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**Preservation of Postvaccinal Immunity to Measles, Rubella, Parotitis, Hepatitis B and Diphtheria in Patients With Juvenile Idiopathic Arthritis Who Undergone Planned Immunization Under the Age of Two: Preliminary Results of Cross-Sectional Study**

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***Background.*** *Patients with juvenile idiopathic arthritis (JIA) can have low levels of antibodies to vaccine antigens due to immunologic features of the main disease, disruptions in vaccination schedule and* *immunosuppressive drugs administration. The aim of the study is to examine the status of postvaccinal immunity and determine the factors associated with preservation of protective level of antibodies in patients with JIA.* ***Methods.*** *This cross-sectional study included patients with JIA at the age from 2 to 17 years old vaccinated under the age of two (before JIA) against measles, rubella, parotitis, hepatitis B and diphtheria. Levels of IgG to vaccine antigens were measured by enzyme immunoassay. The minimum protective level of anti-measles IgG was esteemed as 0.18 IU/ml, antibodies to rubella — 10 IU/ml, for parotitis — COI >1.0, for hepatitis B — 10 mIU/ml, antibodies to diphtheria — 0.09 IU/ml.* ***Results.*** *The study included 90 patients with JIA (71% of girls) at the age (median) 11.3 (7.5; 14.9) years. The age of JIA manifestation was 6.0 (4.0; 8.0) years, disease duration — 4.0 (2.0; 7.3) years. Glucocorticosteroids administration in anamnesis or at study entry was recorded in 24/88 (27%) patients, methotrexate — 81/88 (92%), genetically engineered biologic drugs — 54/89 (61%). Protective level of antibodies to measles virus was revealed in 45 (50%) children with JIA, to rubella virus — in 88 (98%), to parotitis — in 68 (76%), to hepatitis B — in 49 (54%), to diphtherial anatoxin — in 45 (50%). The decrease of postvaccinal immunity level was associated with JIA duration and glucocorticosteroids administration (against diphtheria) duration, as well as drop-out immunization (against measles).* ***Conclusion.*** *Major part of children with JIA have no protection against measles, parotitis, hepatitis B or diphtheria. High risk of progression of such vaccine-preventable diseases in these children demands development of individual programs of immunization.*

***Key words:*** *children, juvenile idiopathic arthritis, preventive vaccination, antibody titer, measles, rubella, parotitis, hepatitis B, diphtheria, risk factors.*

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**RESULTS**

**Table 1.** Structure of patients with JIA and minimum protective level of antibodies

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Percentage of patients with minimum protective level of antibodies against:** | All (n =90) | **Age groups, years** | | | *Р*  **(df =2)** |
| **<7 (n =24)** | **8-12 (n =32)** | **13-17 (n =34)** |
| Measles, abs. (%) | 45 (50) | 16 (67) | 14 (44) | 15 (44) | 0,163 |
| Parotitis, abs. (%) | 61 (68) | 20 (83) | 20 (63) | 21 (48) | 0,163 |
| Rubella, abs. (%) | 88 (98) | 24 (100) | 32 (100) | 32 (94) | 0,186 |
| Diphtheria, abs. (%) | 45 (50) | 15 (63) | 15 (47) | 15 (44) | 0,351 |
| Hepatitis B, abs. (%) | 49 (54) | 15 (63) | 18 (56) | 16 (36) | 0,493 |

**Table 2.** Predictors of preservation of postvaccinal immunity (minimum protective level of antibodies) to measles, parotitis, diphtheria, hepatitis B: results (р) of unifactor regression analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Predictors** | **Minimum protective level of antibodies** | | | |
| **Measles** | **Parotitis** | **Diphtheria** | **Hepatitis B** |
| JIA length | **0,001** | 0,569 | 0,431 | 0,846 |
| Age\* | **0,014** | 0,387 | **0,014** | 0,914 |
| Number of vaccinations | **0,023** | 0,572 | 0,698 | 0,886 |
| Glucocorticosteroids | 0,340 | 0,880 | **0,05** | 0,931 |
| Methotrexate | 0,652 | 0,125 | 0,652 | 0,174 |
| GEBD | **0,013** | 0,253 | 0,897 | 0,215 |

*Note.* # — predictors of preservation of postvaccinal immunity to rubella were not analysed because it sustained in 98% of patients. \* — age at study entry. JIA — juvenile idiopathic arthritis, GEBD — genetically engineered biologic drugs.

**Table 3.** Predictors of preservation of postvaccinal immunity (minimum protective level of antibodies) to measles and diphtheria: results multifactor regression analysis

|  |  |  |  |
| --- | --- | --- | --- |
| **Predictors** | b | **SE** | *Р* |
| **Against measles** *(п* **= 88), R2 = 0,15** | | | |
| JIA length | -0,240 | 0,021 | 0,083 |
| Age\* | -0,068 | 0,022 | 0,652 |
| Number of vaccinations | 0,304 | 0,147 | **0,038** |
| Glucocorticosteroids | 0,057 | 0,134 | 0,643 |
| Methotrexate | 0,100 | 0,212 | 0,369 |
| GEBD | -0,187 | 0,130 | 0,142 |
| **Against diphtheria (п = 88), R2 = 0,13** | | | |
| JIA length | -0,287 | 0,140 | **0,044** |
| Age\* | 0,017 | 0,172 | 0,919 |
| Number of vaccinations | 0,083 | 0,140 | 0,552 |
| Glucocorticosteroids | -0,232 | 0,117 | 0,05 |
| Methotrexate | 0,002 | 0,112 | 0,982 |
| GEBD | 0,188 | 0,130 | 0,151 |
| **Against parotitis (п = 88), R2 = 0,06** | | | |
| JIA length | -0,181 | 0,138 | 0,764 |
| Age\* | -0,073 | 0,173 | 0,221 |
| Number of vaccinations | 0,280 | 0,143 | 0,193 |
| Glucocorticosteroids | 0,050 | 0,119 | 0,558 |
| Methotrexate | 0,059 | 0,111 | 0,226 |
| GEBD | -0,193 | 0,127 | 0,645 |
| **Against hepatitis B (п = 88), R2 =0,04** | | | |
| JIA length | -0,125 | 0,022 | 0,396 |
| Age\* | 0,069 | 0,018 | 0,630 |
| Number of vaccinations | -0,017 | 0,189 | 0,888 |
| Glucocorticosteroids | -0,028 | 0,138 | 0,820 |
| Methotrexate | 0,111 | 0,225 | 0,348 |
| GEBD | 0,142 | 0,141 | 0,303 |

*Note.* \* — age at study entry. JIA — juvenile idiopathic arthritis, GEBD — genetically engineered biologic drugs.

**STUDY LIMITATIONS**

Major limitations of this research are connected with the small sampling size, different patients’ age, disease length and number of previous vaccinations. The small sample size did not allow to perform analysis of risk factors for fully estimation of immunity against rubella and hepatitis B. It should be mentioned that there was no control group for this study, thus, we could not fully estimate the reduction of antibody formation in healthy children without any risk factors. The presence of the control group would make it possible to estimate whether the studied predictors actually affect the reduction of antibody formation or not. The research limitations could affect the accuracy of identification of predictors covering preservation of postvaccinal immunity. It means that studied factors could be wrongly considered as possible predictors (no control group) and the role of other factors which might be important could not be identified (the combination of medications with JIA length, age of administration of certain medications, therapy duration). It is impossible to specify how every single factor (medications, number of vaccinations, disease length, arthritis subtype) could affect the situation itself because some patients received combination therapy, groups were not stratified by age of disease manifestation or disease length. It is possible that larger sampling would allow us to carry out more detailed analysis in subgroups. We neither did not mentioned such factors as therapy length, cumulated doses, treatment combinations. One patient could receive several types of therapy, or may be he had another disease which could affect the drug elimination and indirectly the immune response itself. The measurement error is also possible for the study related to the accuracy of the measurement methods (CV of the methods used to measure antibodies level was 7.5–8%).

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**CONFLICT OF INTERESTS**

**Mikhail M. Kostik** ― receives fees for lecturing from Pfizer, AbbVie, Novartis, Sanofi companies.

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