

Clinical and Immunological Study of the Effect of Different types of Therapy on the Course of Allergic Rhinitis in Children with Hymenolepiasis

Khamidova N.K., Mirzoeva M.R., Narzullaev N.U.

Bukhara State Medical Institute named after Abu Ali ibn Sino, Bukhara, Uzbekistan

ABSTRACT

A detailed analysis of the main clinical and laboratory indicators of children which are suffering from allergic rhinitis (AR) with concomitant hymenolepiasis in the course of antiallergic, antiparasitic and complex therapy is presented. Patients with AR with hymenolepiasis were divided into three groups: 21 patients underwent antiallergic therapy, 22 patients received antiparasitic therapy and 24 patients received complex therapy. The maximum clinical effect was achieved with the use of complex treatment, which we included antiallergic and antiparasitic therapy. The dynamics of immunological indicators after treatment of AR patients with hymenolepiasis only with antiallergic or antiparasitic drugs represents that, despite a positive result, it is insufficient and does not normalize immunological parameters. Complex antiallergic and antiparasitic treatment results a pronounced immunological effect, activates the severity of the immune response, switches the nature of the immune response to suppressive, and also contributes to a more rapid relief of the allergic process in the body.

KEY WORDS: allergic rhinitis, hymenolepiasis.

INTRODUCTION

According to the latest sources which is devoted to the issues of allergic rhinitis (AR), in recent years there have been indications of a frequent combination of this disease with hymenolepiasis of the gastrointestinal tract (GIT) [1,5,11]. In hymenolepidosis, the microbiome of the gastrointestinal tract is disturbed, and all of its stuff are most often involved in this process [2,8,10]. In the intestine, at the same time, there are disorders of parietal digestion (accompanied by impaired absorption, permeability and barrier function of the gastrointestinal mucosa), sensitization of the body develops, as a result of which the level of IgE and histamine increases [3,7,16] and signs of secondary immune deficiency appear [16]. Thus, there is a certain commonality in the development of the pathogenetic mechanism of pseudoallergic rhinitis and pathology of the digestive system [4,9,13]. At the same time, the issues of complex therapy in patients with AR with hymenolepiasis are insufficiently covered in modern literature; the dynamics of clinical and laboratory indicators during the course of complex treatment is poorly covered [6,12,15].

The aim of the study is to analyze the dynamics of the main clinical and laboratory indicators in children suffering from allergic rhinitis (AR) with hymenolepiasis against the background of antiallergic, antiparasitic and complex therapy.

MATERIALS AND METHODS

The main group of the surveyed consisted of 100 children (from 3 to 14 years old) from the number of patients were observed in the children's city diagnostic center and living in a rural environment; research with informed parental consent. Children with hereditary diseases

(according to the parents), suffering from concomitant chronic diseases in the stage of exacerbation, were excluded from the examined group. The main group included 67 sick children with year-round AR and hymenolepiasis; comparison group - 33 sick children (with year-round AR without hymenolepiasis. The age group 3-6 years included 36 children from the AR group with hymenolepiasis and 14 children with AR without hymenolepiasis; the age group 7-14 years included 31 children with AR with hymenolepiasis and 19 children with AR without hymenolepiasis. For a comparative assessment of nasal secretion by the nasocytogram method, we also introduced a group of healthy children (35) without clinical and laboratory signs of AR and hymenolepiasis. In children with hymenolepiasis (38 people - 55.5%), we diagnosed giardiasis; enterobiasis was observed in 12 children (17.6%); ascariasis was diagnosed in 8 (11.7%) cases; 2 children (2.9%) suffered from hymenolepiasis. In a number of patients (8 people - 11.7%), we diagnosed myxparasitosis (giardiasis and ascaris). The work adopted the AR classification proposed by WHO in 2001 in the ARIA materials. A.Ya. Lysenko (2003) [5] we used to assess the clinical form of giardiasis; classification of hymenolepiasis - according to the works of B.A. Astafieva (1987) [6]. The clinical picture of AR was diagnosed on the basis of complaints, anamnesis, and physical examination data. We also used data from a general blood test, microscopy of nasal secretions, and also determined the respiratory, olfactory, and transport functions of the nose. The cellular composition of the nasal secretion was assessed (nasocytography). Clinical examination included examination of ENT organs. Rhinopneumometry was carried out by modifying a computer spirometer - pneumotachometric type on a spirospektr apparatus of the company "Neurosoft" (Russia). According to the indications, X-ray and CT examinations of the paranasal sinuses were performed. To diagnose parasitic invasions, the method of three-fold coproscopy and scraping was used, followed by microscopy from the perianal fold.

In order to evaluate various types of therapy, patients with AR with hymenolepiasis were divided into three groups: 21 patients underwent antiallergic therapy, 22 patients received antiparasitic therapy and 24 patients received complex therapy. With mixed parasitosis, represented by giardiasis and enterobiasis, first, helminthiasis was treated, and then protozoal infection.

RESULTS AND DISCUSSION

Antiallergic treatment, which included zyrtec, loratal, vibrocil, endonasal electrophoresis with 2% calcium chloride solution for 10 days (vitamin therapy was not used, because vitamins are components of the nutrient medium for lamblia and are easily absorbed by parasites, increasing their viability), led to improvement of allergic status: the number of patients with difficulty in nasal breathing, paroxysmal sneezing, rhinorrhea was significantly reduced, and the number of patients with spastic cough, lacrimation and itching in the nose, ears and throat also decreased, but this result was not reliable. Antiallergic therapy had a short-term effect and after the end of the course, the achieved improvement was largely leveled off.

Antiparasitic therapy also had an anti-allergic effect, which, in contrast to anti-allergic treatment, was stable, but less pronounced: a significant difference was revealed only for the difficulty of nasal breathing, although for the rest of the symptoms of the allergic status there was a clear tendency to decrease. The positive effect of antiallergic therapy was felt immediately, the effect of antiparasitic therapy was delayed and was fully manifested only 7-10 days after the end of the antiparasitic treatment. In fact, there were no differences in the

frequency of symptoms after anti-allergic and antiparasitic treatment.

At the same time, when assessing the effectiveness of anti-allergic and complex therapy, statistically significant differences in the frequency of allergic symptoms were not found, although the tendency to reduce it after complex therapy can be clearly traced.

As a result, it was possible to achieve a pronounced and stable remission and a decrease in the number of patients with difficulty in nasal breathing, itching in the nose, paroxysmal sneezing, rhinorrhea, spastic cough compared with the baseline level was significant, and the frequency of spastic cough was significantly reduced and compared with the results achieved after antiallergic treatment. Symptoms such as lacrimation and itching in the throat and ears have completely disappeared. Some positive changes were identified during rhinoscopic examination. Antiallergic therapy reduced the number of patients with watery and mucous discharge to 14 (63.6%), antiparasitic therapy - to 4 (19%), respectively, complex antiparasitic and antiallergic - to 20 (83.3%). The number of patients with false hypertrophy also decreased: to 40.9%, 52.3% and 20.8%, respectively. X-ray of the paranasal sinuses after complex treatment did not reveal proliferative changes in the paranasal sinuses.

After treatment, study were carried out again after 14 days later. In the first group of patients, the disappearance of complaints and an improvement in the rhinoscopic picture was observed on average 5 days after the start of therapy. When analyzing the data of rhinopneumometry, it was noted that in patients of the 1st group FVC, POS, MFV1, SOS25-75, MOS25, MOS50, MOS75, VC increased slightly after treatment, respectively, from 35.5, 45.8, 40, 1, 40.7, 44.9, 46.6, 46.8, 45.1, 38.2 to 35.9, 48.7, 42.6, 43.3, 46.5, 49.1, 48.4, 46.7, 41.6 ($P > 0.05$). In the 2nd group of patients, the improvement on average occurred on the 7th day. The data of rhinopneumometry in the second group increased, respectively, from 35.3; 37; 44.3; 44.7; 44.4; 46.6; 47.7% to 44.9; 46; 52.6; 48.1; 50.1; 53; 48.1%. The data of SOS25-75, MOS50, MOS75 increased by 120.0, 107.2, 125.4%, respectively ($P < 0.001$).

In patients of the 3rd group, the results were the best in comparison with the 1st and 2nd groups. Improvement in clinical and laboratory data occurred on the 3rd day. Rhinopneumometry data in the 3rd group were: 33.1; 42.3; 41.9; 42.3; 42.6; 42.9; 41.3, 40.0 and 34.7%. After complex therapy, these indicators significantly increased to 56.3; 92.1; 90.2; 88.5; 113.6; 93.5%, 103.1; 122.0; 93.5%, exceeding similar indicators in the 1st and 2nd groups. The data for SOS25-75, MOS50, MOS75 and VC increased by 166.7, 149.6, 205.0%, 169.5%, respectively ($P < 0.001$).

The cellular composition of mucosal smears (nasocytograms) significantly improved after all three types of therapy, although the most pronounced changes were observed against complex anti-allergic + antiparasitic treatment, which is especially clearly demonstrated by the dynamics of the content of eosinophils. Antiparasitic and complex therapy led to the disappearance of such symptoms of hymenolepiasis, such as vomiting, flatulence, teeth grinding, itching in the anus, allergic dermatoses; as well as a significant reduction in the frequency of abdominal pain, frequent bowel movements, nausea, nervousness / irritability, and weight loss.

The results of studying the dynamics of immunological indicators after antiallergic treatment showed that there is a tendency to normalize the content of CD3 + -, CD4 + -, CD8 + -, CD20 + - lymphocytes, these indicators exceeded the values obtained before treatment, respectively in 1.17, 1, 10, 1.26 and 1.19 times, at the same time they did not reach normal values and were lower than them, respectively, in 1.13; 1.13; 1.36 and 1.14 times.

Differences in the intensity of changes in the content of CD4 + - and CD8 + - both before

and after treatment, caused a significant decrease in the value of IRI after treatment, although this indicator exceeded similar values in the control group. The number of CD20 + - lymphocytes after treatment did not differ significantly from the initial value. The most pronounced changes concerned the concentration of total serum IgE, which was 8.9 times higher than that in the control group and decreased after treatment by more than three times, while remaining at the same time more than two times higher than normal values.

Before treatment, the indicators of ASL content to tissues of various organs were significantly increased. The maximum increase (2.7 times) in the number of ASL was observed in the intestinal tissues, which is probably due to the localization of parasites and their direct effect on the tissues. There was a less pronounced, but nevertheless significant increase in the content of ASL to the tissues of the trachea and lungs (2.0 and 2.4 times, respectively). Treatment led to a decrease in their number, but not to normal values: the content of ASL to the tissues of the trachea, lungs and intestines remained above normal values by 1.5, 1.6 and 2.1 times, respectively.

The content of CD20 + - lymphocytes corresponded to the changes identified in the group of patients with AR. The dynamics of changes in the level of total serum IgE was of the same type: the concentration of IgE exceeded the indicator in the control group by 9.1 times, having decreased after antiallergic therapy by 3.6 times, but at the same time significantly exceeding the normal values more than twice.

The content of ASL to the tissues of the trachea and lungs was increased, respectively, by 2.9 and 3.2 times, the intestine - by 2.6 times, antiallergic therapy decreased these indicators, but they exceeded the normal values by 1.6, 1.2, respectively. and 1.9 times. The index of ASLs specifically sensitized to intestinal hypertension in patients with AR with PI was $5.71 \pm 0.27\%$ before treatment, which is reliably 2.76 times higher than the values in the control group (2.07 ± 0.16). Antiallergic therapy led to a slight increase in the number of CD20 + lymphocytes and a sharp (3.63 times) decrease in the level of total nonspecific serum IgE. The same trend and severity of the dynamics of indicators of cellular immunity and ASL to TA of the trachea, lungs and intestines is observed in the group of patients with AR with PI, that is, there is a significant increase in the indicators of CD3 + -, CD4 + -, CD8 + -, CD20 + lymphocytes 1.15 ; 1.08; 1.20; 1.14 times compared with the parameters before treatment, but they remained significantly lower than those in the control group at 1.13; 1.13; 1.36 and 1.14 times, respectively. The results of studying the blood levels of ASL to TA of the trachea, lungs and intestines after treatment demonstrate that in children with AR with hymenolepiasis, these indicators significantly exceed the control values of the corresponding indicators in this age group: for ASL that bind TA trachea - $3.91 \pm 0.31\%$ versus 2.21 ± 0.15 , lungs - $2.64 \pm 0.15\%$ versus 2.14 ± 0.18 , intestines - $4.91 \pm 0.31\%$ versus 2.50 ± 0.19 . Particularly noteworthy are the high rates of ASL to the TA of the trachea and intestines, which are 1.77 and 1.96 times higher than the control values, which is explained by the common immune system of the respiratory and digestive tracts.

The dynamics of immunological parameters of patients of the 2nd group (ARs who received specific antiparasitic treatment (for giardiasis - metronidazole (Macmiror); hymenolepiasis - niclosamide (fenasal); enterobiasis - ascariasis - albendazole without antiallergic drugs in what -th degree may indicate the role of parasites in the induction of allergies.

Antiparasitic therapy led to a significant improvement in CD3 + and CD4 + lymphocytes, and the content of T-helpers did not differ from normal values. Positive dynamics was also

observed for CD8 \pm lymphocytes - their content significantly increased in comparison with the value before treatment, but nevertheless was inferior to the control value. The reduced content of CD20 \pm lymphocytes increased, not significantly differing from the control values. The sharply increased content of total serum IgE decreased by more than two times, but its concentration was nevertheless more than three times higher than the normal value. Antiparasitic therapy reduced the content of ASLs to TAGs of the trachea, lungs and intestines, however, these indicators did not reach the control values.

Comparative analysis of indicators of cellular immunity - CD3 \pm -, CD4 \pm -, CD8 \pm -, CD20 \pm - lymphocytes and ASL to TAG of the trachea, lungs and intestines shows that the direction and severity of the dynamics of indicators are similar to those of group 1. So, there is a significant increase in relation to the initial level before treatment of all indicators of cellular immunity - CD3 \pm , CD4 \pm , CD8 \pm , CD20 \pm lymphocytes (by 1.21; 1.14; 1.18 and 1.13 times, accordingly), relative to the control values, there are significant differences in the indicators of CD3 \pm and CD8 \pm lymphocytes (51.88 ± 1.46 versus 62.07 ± 0.45 and 18.50 ± 0.33 versus $20, 71 \pm 0.67$, respectively), indicating insufficient effectiveness of the treatment.

The dynamics of an increase in the indices of subpopulations of T-lymphocytes, different in severity, leads to a decrease in IRI and some suppression of the helper effect of the body's immune response, which also continues to differ significantly from the norm by 1.11 times, and the reaction of the immune response is still of a helper nature.

The content of CD20 \pm lymphocytes significantly increased after treatment, but this indicator remained below the same parameter in the control group. A sharp decrease in the level of total nonspecific serum IgE was observed (201.38 ± 11.31 versus 60.86 ± 2.08 in the norm).

Analysis of ASL indices to TAG trachea, lungs and intestines showed a significant decrease in values relative to those before treatment (4.25 ± 0.25 versus 6.14 ± 0.21 ; 2.63 ± 0.18 versus 4.54 ± 0.26 ; 4.38 ± 0.38 versus 5.71 ± 0.27 ; 2.50 ± 0.33 versus 2.50 ± 0.20), respectively. ASL to TAG trachea, lungs and intestines, significantly decreasing after treatment, remain at 1.45; 1.41; 2.11 times higher than the corresponding values in the group of practically healthy children.

Insufficient effectiveness of the specific antiparasitic treatment of children with AR with hymenolepiasis is indicated by indicators of the content in the peripheral blood after treatment of CD3 \pm - (53.36 ± 0.96), CD4 \pm - and CD8 \pm lymphocytes (34.00 ± 0.49 ; $20, 36 \pm 0.39$), as well as CD20 \pm lymphocytes (11.55 ± 0.16), which significantly increased relative to the values before treatment (43.09 ± 0.48 ; 31.88 ± 0.40 ; 16.32 ± 0.35 and 10.76 ± 0.51 , respectively), at the same time remaining significantly reduced relative to the indicators of practically healthy children (56.21 ± 0.54 ; 38.00 ± 0.39 ; 26.14 ± 0.35 and 14.79 ± 0.38 , respectively). (IS for CD3 \pm - (1.05 times, CD4 \pm - and CD8 \pm lymphocytes (IS = 1.12 and (IS = 1.28 times, respectively, relative to the values of practically healthy children. an increase in the subpopulations of T-lymphocytes of T-helpers and T-cytotoxic lymphocytes leads to a significant decrease in IRI relative to the indicator before treatment (1.65 ± 0.03 versus 1.96 ± 0.03), but remains significantly increased concerning IRI of practically healthy children (1.65 ± 0.03 versus 1.46 ± 0.03), and the reaction of cellular immunity is of a helper nature.

The IgE indicator in AR patients with hymenolepiasis after treatment significantly exceeds (3.05 times) the IgE value in the control group, although it significantly decreases relative to the indicator before treatment, which is noted against the background of significantly low B-lymphocyte counts in the dynamics of the disease.

Conducted specific antiparasitic treatment in this group of patients led to a significant decrease in ASL to TAG of the trachea and intestines, as evidenced by the values of these parameters before and after treatment (4.73 ± 0.30 versus 6.38 ± 0.19 and $3, 36 \pm 0.15$ versus 6.50 ± 0.19 , respectively), but at the same time they significantly exceeded the indicators of practically healthy children (4.43 ± 0.30 versus 2.21 ± 0.15 and $3, 36 \pm 0.15$ and 2.50 ± 0.20 , respectively), (the IS, respectively, is (2.14 and (IS = (1.34 times).

The dynamics of immunological parameters was also characterized by positive shifts in the content of CD3 +, CD4 + and CD8 + lymphocytes. The values of these parameters significantly increased in comparison with the initial values, but were significantly lower than the normal values.

The level of CD20 + lymphocytes was also decreased in comparison with the control, and after treatment it increased, but did not reach normal values. The level of total serum IgE after a course of antiparasitic therapy decreased sharply, but its content was more than three times higher than the initial level.

Changes in the content of ASL were similar - their level decreased, the decrease was significant for ASL against TAG of the trachea and intestines, however, their values were higher than the parameters of the control group.

At the same time, the specific antiparasitic treatment carried out contributed to the normalization of ASL indicators to TAG of the lungs and kidneys, which significantly decreased relative to the indicators before treatment (1.73 ± 0.19 versus 2.82 ± 0.12 ; 2.55 ± 0.16 versus 3.79 ± 0.11 and 1.64 ± 0.15 versus 3.32 ± 0.14 , respectively) and slightly different from the indicators of practically healthy children (1.73 ± 0.19 versus 1.64 ± 0.13 ; 2.55 ± 0.16 versus 2.14 ± 0.18 and 1.64 ± 0.15 versus 1.93 ± 0.13 , respectively) These data are also consistent with the indices of antigen-binding lymphocytes to TAG of the trachea and intestines, which significantly decreased relative to the indices before treatment (4.43 ± 0.30 versus 6.38 ± 0.19 and 3.36 ± 0.15 versus 6.50 ± 0.19 , respectively), but significantly higher than the control group). The results of the use of complex antiallergic and antiparasitic therapy have shown that it has a maximum effect on immunological parameters. If after complex therapy a significant increase in CD3 + - lymphocytes did not lead to the normalization of this indicator, then the content of CD4 + -, CD8 + - and CD20 + - lymphocytes did not differ from the indicators of the control group, the level of CD3 + - CD4 + -, CD8 + - and CD20 + - lymphocytes did not differ from the norm; IRI normalized, in contrast to AR patients with hymenolepiasis, who received either antiallergic or antiparasitic treatment. Complex therapy maximally reduced the concentration of serum IgE. Complex anti-allergic and antiparasitic treatment promoted an intensive decrease in the content of ASL in the peripheral blood to the TAG of the trachea, lungs and intestines to values close enough to normal values, whereas in patients of groups 1 and 2 who received monotherapy, the content of ASL to TAG of a number of organs (in group 1 - trachea, lungs and intestines, in group 2 - trachea and intestines) remain significantly higher than the values of practically healthy children. As a result of complex therapy, there is an increase in all indicators of cellular immunity, for example, for CD3 + lymphocytes, the degree of increase was $T_{II} = T_{I1.32}$ times, for CD20 + lymphocytes - $T_{II} = T_{I1.25}$ times, for CD4 + lymphocytes - $T_{II} = T_{I1.17}$ times, and for CD8 + lymphocytes - $T_{II} = T_{I1.30}$ times, while with only antiallergic treatment, $T_{II} = 11.17$, $T_{II} = 11.19$, $T_{II} = 11.10$, respectively, $T_{II} = 11$, 26 times and during antiparasitic - $T_{II} = 11.21$, $T_{II} = 11.31$, $T_{II} = 11.14$, $T_{II} = 11.18$. A more intense increase in the content of CD8 + lymphocytes ($T_{II} = T_{I1.30}$ times) over that for CD4 + lymphocytes ($T_{II} = T_{I1.17}$) was noted,

which results in the transition of the observed helper nature of the immune response ($IRI = 2, 01$) into suppressor ($IRI = 1.56$). Normalization of the values of B-lymphocytes ($11.45 \pm 0.34\%$ versus $11.50 \pm 0.33\%$ in control) and a significant decrease in the IgE level ($76.18 \pm 6.87\%$ versus $60.86 \pm 2, 08\%$ in control), indicating a pronounced decrease in allergic reaction.

One of the most pronounced effects of complex therapy is a significant decrease in ASL to tracheal TAG (up to $2.45 \pm 0.21\%$ versus $2.93 \pm 0.16\%$ in the control), where the degree of decrease is 2.51 times as compared with $IS1 = 1.67$ times in the 1st and $IS1 = 1.44$ in the 2nd group of patients in comparison with the indicators before treatment; ASL to TAG lungs (up to $2.36 \pm 0.15\%$ versus $1.86 \pm 0.18\%$), where the degree of reduction is 2.42 times compared to $IS1 = 1.51$ times in the 1st and $IS1 = 1.73$ in the 2nd group of patients in comparison with the indicators before treatment; TAG of the intestine (up to $2.55 \pm 0.16\%$ versus $2.07 \pm 0.16\%$), where the degree of decrease is 1.78 times in comparison with $IS1 = 1.00$ times in the 1st and $IS1 = 1.30$ in the 2nd group of patients in comparison with the indicators before treatment. In the 3rd group of AR patients with hymenolepiasis, who received combined antiallergic and antiparasitic treatment, the dynamics of the studied parameters of cellular immunity: CD3 + lymphocytes, CD20 + lymphocytes, CD4 + and CD8 + lymphocytes, as well as IRI characterizes the stable direction of their changes towards an intensive increase to the original values. In this case, the indicators of IRI characterize the immune response as a pronounced suppressor, whereas in patients of groups 1 and 2, IRI had the highest values (1.74 and 1.78, respectively), and the immune response in these groups was pronounced helper character. Complex treatment promotes an intensive decrease in the content of ASL in the peripheral blood to the hypertension of the trachea, lungs, and intestines to values that are quite close to the initial values. ASL to TAG of a number of organs (in the 1st group - the trachea, lungs and intestines, in the 2nd group - the trachea and intestines) remain significantly high compared to the values of practically healthy children.

CONCLUSION

The expected high clinical effect was achieved with the use of complex treatment, which we included antiallergic and antiparasitic therapy. Antiallergic therapy led to a rapid improvement in the condition of patients, and antiparasitic therapy consolidated this effect. The most pronounced positive dynamics according to rhinopneumometry data was also observed after complex treatment. Analysis of the results of indicators of cellular immunity and ALS in the group of patients with AR children with hymenolepiasis shows a decrease in the content of populations and subpopulations of T-lymphocytes and B-lymphocytes in the peripheral blood and the prevalence of the activity of the helper link of immunoregulatory T-lymphocytes, an increase in ASL to TA trachea, lungs and intestines, increased IgE. The studies of the dynamics of immunological indicators after treatment of AR patients with hymenolepiasis only with antiallergic or antiparasitic drugs showed that, despite a certain tendency towards the correction of the revealed deviations, in some cases reliable, it is clearly insufficient and does not lead to the normalization of immunological parameters. Complex antiallergic and antiparasitic treatment has a pronounced immunological effect, activates the severity of the immune response, switches the nature of the immune response to suppressive and also contributes to a faster relief of the allergic process in the body.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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