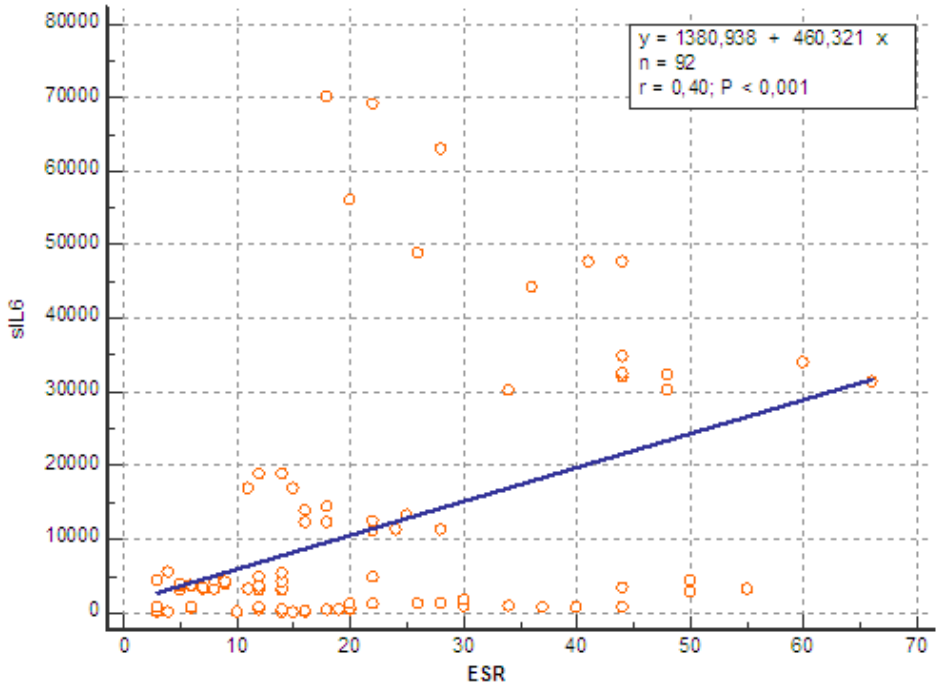

Fig. 2. Linear regression analysis of the direct relationship between ESR (mm/h) and IL-6 in the synovial fluid (pg / ml): ESR – erythrocyte sedimentation rate, sIL6 – interleukin 6 in the synovial fluid

Table 5

The results of constructing the model of "inactive" arthritis by the method of logistic and multiple linear regression in children with JIA based on laboratory tests

Parameter	R^2	Standard error	T-test	OR	95% CI	*p*
	–0.003841	0.009596	–0.400	0.9913	0.8934– 1.0998	0.8638
CRP, mg /l	–0.01390	0.02447	–0.568	0.9443	0.7508– 1.1878	0.6246
IL-6 serum, pg /ml	–0.03193	0.02386	–1.338	0.8366	0.6151–1.1379	0.2557
TNFα serum, pg /ml	0.1144	0.06898	1.659	2.2208	0.7480– 6.5938	0.1507
I IL-6 synovial, pg /ml	–0.000009239	0.00000764	–1.209	0.999	0.9997– 1.0001	0.2913
TNFα synovial, pg /ml	0.02611	0.01474	–1.772	1.1221	0.6138– 1.1007	0.1882

Table 6

The results of constructing the model of "active" arthritis by the method of logistic and multiple linear regression in children with JIA based on the duration of the inactive stage between intra-articular injections of triamcinolone acetonide

Time, months	R^2	Standard error	T-test	OR	95% CI	*p*
More than 6	–0.7745	0.04702	–16.470	5.09	0.956– 1.000	< 0.001
3–5	0.1311	0.09810	1.337	2.03	0.393–4.643	0.1312
Less than 3	0.5849	0.1249	4.683	2.09	0.534–0.749	< 0.001
Less than 2	0.5849	0.1151	5.081	8.9	0.680–0.868	< 0.001

DISCUSSION

Our study analyzed the effectiveness of intra-articular injections of long-acting corticosteroids (triamcinolone acetonide) in children with oligoarticular-onset JIA. The main aim of the research was to find possible predictors (clinical, instrumental or laboratory) of early ineffectiveness of is-IAI in children with chronic oligoarticular JIA. Sample homogeneity, the volume of laboratory and instrumental diagnosis, and management of the participants in one medical center allowed to study the nature of the disease onset, the dynamics of the articular syndrome, and the effectiveness of monotherapy with corticosteroids.

Moreover, the parents had a great interest in the course of the study. It is known that parents do not agree to early aggressive therapy with methotrexate. This opinion is based on the amount of information available on the Internet about side effects of methotrexate, conclusions of specialists not related to rheumatology, and a fear of lifelong treatment. In addition, a small number of affected joints and seemingly low activity of the disease leave hope for a favorable outcome or misdiagnosed JIA (in the opinion of most parents). In this situation, parents of the child would rather agree to the next intra-articular injection of triamcinolone into the inflamed joint than to methotrexate therapy.

Therefore, this study was aimed at searching for the clinical, instrumental, and laboratory predictors that could help to forecast early ineffectiveness of local steroid therapy. However, it is worth noting that our conclusions do not reflect the degree of intensity of the disease course, possible risks of articular syndrome progression and eye lesion development, and unfavorable outcomes of the disease.

In the Russian literature, the need for application of local steroid therapy in children with JIA is mostly described in works published earlier than 2010, despite the fact that the national clinical rheumatology guidelines contain this treatment option [8, 9]. I.M. Vorontsov and N.N. Kuzmina in their studies indicated subtypes of JIA with lowly aggressive course and sometimes complete recovery [10, 11]. A meta-analysis of data from various trials showed the effectiveness of local intra-articular corticosteroid injections in JIA.

These results of retrospective studies on JIA treatment are available only in English-language publications [12–14]. Currently, in Europe and the USA, the long-acting steroid which is approved and most commonly used in JIA for intra-articular treatment is triamcinolone hexacetonide (TH). In the Russian Federation, the drug that is certified and approved for intra-articular injection in JIA is triamcinolone acetonide (TA).

Triamcinolone acetonide (TA) is a synthetic corticosteroid with anti-inflammatory properties. The drug in the form of a sustained-release suspension is poorly soluble and deposits in the articular cavity, providing a long-term effect on the inflamed synovium. Triamcinolone decreases the expression of proinflammatory cytokines (TNFα, IL-1β, IL-6), chemokines, and growth factors (VEGF, IGF, PDGF, CSF-1), blocks proteolytic activity of matrix metalloproteinases (MMP-2, MMP-3, MMP-9), and reduces migration of inflammatory cells in the synovial cavity. Moreover, the drug decreases the proliferative capacity of synoviocytes associated with reduction of NF-κB transcriptional activity [15–17].

Most multicenter studies have demonstrated high effectiveness, good tolerance, and safety of intra-articular injections with triamcinolone hexacetonide. Triamcinolone acetonide was viewed as an alternative form acceptable for intra-articular injections, that demonstrated good clinical effects [18–20]. Long-term effectiveness of early local therapy with triamcinolone hexacetonide / acetonide in JIA was also described in more recent studies, however, triamcinolone hexacetonide was preferred [21–23].

In the present study, effectiveness of non-systemic corticosteroid therapy of JIA was related to a number of determining factors: the first injection of triamcinolone at an earlier stage of oligoarticular JIA, solely intra-articular administration of triamcinolone with preliminary dilution of the drug, and special post-injection regimen. The optimal timing for is-IAI in children with JIA should be strictly limited to 6–12 months after the onset of the disease. The following injections can be performed in the inflamed joints without signs of disease progression [24].

Preliminary dilution of triamcinolone and active / passive joint movements improve the penetration of

the corticosteroid into the inflamed synovial membrane. Reduced axial loads on the lower extremity decrease risks of aseptic necrosis and contribute to prolonged therapeutic effect [25]. Long-term effects of intra-articular administration of triamcinolone is related to anti-inflammatory, anti-proliferative, immunosuppressive, and vasoconstrictive effects on the synovial membrane. Triamcinolone has the slowest joint clearance and is the most potent in producing synovial atrophy. The "scalding" effect of triamcinolone on the inflamed synovial tissue can be associated with vasoconstriction of blood vessels in the subsynovial layers and return of cell sensitivity to pro-apoptotic factors [26].

The present study demonstrated the effectiveness and safety of non-systemic corticosteroid therapy with triamcinolone acetonide in children with oligoarthicular-onset JIA. The research did not identify predictors of oligoarticular JIA which could directly indicate possible ineffectiveness of steroid therapy beforehand. However, the study revealed that the degree of aggressiveness of JIA was inversely proportional to the duration of the inactive phase of arthritis between two consecutive is-IAIs. Moreover, the study revealed a direct relationship between ESR and the concentration of IL-6 in the synovial fluid. Summarizing the data of the 7-year follow-up of children with oligoarticular JIA, we can state that about one third of the children achieve stable remission against the background of local steroid therapy.

CONCLUSION

Local corticosteroids are effective and safe in children with oligoarticular-onset JIA. Rational use of isolated intra-articular injections in children with JIA contributes to assessment of the degree of disease aggressiveness. Application of treat-to-target principles and early disease-modifying anti-rheumatic drugs in patients with oligoarticular-onset JIA artificially reduce the effectiveness of steroid therapy in pediatric rheumatology.

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