

Introduction

Juvenile idiopathic arthritis (JIA) often causes significant functional impairment throughout the lifespan [1,2]. Medical workers who are aware of the JIA's clinical course specifics in adolescence can provide better assistance at the transition stage when a patient's healthcare shifts from a pediatric to an adult health services [3, 4,5]. The patient's transmission is a multidimensional, interdisciplinary and active process, which addresses the medical, socio-psychological and educational/professional needs of adolescents with JIA [6,7,8]. Previous studies ([The link](#)) have shown that the use of specific questionnaires (CHQ, Peds-QL) don't allow fully assess psychometric changes in young adults. In particular, the interpretation of these studies' results on Peds-QL is limited due to a small sample size [10]. On the contrary, when using HR-QOL, Haverman L. et al. (2011) found significant changes in the quality of life in children and adolescents with JIA [11].

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The HAQ (Moroz & Bezsheiko, 2018) questionnaire is widely used in clinical practice for the study rheumatic diseases in adults, particularly in rheumatoid arthritis [12]. This questionnaire is a useful tool for evaluation of functional status, its change during treatment (Frankova & Semenoga, 2014). HAQ score is also associated with disease activity, mortality, and need in joint replacement [12, 13]. Most often, for the quality of life (QoL) assessment in adult patients, the SF-36 questionnaire is used [13]. Indeed, QoL in adulthood may be influenced by sociological, economic, philosophical and ethical factors, which can be less informative in childhood. For patients in the transitional period from pediatric to adult medical care, it is necessary to investigate the effectiveness of various medical examination methods for measuring QoL.

The study aimed to determine the impact of the disease on the QoL in young adults with JIA during the transition from a pediatric to an adult healthcare service.

Materials and methods

materials

A study sample included 89 young people aged 16 to 22 years old with a history of JIA, regardless (1) of the active inflammation severity at the time of examination and 25 healthy young volunteers that formed the control group. The experimental group comprised of patients from different Ukrainian who were diagnosed with the JIA according to the classification criteria of the International League of Associations for Rheumatology - ILAR [14] between 1984 and 2014 without severe concomitant pathology. Upon reaching adulthood, all patients with JIA were examined by an adult

rheumatologist during outpatient visits or inpatient at the Oleksandrivka City Clinical Hospital in Kyiv between April 2015 and February 2017. In the study were analyzed demographic and clinical data, including age, gender, delayed diagnosis of JIA, disease duration, number of swollen joints, limitation of joint mobility, disease activity, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Pain and overall well-being were measured using the visual analogue scale (VAS). The functional status was evaluated using the HAQ questionnaire (Health Survey). Disease activity and the presence of remission were determined according to the American Association of Rheumatologists criteria [15].

methods

First Method

Additionally, the data regarding current JIA treatment were analyzed, including the use of non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids (GCs), methotrexate, leflunomide, hydroxychloroquine, azathioprine and biological therapy (IL-1Ra, anti-TNF agents (etanercept, adalimumab), abatacept and tocilizumab). The QoL of patients with JIA and the control group was assessed using the Short-Form-36 questionnaire (SF-36). We used licensed access containing (license No. QM037587) for Non-Profit Academic Research from the Management of Scientific Grants and Research (OGSR) provided by OptumInsight Life Sciences, Inc..

Second Method

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Statistical analysis

Statistical analysis was performed using descriptive statistics, Student's criteria for unbound variables, and one-way ANOVA dispersion analysis. The data are presented as the mean \pm standard deviation (SD) for continuous variables and numbers (percentages) for categorical variables. Statistically significant was the probability value $p < 0,05$. The correlation was determined by the Pearson method for a two-way mixed model. In the analysis, software packages "Statistica 6.0" was used by Copyright StatSoft, Inc. 1984-2001.

Results

There was conducted an analysis of demographic and anthropometric data from 89 young patients with JIA and 25 healthy volunteers (Table 1). The mean age of patients was 19.4 ± 1.8 years, which did not significantly differ from the mean age in control group. The average duration of the disease was 8.7 ± 5.1 years and the average age of

the disease onset - 10.2 ± 4.9 years. The mean time from the disease's onset to the diagnosis was estimated at 15.6 ± 25.9 months.

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The oligoarthritis form of JIA was diagnosed in 34 patients, including 20 patients with persistent and 14 with common form. The polyarthritis variant was found in 24 patients, from whom 10 had seropositive and 14 had seronegative polyarthritis. Enthesitis-related arthritis and psoriatic arthritis were diagnosed in 18 patients, and systemic JIA - in 13 patients.

Most patients (67.4%) had previously received glucocorticoids (GCs) before baseline period, and at the time of observation, only 27% received GCs. 14 patients received only NSAIDs. 75 patients received DMARD, including methotrexate (n=55), plaquenil (n=12), sulfasalazine (n=6), azathioprine (n=2). 23 patients received immunobiological therapy before or at the time of examination; 19 patients were prescribed monoclonal antibodies to the TNF-19 (etanercept - 16 patients, adalimumab - 3 patients), 2 - tocylumizabac, and remaining 2 - rituximab. Remission was diagnosed in 37 (41.6%) patients with a history of JIA.

Table 1. Demographic characteristics of patients with JIA.

	Patients with JIA (n=89)
Sex (M/F)	41/48 (control group -12/13)
Middle age	19.4±1.8 (control group - 20.1±1.9)
Duration of the disease, years	8.7±5.1
Age at onset of JIA, years	10.2±4.9
Time from onset to the diagnosis, months.	15.6±25.9
Persistent oligoarthritis	20 (22.5%)
Common oligoarthritis	14 (15.7%)
Polyarthritis RF +	10 (11.2%)
Polyarthritis RF -	14 (15.7%)
Enthesitis-related arthritis + psoriatic arthritis	18 (16.9%)
Systemic JIA	13 (14.6%)
GCs took earlier / at the moment	60 (67.4%)/24 (27%)
Remission	37 (41.6%)
NSAIDs	14
DMARD (n=75)	
Methotrexate	55/75
Plaquenil	12/75
Sulfasalazine	6/75
Azathioprine	2/75
Immunobiology (n=23)	
Anti-TNF (ETA / ADA))	19/23 (16/3)
Tocilizumab	2/23
Rituximab	2/23

Table 1: This is caption

All patients from JIA and control group received quality assessment questionnaires SF-36 and functional status HAQ. The results of the evaluation are presented in Table 2.

Table 2. Quality of life in young patients with JIA and control group

Indexes	Patients with JIA (n=89)	Control group (n=25)	p
HAQ	0.3±0.4		
VAS patient	34.6±23.3		
VAS doctor	27.9±24.3		
SF- 36			
SF-36 physical indexes			
PF	74.3± 20.9	94.7±8.7	0.0002
RF	64.6±29.9	83.8±19.5	0.02
BP	59.0±24.2	84.5±21.6	0.0002
GH 56.5±22.6		60.1±17.1	0.54
VT	58.2±19.1	59.8±20.0	0.77

SF-36 psychological indexes			
SF	75.8±21.2	80.5±18.2	0.41
RE	69.2±33.8	75.0±26.7	0.52
MH	69.3±18.6	68.4±18.9	0.86
PCS	46.3±8.7	55.7±6.9	0.0001
MCS	47.0±10.5	45.1±11.7	0.52
PHQ-9	5.8 ±5.5	4.3 ±3.1	0.12

* Notes: PF - physical functioning; RP - role functioning due to physical condition, BP - pain intensity, GH - general health status, VT - vital activity, SF - social functioning, RE - role function, conditioned by emotional state, MH - mental health, PCS - Physical well-being, MCS - psychological well-being.

HAQ	0.3±0.4	80.99±18.29	34.55
VAS patient -	34.6±23.3	75.99±26.79	32.33
VAS doctor	27.9±24.3	68.99±18.99	26.55

As can be seen from Table 2, patients with JIA had a worse ($p<0.001$) physical well-being (46.3 ± 8.7) compared with the control group (55.7 ± 6.9). In them, there was a decrease in the indices corresponding to the physical condition ($p<0.001$), role functioning due to the physical condition ($p=0.02$), and the intensity of pain ($p<0.001$), compared with the control group. However, the indicators responsible for psychological well-being in patients with JIA did not differ from the control group.

In the analysis of functional activity communication for HAQ (Table 3), there was found a strong negative effect on physical functioning ($r = -0.56$, $p<0.001$), a role-based functioning due to physical condition ($r = -0.33$, $p <0.001$), pain intensity ($r = -0.60$, $p<0.001$), general health ($r = -0.40$, $p = 0.01$), vital activity ($r = -0.46$, $p <0.001$), social functioning ($r = -0.48$, $p<0.001$), and mental health ($r = -0.42$, $p<0.001$), as well as in the total score for the physical ($p<0.001$) and psychological ($p<0.05$) well-being.

Table 3. Communication of functional activity with quality of life.

	PCS	MCS	PF	RF	BP	GH	VT	SF	RE	MH
HAQ	-0.59	-0.25	-0.56	-0.32	-0.60	-0.40	-0.46	-0.48	-0.08	-0.42
P	<0.001	0.035	<0.001	0.006	<0.001	0.001	<0.001	<0.001	НД	<0.001

Figure 1 shows the results of the SF-36 questionnaire for young patients with JIA and those in the control group, where the apparent lower levels of physical health (PCS) ($p<0.001$), role-based physical functioning are evident) - RF ($p<0, 05$), pain intensity - BP ($p<0.001$) and physical functioning - PF ($p<0.001$) in patients with JIA compared with healthy subjects.

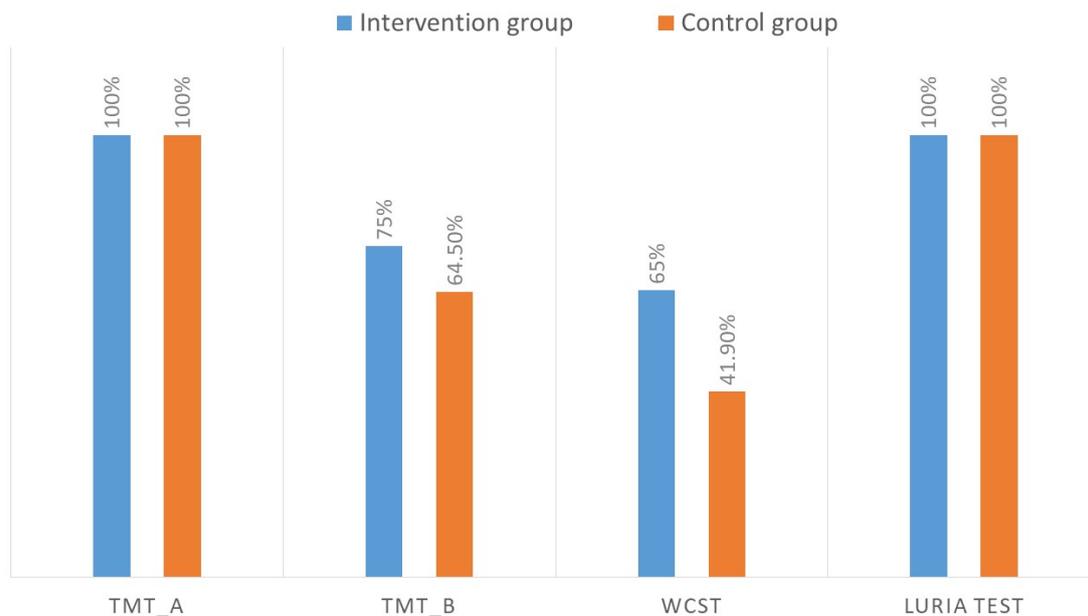


Figure 1: Quality of life in young patients with JIA and healthy individuals according to the SF-36 questionnaire.

*Notes: * - statistical significance $p < 0.001$, † - statistical significance $p = 0.05$

Discussion

Heading 3

As we expected, QoL in patients with JIA was worse than in the control group. Our findings were confirmed by data published earlier that showed a worse QoL in young people with JIA than in the control group of the corresponding age and sex [9, 16, 17, 18, 19, 20, 21]. However, our results in patients with JIA and healthy individuals are different from the data from Wipff J. et al., where authors analyzed data on patients with JIA at the stage of transmission of patients from child to an adult healthcare services during biologic therapy [22]. The SF-36 score for physical and psychological

health was less influenced by the JIA in our sample than in previously published studies. These results were quite unexpected because in Ukraine biological therapy is not available for many patients [16, 18, 19, 20, 22]. There are several possible explanations for these results, including:

- Our patients often received GCs, which reduced the activity of the disease.
- Our sample included not only patients with JIA in the active phase that needed constant observation but also those who were in complete clinical remission and did not require medical therapy.
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- Our results confirmed that JIA's greatest impact was on "physical functioning" and "pain intensity," which are parts of the physical well-being SF-36 factor. Thus, JIA has a greater impact on physical health than on the mental health of patients, which corresponds to scientific data [16, 18, 19, 20, 23, 24].

There is evidence of a negative relationship between QoL and the duration of the disease by the results of work by Minden K. et al. [25]. Foster et al. also noted this tendency in patients with JIA [16]. However, in our study, we did not detect the effect of the duration of the disease on the QoL indicators, although we observed the negative correlation between functional activity limitation and all components of the QoL according to the SF-36 as established, and in the previous work [1] we have shown that QoL depends on the X-ray definite degree of JIA's progression .

Since our study showed that physical activity is most strongly affected by pain intensity, treatment with JIA should not be directed solely at the fight against inflammation through the use of NSAIDs. It is advisable to use analgesics and procedures for severe pain, including physiotherapy and/or hypnosis [26].

Patients with JIA may also have a low QoL while in remission. In our study, it was found that 3 out of 33 patients in the remission stage had a low physical well-being. In 5 out of 33 patients - a low level of mental well-being. These data coincide with the results of the study [22], in which 8/38 patients with JIA in the remission stage had a low physical well-being.

Our study has some limitations. First, our study had cross-sectional design study that limited the assessment of the natural course and QoL prognostic factors of the JIA. Second, data on the educational and socio-economic status of patients with JIA and their parents have not been collected. These factors may influence SF-36 results. Previous studies have shown that psychological factors, therapies, geographical origin, and socioeconomic differences can have an effect on pain in the JIA [27, 28]. Third, we did not evaluate the effect of treatment on QoL, especially on biological therapy, although a number of studies have shown that QoL with JIA is improved against the background of biological therapy [29, 30].

Our research also has the strengths:

1. The experimental group consisted of patients with JIA that met the criteria for ILAR in the transition period.
2. The results of evaluation were compared with the control groups comprised of healthy individuals.

3. This is the first study in Ukraine that included biologic therapy as a potential factor affecting QoL in the transition period.

Conclusion

Juvenile idiopathic arthritis had the greatest influence during the transition from pediatric to adult rheumatological service to a physical functioning and pain intensity on SF-36 physical well-being scale. It indicates a greater effect of the disease on the physical than on the mental health in patients with JIA.

Another conclusion

Звичаний текст тут.

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