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Strategies for the treatment of chronic bronchitis in children, taking into account sexual development

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Abstract: A study was carried out to study the characteristics of sexual development and measures of secondary prophylaxis in patients with chronic bronchitis. The study included 84 children with chronic bronchitis aged 10 to 16 years. Of them, 37 (44%) are girls and 47 (56%) are boys. Moderate - severe course of the disease was revealed in 43 (51,2%) children, severe - in 41 (48,8%). It was revealed that chronic bronchitis adversely affects the sexual development of children of both sexes. The pace of development of secondary sexual characteristics occurs gradually and does not complete until the end of puberty. The comprehensive stage-by-stage secondary prophylaxis we proposed for children with chronic bronchitis disease contributed to the improvement of both the underlying disease and sexual development.

Keywords: Chronic Bronchitis; Sexual Development; Hypophysial Hormones; Secondary Prophylaxis.

Introduction

Chronic diseases of the lower respiratory tract is one of the serious public health problems in all countries of the world due to frequent disability at a young working age, a decrease in the quality of life of patients due to frequent and prolonged exacerbations [1;6;7;8]. On a global scale, special attention is paid to research on the mechanisms of development of chronic non-specific lung diseases, as well as the diagnosis of extrapulmonary systemic manifestations in the early stages of development [4;9] and effective methods of treatment and prophylaxis. In this regard, the timely diagnosis of chronic non-specific lung diseases in children, the determination of factors contributing to the delay in the sexual development of patients of priority. In addition, one of the most pressing issues of scientific research on this problem is the development of secondary preventive measures and its effectiveness, as well as improvement of measures aimed at improving the quality of life of patients.

There are few works on the study of sexual development disorders in children with chronic bronchitis [3;5], and the results are contradictory. The authors are united in that the problem of impaired puberty in chronic diseases of the lower respiratory tract really exists.

The aim: To assess the state of sexual development of children with chronic bronchitis and to develop measures for secondary prevention and treatment.

Methods

84 (obstructive - 46, non-obstructive -38) children with chronic bronchitis (CB) aged 10 to 16 years were examined. According to the duration of the disease, the patients were divided as follows: 5-6 years - 32 (38%), 7 years -14 (16,7%), 8 years -13 (15,5%), 9 years - 12 (14,3%), 10 years or more - 13 (15,5%) children. According to the severity of the condition, the patients were divided as follows: moderate - severe course of the disease was revealed in 43 (51,2%) children, severe - in 41 (48,8%).

The function of external respiration (FER) was investigated using a spirometer of «Medicor» firm (Hungary). The main functional manifestation of respiratory failure was impaired bronchopulmonary patency, the Tiffno index was reduced to 64,7 ± 6,18%. Patients were divided as follows depending on the parameters of the FER: degree I of impairment of the FER was observed in 60%, degree II in 24% and degree III in 16% of patients.

Sexual development is assessed by the appearance and severity of marked secondary sexual characteristics according to the method of J. M. Tanner (1969). A genetic analysis in boys was also performed.

In the blood serum of the examined children, the levels of hormones were determined by the immunoenzymatic method: thyroid-stimulating hormone (TSH, mlE/l), free thyroxine (T4, µg/dl), triyodtironin (T3, ng/ml), follicle-stimulating (FSH, MLE / ml), luteinizing hormone (LH, MlE /ml), testosterone (T, nmol/l), estradiol (E2, pg / ml).

Complex treatment and stage by stage secondary prophylaxis was carried out using reamberin, calcium D3, aevit and thymus preparations.

The main pharmacological effect of reamberin is due to its ability to enhance the compensatory activation of aerobic glycolysis, reduce the degree of inhibition of oxidative processes in mitochondria, and also to increase the intracellular fund of macroergic compounds. Reamberin has antihypoxic, antioxidant, antidepressant and microcirculatory enhancing effects. Reamberin was administered intravenously. Depending on the severity of the disease, the course of treatment was 7-10 days.

Results and Discussion

A significant number of sexual development disorders were revealed in patients with chronic bronchitis.

Genetic studies have shown that in patients with chronic bronchitis disease, genital sizes were significantly (P <0,001) delayed at the age of 14, 15 and 16 years.

The analysis of the formation of secondary sexual characteristics in boys with chronic obstructive pulmonary disease showed that at the age of 15–16 years, P1 Ax1 was observed in 10 (71,4%) of 14 patients, and only 4 (28,5%) showed P2 Ax2. It was found that all 100% of boys with chronic bronchitis were lagging behind in the formation of secondary sexual characteristics in relation to healthy ones. In general, delayed sexual development (DSD) was detected in 85,7% of examined boys with chronic bronchitis disease. The analysis of SD depending on the duration and severity of the disease showed that the degree of DSD correlates with the duration and severity of CB (r = 0,50; r = 0,39 (P <0,05)). So, signs of DSD in the group of patients with a disease duration of 5-6 years were revealed in 66,7%, with duration of 7 years - in 88,9%, 8 or more years - in 100% of boys with chronic bronchitis disease.

A clinical examination of sick girls revealed that by the age of 16, 54.4% had sexual hairiness in the P2Ax2 stage, and only 33,3% of patients in the P3Ax3 stage, while in the group of healthy peers this formula looks like P3-4Ax3. In addition, in all age groups, there was a tendency to lengthen the duration of passage of individual stages of development of the mammary glands in comparison with the group of healthy girls. The mammary glands by the age of 16 in 24,4% of patients were in the Ma3 stage, and in the remaining patients they did not exceed II degree according to Tanner. It is known that the most objective indicator of puberty for girls is the time of the first menstruation.

According to Kamilova R. T [2], the average age of menarche in our republic is 13 years 2 months. The analysis of our data showed that at the age of 13 among the girls with chronic bronchitis, no persons with the onset of menstruation were revealed. Impairment of the formation of menstrual function was more often revealed in sick girls who used systemic glucocorticoids for treatment. The frequency of delayed sexual development among girls with chronic bronchitis was often found in older age groups and made 82,7%.

An elevated serum level of thyroid stimulating hormone (TSH) was found in all examined girls and boys with chronic bronchitis (2,15 ± 0,08 mlE / ml –3,24 ± 0,2 mlE /ml, respectively 1,21 ± 0,05 mlE /ml – 1,69 ± 0,09 mlE / ml) compared with the control group (P <0,001). The content of the free thyroxine fraction (T4) was significantly (P <0,05; P <0,001) reduced (5,21 ± 0,03 μg /dl) compared with healthy (9,25 ± 0,52 μg /dl).

Functional disorders in the pituitary-gonadal system were confirmed by the results of studies of the content of gonadotropins and sex hormones in the blood serum.

The increase in the secretion of gonadotropic pituitary hormones during puberty in healthy boys is heterogeneous, in almost all age groups luteinizing hormone (LH) prevails over follicle-stimulating hormone (FSH). The results of our studies show that patients with chronic bronchitis aged 10-11 years showed some increase in the level of FSH (1,26 ± 0,1 MlE/ml) compared with the group of healthy children of this age (1,07 ± 0,01 MlE/ml P> 0,05) and a significant decrease in LH (1,18 ± 0,26; 0,73 ± 0,32 MlE / ml, respectively) and an unreliable increase in testosterone (3,57 ± 0,67 nmol/l). This, apparently, is due to the fact that in children at the beginning of puberty in response to hypoxia, the

concentration of FSH increases compensatorily, and LH remains lowered (P <0,001). The synergism of the action of these hormones is impaired from this age. In healthy boys, the level of testosterone concentration in the blood from 13 years old to 16 years old increases 1,9 times, from 7,05 ± 0,90 nmol /l to 13,44 ± 0,87 nmol /l.

In patients with chronic bronchitis (CB) from the age of 14, the level of testosterone begins to decrease significantly (7,8 ± 0,42 nmol /l) compared with the control group (9,49 ± 0,36 nmol/l P <0,01). A decrease in testosterone indicates that in patients with CB, the sensitivity of gonads to LH is reduced. The low genetic indicators revealed by us in boys with chronic kidney disease are interrelated with low levels of FSH, LH and T r = 0,33; r = 0,38. In patients with severe CB and with a disease duration of more than 7 years, testosterone levels decreased sharply (P <0,001). They lagged behind in sexual development by about 3 years, later entered the period of puberty than patients with a mild and moderate course.

The results of a study of the pituitary-ovarian system in girls with CB showed significant changes in the production of some sex hormones. The peak increase in pituitary FSH secretion in healthy girls occurs at the age of 12-13 years (7,9 ± 0,14 MlU / ml), LH at the age of 16 years (5,48 ± 0.71 MlU/ ml). In sick girls with CB in the blood serum, a significant decrease (P <0,05) in the level of FSH at the beginning of the puberty (3,42 ± 0,2 MlU/ml) was noted. The content of LH throughout the course of pubertal development was significantly lower (P <0,001) and remained low in late puberty (1,15 ± 0,19 MlU / ml). The level of estradiol in girls with CB was significantly (P <0,001) low in the older age groups (44,6 ± 5,74 pg/ml) compared to the group of healthy girls (108,0 ± 4,6 pg /ml).

Drawing a conclusion, we can say that, for children with chronic diseases of the lower respiratory tract, the puberty is more difficult than for healthy children. Chronic hypoxia accompanied by chronic bronchitis causes a state of chronic stress in the body of children, which contributes to a significant reduction in sexual development and the secretion of hormones of the studied parts of the endocrine system.

Considering the pathogenesis data on the role of hypoxia and intoxication, immune-endocrine shifts in sexual development disorders in chronic bronchitis disease, which are interdependent, we proposed a complex therapy regimen and developed the 2nd and 3rd stages of comprehensive prevention taking into account delayed sexual development in chronic bronchitis (table 1).

Table 1. Treatment regimen for patients with chronic bronchitis with delayed sexual development

Stage of treatment	Medicines, dosage, method of usage	Duration
Stage I, in combination with conventional therapy, in a hospital	- Reamberin 10 ml / kg intravenous drip. - Aevit 1 capsule daily orally. - Calcium D3 (500 mg Ca ++ and 400 IU of vitamin D) 1 tablet 2 times a day, orally. - Thymus preparations of 50 mcg intramuscularly.	7–10 days a month 6 days a month 6 days

Stage II for the purpose of secondary prevention, after 6 months	- Reamberin 15ml / kg intravenous drip. - Aevit 1 capsule 2 times a day, orally. - Calcium-D3 1 tablet 2 times a day.	8 days 2 months 3 months
Stage III for the purpose of secondary prevention, after 12 months	- Reamberin 10ml / kg intravenous drip. - Aevit 1 capsule 1 time per day, orally -Calcium-D3 1 tablet 2 times a day, orally - Thymus preparations of 100 mcg once a day i/m.	7 days 2 months 3 months 6 days

Stage I of complex therapy, patients received along with conventional therapy in a hospital. To determine the effectiveness of complex therapy, the patients were divided into two groups: group I consisted of 36 patients with chronic bronchitis, who received our treatment regimen in a complex of standard therapy, and group II consisted of 33 patients who received traditional complex treatment.

A comparative study of the effectiveness of complex therapy with traditional therapy revealed a faster positive clinical dynamics, elimination of symptoms of exacerbation of chronic bronchitis. The positive results of this method of treatment were confirmed by the parameters of the study of the function of external respiration (FER) in dynamics. After complex treatment in patients of the main group, the number of children with normal FER indicators increased 2 times, 1,5 times more patients were revealed with I degree of disturbances in the ventilation function of the lungs. Along with this, the number of children with a II or III degree of respiratory dysfunction significantly decreased. In the control group of children who received traditional complex treatment, no marked dynamics of the studied parameters of the lung ventilation function was observed.

Patients of the main group for the purpose of secondary prevention after 6, 12 months repeatedly received II and III stage of complex treatment.

In patients receiving secondary prophylaxis, after a year, the content of free T4 (9,1 ± 0,62 ng /ml) in all age groups significantly increased compared with the control group T4(5,1 ± 0,46 ng /ml P1 <0,001), and the level of TSH (2,3 ± 0,06 mlU /ml) decreased to a healthy concentration (2,12 ± 0,14 mlU /ml P1 <0,001), while in the control group the level of TSH remained high (3,1 ± 0,1 mlU/ml).

A comparative analysis carried out a year later showed that in patients receiving secondary prophylaxis, the size of the testicles significantly (P <0,05; P <0,001) increased and the length of the testicle reached 2,5 cm already at the age of 12 years, the size of the penis also had rather growth effect, while in the control group there were no significant changes in genetic parameters, P> 0,1. In patients who received secondary prophylaxis after a year, along with an increase in the size of the genital organs, pubic hair and axillary zone were revealed at the age of 12-14 years. At the age of

15-16 years, hair growth appeared, spreading over the pubic joint and the hair became darker (P3), which corresponded to stage III according to Tanner. In the control group of patients, this symptom was revealed at the age of 15-16 years in only 48%.

Complex treatment and secondary prophylaxis in patients of the main group resulted in abrupt increase in LH at the age of 15-16 years (6,9 ± 0,48 MU/ml) compared with the control group (2,96 ± 0,62 MU/ml). A significant increase in the concentration of FSH in patients of the main group was noted compared with the control indices (4,9 ± 0,36 MlU/ml versus 2,9 ± 0,37 MlU/ml, P <0,05).

An increase in the concentration of estradiol in girls and testosterone in boys occurred after two years of stage treatment. At the age of 14 years in boys, the concentration of testosterone in the blood significantly (P <0,01) increased 9,12 ± 0,26 nmol /l compared with the control group 8,14 ± 0,29 nmol /l. In girls aged 14–15 years, estradiol concentration was significantly higher than in the control group (108,3 ± 4,5 pg /ml versus 68,0 ± 4,21 pg /ml, P <0,01).-spasi-

Conclusion

The data obtained allow us to conclude that treatment of chronic obstructive pulmonary disease is a complex therapeutic problem and requires the use of a complex of therapeutic agents aimed at all pathogenesis links involved in the formation and course of these diseases in children. The complex stage-by-stage secondary prophylaxis we proposed for children with chronic bronchitis was quite effective and contributed to the improvement of both the underlying disease and indices of external respiration functions. In addition, secondary prevention of CB during the puberty resulted in improvement in sexual development.

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