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GROWTH AND DEVELOPMENT OF CHILDREN WITH HIV/AIDS

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There were observed 241 HIV-infected children. Indexes of children's physical development (PD) such as weight-to-growth, height-for-age, weight-for-age, and BMI-for-age were studied, depending on the age (less than 12 months, 12-35 and 36-59 month-old children), stage of disease, immunosuppression severity and HIV replication activity. It was revealed that PD indexes of children less than 12 months may not be used as predictors of HIV severity and progression rate. Adequate prognosis in regard of severity and progression rate according to PD indexes is possible only in children older than 1 year old.

Keywords: Human immunodeficiency virus, acquired immunodeficiency syndrome, physical development, children.

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Introduction

Physical development (PD) is one of the main criteria of children's health. It has the value of objective criteria for individual organism's development due to relative simplicity and accessibility of research methods of children's PD, as well as the most information of materials obtained (Kapitonov, 2005).

The fact that HIV infection in children results in significant disturbances of PD is well known (Berhane et al., 1997; McKinney et al., 1994; Miller, 2000). Accordingly, the more pronounced clinical signs of disease, the more clear symptoms of lag in PD (Moye et al., 1996). Saavedra et al. (1995) reported that children with AIDS lag in growth stronger than children in a less advanced stage of the disease. Berhane et al. (1997) observed that in Ugandan HIV-infected children weight loss followed by 5-fold increase in mortality, compared with the age norm (Z-index of less than 1.5). Saavedra et al. (1995) described a similar relationship between weight loss, disease progression and survival in the U.S.A.

However, relationships between children's PD and other factors that influence on the progression of HIV infection (the level of viral RNA in plasma, immunodeficiency severity) are still not well studied. Thus, the main question "Is it possible to rely on indicators of children's PD at estimation the risk of adverse outcome?" remains poor understood.

Thus, the purpose of our study was to investigate PD disturbances in HIV-infected children, depending on the viral replicative activity and immunodeficiency severity during the natural course of the disease.

Materials and methods

Objective of the study was 241 HIV-infected children. The children were divided into 3 groups according to age: I group - 19 children less than 12 months, II group - 107 children aged between 12-35 months, III group - 115 children aged between 36-59 months.

We studied PD of HIV-infected children, depending on the stage of disease, immunosuppression severity and HIV replicative activity. Stage of HIV infection was determined according to the revised WHO clinical classification of HIV-infection in children (WHO, 2005), immunosuppression severity according to the WHO classification

of HIV-associated immunodeficiency in children (Geneva, 2006). Empirical value of the level of HIV RNA in blood which is equal to 100.000 cop/ml was selected as the boundary separating HIV replicative activity.

Anthropometric measurements and their evaluation were conducted according to the WHO Child Growth Standards (WHO, 2006a). Since the single anthropometric measurements (height or body weight) had limited values, we calculated such metrics as body weight for the given height (exhaustion), body length for the given age (stunting), body weight for the given age (integral index of physical development), as well estimated the ratio of body weight (in kg) to the body length in a prone position, or to the height in a standing position (in m^2) (body mass index-age) according to the WHO standard indicators of child's development (WHO, 2006b).

Because the height or weight of children are very often were at the end of the distribution curve (e.g., below the 5th percentile), we used Z-index, which is a standardized measure to assess the relative growth rate or weight gain regardless of whether there are entry points of these indicators on the standard curve.

A child with a height-age index, a measure of linear growth of more than two standard deviations (-2SD), was assessed as stunted, that reflecting a presence of chronic malnutrition. If the value of this indicator was more than three standard deviations (-3SD), this state regarded as a severe growth retardation.

A weight-growth index allowed assessing the nutritional status of child in the present. Children who had index values more than two standard deviations (-2SD) regarded as being underweight for growth and having a moderate degree of exhaustion. If a child was detected deviation of more than three standard deviations (3SD), his/her condition was regarded as a severe degree of exhaustion.

An index "weight-for-age" was used as a good general indicator for the determination of nutrition status. Children who had values of more than two standard deviations (-2SD), were considered as having a moderate degree of malnutrition, whereas children with more than three standard deviations (3SD) were regarded to have a severe degree of malnutrition.

The results obtained and discussion

PD of children less than 12 months. In the separation of children less than 12 months by disease stages, no statistically significant difference was revealed.

In the separation of this age group by HIV replicative activity statistically significant difference was found only when comparing the indicators of body mass index: in children with low HIV replicative activity ($\leq$100.000 cop/ml) it was -2.31$\pm$0.66, whereas in children with viral load over 100.000 cop/ml it was -1.39$\pm$0.41 ($p \leq 0.05$).

Thus, in children less than 12 months viral load can not be used as a prognostic factor of unfavorable outcome.

In the separation of children according to immunosuppression level, we obtained the discouraging results: the more severe the immunodeficiency, the PD indicators were closer to the norm. Absence of adequate correlation between the percentage of CD4 + lymphocytes and children's PD suggests that PD in any way can not serve as a predictor of immunodeficiency severity in HIV-infected children less than 12 months, as well as the level of CD4 + T-lymphocytes has no predictive value when assessing the risk of nutrition disorders in children. This is due to the immaturity of the immune system of early age children, resulting in even a fraction of CD4+ lymphocytes does not reflect the true picture of the formation of the adaptive immune response.

Thus, in children less than 12 months, PD does not reflect the severity of disease, as well as there was no dependence on the level of replicative activity and immunodeficiency severity. The abovementioned means that in children less than 12 months the prediction of risk of adverse disease course is not possible in terms of immunodeficiency level and

viral load, because even such a sensitive sign as PD does not response to changes in the immunological status of patient and viral replicative activity.

PD of 12-35 month-old children. In children aged between 12-35 months, disease progression was accompanied by more serious PD disturbances. The separation by HIV replicative activity also showed that children with high replicative activity had more pronounced delay in linear growth and malnutrition than the children controlling virus replication (Table 1).

TABLE 1. DISTURBANCES IN CHILDREN'S PHYSICAL DEVELOPMENT, DEPENDING ON THE DISEASE STAGE AND HIV REPLICATIVE ACTIVITY

Indicator	Stage III	Stage IV
Weight-to-growth (z)	-0.33±0.28	-2.08±0.23***
Height-for-age (z)	-1.5±0.42	-1.8±0.27
Weight-for-age (z)	-1.05±0.24	-2.52±0.16***
BMI-for-age (z)	-0.12±0.32	-1.92±0.6***

Index	≤ 100 000 cop/ml	> 100 000 cop/ml
Weight-to-growth (z)	-1.51±0.64	-1.74±0.31
Height-for-age (z)	-0.22±0.92	-1.85±0.38*
Weight-for-age (z)	-1.22±0.45	-2.25±0.26*
BMI-for-age (z)	-1.49±0.75	-1.53±0.35

Note: * - significant differences between comparing groups.

Thus, we can see a close relationship between child's PD state and disease progression, which is bilateral in nature: HIV infection modifies the nutritional status of the child as a result of malabsorption, increased nutrient requirements and metabolic disorders, especially against opportunistic and other infections, whereas nutrient deficiency, in its turn, leads to the disease progression.

The separation by immunosuppression severity reflected the natural course of HIV infection, in which with disease progression worsening of signs of exhaustion and malnutrition were marked, that was confirmed by statistical significance (Table 2).

TABLE 2. DISTURBANCES IN CHILDREN'S PHYSICAL DEVELOPMENT, DEPENDING ON IMMUNODEFICIENCY LEVEL

Index	Mild	Moderate	Pronounced	Severe
Weight-to-growth (z)	-1.53±0.64	-0.77±0.53	-1.54±0.28	-2.28±0.34^^#
Height-for-age (z)	-1.09±0.52	-1.04±0.72	-1.98±0.43	-2.04±0.4^
Weight-for-age (z)	-1.71±0.49	-1.41±0.36	-2.15±0.26^	-2.74±0.22*^^#
BMI-for-age (z)	-1.33±0.68	-0.94±0.67	-1.3±0.32	-2.06±0.4^

Notes: * - reliability between indexes of children with mild immunodeficiency; ^ - reliability between indexes of children with moderate immunodeficiency; # - reliability between indexes of children with pronounced immunodeficiency

PD of 36-59 month-old children. In children in this age group we revealed the dependence of PD indicators on disease progression, which is statistically reflected by all anthropometric indicators. The separation by replicative activity has demonstrated once again how child's nutrition status is very sensitive to increase of HIV level in child's organism (Table 3).

TABLE 3. DISTURBANCES IN CHILDREN'S PHYSICAL DEVELOPMENT, DEPENDING ON THE DISEASE STAGE AND HIV REPLICATIVE ACTIVITY

Indicator	Stage III	Stage IV
Weight-to-growth (z)	0.29±0.17	-1.16±0.28***
Height-for-age (z)	-1.57±0.16	-2.54±0.25***
Weight-for-age (z)	-0.75±0.14	-2.27±0.22***
BMI-for-age (z)	0.43±0.17	-0.9±0.29***

Index	≤ 100 000 cop/ml	> 100 000 cop/ml
Weight-to-growth (z)	0.19±0.29	-0.97±0.34**
Height-for-age (z)	-1.31±0.26	-2.23±0.36*
Weight-for-age (z)	-0.66±0.23	-1.98±0.33**
BMI-for-age (z)	0.3±0.31	-0.72±0.35*

Note: * - significant differences between comparing groups

Adequate reflection of the natural course of disease was obtained also after separation by immunosuppression severity. In this case, the worsening of immunodeficiency leads to rough deviation of PD indicators (Table 4).

TABLE 4. DISTURBANCES IN CHILDREN'S PHYSICAL DEVELOPMENT, DEPENDING ON IMMUNODEFICIENCY LEVEL

Index	Mild	Moderate	Pronounced	Severe
Weight-to-growth (z)	0.29±0.24	-0.74±0.38*	-0.26±0.39	-1.07±0.43**
Height-for-age (z)	-1.86±0.19	-1.42±0.29	-2.04±0.33	-2.36±0.43
Weight-for-age (z)	-0.89±0.21	-1.33±0.31	-1.42±0.37	-2.12±0.37**
BMI-for-age (z)	0.48±0.23	-0.6±0.39*	-0.08±0.38	-0.84±0.44**

Note: * - moderate/insignificant and severe/insignificant differences between comparing groups

Thus, in children of 36-59 months, disease stage, severity of immunosuppression and viral load are highly significant predictors in assessment the risk of adverse outcome, like in children of 12-35 months. However, according to our study, PD indicators of HIV-infected children, whose measurement is more accessible in resource-limited settings, can testify to disease progression at early stages.

Conclusion

The results of our study are very valuable, as they prove the use of PD indicators to determine the risk of adverse outcome (e.g., lethality, deterioration of patient's health, absent or unsatisfactory dynamics in treatment course), especially in countries with limited resources, lack of access to routine implementation of immunological and virological tests. However, for children less than 12 months we recommend frequent examination involving all the specialized expertise to maximize the early detection of signs of disease progression and timely administration of antiretroviral therapy, because children in this age group had no significant predictive signs of risk for adverse outcome.

The abovementioned makes it possible to do the following conclusions:

PD indicators of children less than 12 months may not be used as predictors of HIV severity and progression rate.

Adequate prognosis in regard of severity and progression rate according to PD indicators is possible only in children older than 1 year old.

PD monitoring in children older than 1 year old will allow using not only its predictive possibility, but also control the effectiveness of antiretroviral therapy, along with the

monitoring of blood viral RNA and the levels of CD4+ T-lymphocytes, especially in developing countries which have no access to routine implementation of immunological and virological tests.

References

Berhane, R., Bagenda, D., Marum, L. et al., 1997. "Growth failure as a prognostic indicator of mortality in pediatric HIV infection", J. Pediatrics, Vol.100, p.e7

Kapitonov, V., 2005. "Genetic approach in evaluating the growth characteristics and child's development," Pediatrics [Pediatriya], in Russian, No.3, pp.58-60

McKinney, R., Wilfert, C., 1994. "Growth as a prognostic indicator in children with human immunodeficiency virus infection treated with zidovudine. AIDS Clinical Trials Group Protocol 043 Study Group," J. Pediatrics, Vol.125, pp.728-33

Miller, T., 2000. "Nutrition in paediatric human immunodeficiency virus infection," Proc. Nutr. Soc., Vol.59, pp.155-162

Moye, J., Rich, K., Kalish, L., et al., 1996. "Natural history of somatic growth in infants born to women infected by human immunodeficiency virus," J. Pediatrics, Vol.128, pp.58-67

Saavedra, J., Henderson, R., Perman, J., Hutton, N., Livingston, R., Yolken, R., 1995. "Longitudinal assessment of growth in children born to mothers with human immunodeficiency virus infection", Arch. Pediatr. Adolesc. Med., Vol.149, pp.497-502

WHO, 2005. Report of the technical consultation on clinical staging of HIV/AIDS and HIV/AIDS case definition for surveillance, Copenhagen, WHO Regional Office for Europe

WHO, 2006a. Antiretroviral therapy of HIV infection in infants and children in resource-limited settings, WHO Child Growth Standards, towards universal access: Recommendation of a public health approach, Geneva

WHO, 2006b. Standard indicators of child's development (length / height-age, weight-for-age, body mass-body length, body weight, height and body mass index, age): Methods and developments, in Russian