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Influence of recovery treatment based on the haloaerosoltherapy upon non-specific defense of children with recurrent respiratory diseases

Key words: *children, recurrent respiratory diseases, recovery treatment, haloaerosoltherapy.*

Respiratory diseases in children remain an actual problem in medicine [9, 16], and recurrent respiratory diseases (RRD) occupy a special place among them [16, 19, 21]. Recurrent episodes of the disease, especially on the background of residual changes following acute respiratory diseases (ARD), may have a protracted duration and further contribute to the formation of chronic diseases of the bronchopulmonary system [1, 3, 7, 20].

Accounting the important role of the immune system, which goes through a formative stage during childhood, special attention should be paid to the evaluation of changes in the indices of non-specific defense, which defines the first line of defense against infectious agents [8, 11, 18]. Studies by different researchers indicate changes in the macrophage branch of the immune system [2, 11, 13] in children with frequent ARD, which can persist even after the subsidence of acute manifestations.

Therefore, children with RRI require long-term control and comprehensive rehabilitation with predominant use of non-medicamental methods to provide adequate immune correction [5, 6, 10, 14]. In this aspect, haloaerosoltherapy (HAT) is of worth attention, since it directly influences the drainage function of the bronchi due to the hyperosmolar effect, is characterized by bactericidal action and indirectly provides correction of immune disorders [4, 15, 17].

Objective was to study the influence of different treatment complexes (TC) based on HAT with increased concentration of rock-salt aerosol upon non-specific defense at children with RRD.

Materials and methods. 74 patients aged 6 to 11 years were examined, all children were beyond acute period. The inclusion criteria were four or more recurrences of ARD during the year, that is, among them: rhinopharyngitis, laryngitis, tracheitis or bronchitis. The control group consisted of 12 practically healthy children of the same age. The analysis of indices of non-specific resistance of the organism was carried out on the basis of the assessment of phagocytic activity of neutrophils (PhAN) and monocytes (PhAM), as well as their phagocytic numbers (PhNN and PhNM).

The spontaneous and induced phagocytic reserve of neutrophils (PhR) was also evaluated by nitro blue tetrazolium test (NBT-test). The content of lysosomal cationic proteins (LCP) in neutrophils was determined, the percentage of positive cells (LCP%) and the intensity of the test by the cytochemical coefficient (CCC LCP) were taken into account. Simultaneously, the content of the myeloperoxidase enzyme (MPO) with the determination of the percentage of positive cells (MPO%) and the calculation of the cytochemical coefficient (CCC MPO) was studied.

The treatment was conducted within two treatment complexes (TC). TC-1 (standard) included 18 sessions of haloaerosoltherapy with increased intensity of haloaerosol influence [12]. The concentration of rock salt aerosol varied from 40 mg/m^3 at the beginning to 35 mg/m3 at the end of the 30 minute session, aerosol particles up to 6 μm in size ranged from 70% to 75%. Such parameters provide direct influence on the mucosa of different levels of the respiratory tract and allow taking into account the peculiarities of the pathogenesis of the pathological process.

The course of treatment included a period of adaptation to the haloaerosol for 2–3 days, with the duration of procedures from 10 to 30 minutes, and the main period, with

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the duration of sessions for 30 minutes each. TC-2 provided reduction of the haloaerosoltherapy course to 13 procedures with the simultaneous prescription of singlet oxygen therapy (SOT) in the form of oxygen foam, which was received by MIT–C device produced in Ukraine, within 12 procedures of 200 ml. The statistical processing of the results was carried out using the standard program package «Statistica 6.0 for Windows».

Results and discussion. Before treatment in children with RRD, in comparison with the control group of practically healthy children, inhibition of the absorption properties of neutrophils and monocytes was observed. Thus, there was a significant decrease in the PhAN to 44,0±1,22%, compared to 50,3±0,76% in the control (p<0,001), and some decrease in PhNN to 3,24±0,09 at norm 3,54±0,13 (p<0,1), which contributes to the weakening of anti–infective defense.

The decrease of absorption properties of monocytes has been also revealed. Thus, the values of PhAM and PhNM were significantly lowered to 35,3±0,93% versus 42,5±0,95% in the control group (p<0,001), and to 2,72±0,07 at normal level 2,99±0,04 (p<0,01) accordingly, which may affect the antigen presentation process.

Neutrophils also revealed a significant decrease in the spontaneous NBT–test to 23,1±0,76%, compared to 27,1±0,80%, in the control (p<0,001) and induced NBT–test to 29,5±0,77%, with a norm of 35,5±0,92% (p<0,001), indicating a lack of functional reserves of the phagocytic activity of neutrophils, and is confirmed by a decrease in the PhR, which corresponded to 6,41±0,49%, against 8,47±0,65% in healthy children (p<0,02).

Study of intracellular microbial cytotoxic properties of neutrophils revealed a significant decrease in MPO% levels, which was 90,3±0,55% with a norm of 92,3±0,63% (p<0,02), and a CCC of MPO equal to 1,75±0,04 vs. 2,06±0,05% in control (p<0,001), which reflects the inhibition of the ability of intracellular destruction of a alien antigen. Changes in oxygen–independent antimicrobial properties of neutrophils were less significant. Thus, the percentage of LCP was 88,9±0,60%, compared with 90,3±0,45% in the control group (p<0,1), and the value of CCC LCP was 1,46±0,03, compared with 1,55±0,04 within normal ranges (p<0,1).

Thus, in children with RRD even beyond of the acute period there was a significant reduction in anti–infective defense due to inhibition of the absorption properties of neutrophils and monocytes and suppression of intracellular

Table. Changes of nonspecific defense indices in children with recurrent respiratory diseases under the influence of different treatment complexes

Indices, units	Control group (n=12)	TC-1 (n=35)		TC-2 (n=39)	
		before treatment	after treatment	before treatment	after treatment
PhAN,% p	50,3±0,76	44,1±1,35**	49,3±1,19 <0,01	44,0±1,08**	48,6±1,26* <0,01
PhNN p	3,54±0,13	3,25±0,11*	3,65±0,10 <0,01	3,24±0,08*	3,57±0,09 <0,01
spontaneous NBT-test,% p	27,1±0,80	23,1±0,94**	26,6±0,76 <0,01	22,9±0,59**	26,2±0,77 <0,001
induced NBT-test,% p	35,5±0,92	29,4±0,89**	33,6±1,03* <0,01	29,6±0,66**	33,3±0,64* <0,001
PhR,%	8,47±0,65	6,23±0,57**	7,06±0,53*	6,59±0,41**	7,00±0,58*
MPO,% p	92,3±0,63	90,8±0,55*	93,7±0,39 <0,001	89,6±0,54**	92,3±0,58 <0,01
CCC MPO p	2,06±0,05	1,76±0,05**	2,05±0,05 <0,001	1,74±0,03**	1,98±0,04 <0,001
LCP,% p	90,3±0,45	89,3±0,60*	91,5±0,43 <0,01	88,5±0,61*	91,1±0,36 <0,001
CCC LCP p	1,55±0,04	1,47±0,03*	1,57±0,02 <0,01	1,45±0,02	1,59±0,02 <0,001
PhAM,% p	42,5±0,95	36,6±1,06**	42,9±1,39 <0,001	33,9±0,81**	40,9±0,96* <0,001
PhNM p	2,99±0,04	2,85±0,07*	3,07±0,09 <0,1	2,60±0,07**	3,04±0,12 <0,01

Notes:** – statistically valuable difference (p<0,05) between results in comparison with norm (control group);
* – tendency to statistically valuable difference between results in comparison with norm;
p – statistical accuracy of difference between results before and after treatment.

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antimicrobial activity, which may be a pathogenetic ground for the progression of infectious inflammatory process and requires appropriate immunocorrection.

As a result of the recovery treatment carried out, positive dynamic of the nonspecific defense indices under study was observed on the background of the absence of significant differences between the treatment complexes (see table).

Thus, under the influence of TC-1 (standard HAT course) there was a significant increase and normalization of the PhAN and PhNN. Monocytes also indicated an improvement in their absorption capacity, mainly due to a significant increase and normalization of the PhAM value; the PhNM increased slightly ($p<0,1$), but normalized.

The research also showed that TC-2 results in a significant improvement in the functional status of neutrophils, according to the spontaneous and induced NBT test ($p<0,01$), with a slight increase in the PhR level up to $7,06\pm0,53\%$. However, after treatment, the values of the induced NBT–test and PhR haven't reached the normal values. Improvement of the function of intracellular destruction of the alien antigen in neutrophils was manifested in the significant increase in the MPO% index and the values of the CCC MPO that were normalized. Strengthening of the phagocytic function of neutrophils after the standard HAT course was confirmed also by a significant increase and normalization of LCP% and CCC LCP indices.

The use of the reduced regime of HAT (TC-2) also contributed to the positive dynamics of the indices under study. The levels of PhAN and PhNN have significantly increased and normalized. Monocytes also significantly increased and PhAM ($p<0,001$) and PhNM ($p<0,01$) normalized, which contributes to the development of an adequate immune response to the antigenic stimulus.

The value of the spontaneous and induced NBT–test increased significantly, indicating an improvement in their metabolic characteristics, while the level of the induced NBT–test did not reach the norm ($p<0,1$), and the level of PhR increased slightly and did not reach the value of healthy children ($p<0,1$). At the same time, there was a significant improvement in the bactericidal properties of neutrophils according to the MPO%, LCP% and the corresponding cytochemical coefficients, the values of which have been normalized.

That is, the duration of the HAT course may be shortened, but only with the simultaneous prescription of an additional therapeutic factor, in particular singlet–oxygen therapy.

Conclusions. In children with RRD out of acute period, a decrease in the absorption capacity of neutrophils and monocytes was observed, which was accompanied by a significant decrease in the functional reserves of neutrophils and a predominant inhibition of their oxygen–dependent mechanisms of intracellular bactericidal activity. These changes can disrupt an adequate immune response and indicate a reduction in anti–infective defense, which can contribute to the protracted course of the pathological process and requires the necessity of recovery treatment and immunocorrection.

The use of the proposed TC based on HAT in children with RRI resulted in the improvement of the studied indexes with the normalization of most of them, which contributes to the improvement of antigen presentation and anti–infection defense in general and allows preventing the progression of the pathological process and the development of chronic pathology of bronchopulmonary system.

The absence of a significant difference in the effectiveness of the proposed TC indicates the possibility of reducing the duration of the course of HAT, subject to the additional prescription of another therapeutic factor, in particular, SOT.

Monitoring of cellular immunity, as well as monitoring of the long–term results of various courses of recovery treatment, including haloaerosoltherapy, is also relevant for children with RRD out of acute period.

Список літератури

1. Восстановительное лечение часто болеющих детей и детей с хроническими очагами инфекции носоглотки / У.В. Лиханова, Е.И. Кондратьева, Н.П. Степаненко и др. Вопросы курортологии, физиотерапии и лечебной физической культуры. 2014. № 2. С. 33–37.
2. Эффективность применения иммунокорригирующих препаратов для профилактики респираторных инфекций и их осложнений у часто болеющих детей младшего школьного возраста / Р.В. Майоров, М.В. Черешнева, С.Д. Верзилин и др. Медицинская иммунология. 2013. Т. 15, № 3. С. 255–262. doi: 10.15789/1563–0625–2013–3–255–262.
3. Кривопустов С.П. Антибіотикорезистентність у педіатрії. Роль фітотерапії з доведеною ефективністю. Medical Nature. 2017. № 2 (22). С. 25–27.
4. Лемко І.С., Лемко О.І. Спелео– та галоерозольтерапія на Закарпатті – становлення, сьогодення, перспективи. Актуальные вопросы физиотерапии и курортологии: Материалы научно– практической конференции с международным участием, посвященной 150–летию со дня рождения профессора А.Е. Щербака (1863–1934). Актуальные вопросы курортологии, физиотерапии и медицинской реабилитации: Труды. Том XXIV. Ялта, АР Крым, 10–11 октября 2013. С. 132–138.
5. Лемко О.І., Вантюх Н.В., Лукащук С.В. Можливості застосування фізичних і преформованих лікувальних факторів в імунореабілітації дітей, які страждають на рецидивуючі бронхіти. Збірник наукових праць співробітників НМАПО імені П.Л. Шупика. Випуск 26. Київ, 2016. С. 44–50.
6. Лукащук С.В., Лемко О.І. Часті та рецидивуючі респіраторні інфекції у дітей: сучасний стан проблеми (огляд літератури). Проблеми клінічної педіатрії. № 3–4. 2016. С. 66–71.
7. Лукащук С.В., Лемко О.І. Принципи ведення дітей із частими та рецидивними захворюваннями дихальних шляхів (огляд літератури). Сучасна педіатрія. № 7. 2016. С. 48–52. doi: 10.15574/SP.2016.79.48.
8. Марушко Ю.В., Мовчан О.С., Марушко Т.В. Функціонування системи місцевого імунітету та її особливості в дітей, які часто хворіють на респіраторні інфекції. Український медичний часопис. 2014. № 1 (99). С. 41–44.
9. Мойсеєнко Р.О., Дудіна О.О., Гойда Н.Г. Аналіз стану захворюваності та поширеності захворювань у дітей в Україні за період 2011–2015 роки. Современная педиатрия. 2017. № 2 (82). С. 17–27. doi: 10.15574/SP.2017.82.17.
10. Муквіч О.М., Омельченко Л.І. Профілактика рекурентних гострих респіраторних інфекцій у дітей шкільного віку. Дитячий лікар. 2013. № 6 (27). С. 65–70.

References

1. Likhanova UV, Kondrateva EY, Stepanenko NP, et al. Vosstanovitelnoie lecheniie chasto boleiushchikh detei i detei s khronicheskimi ochagami infektsii nosoglotki (The rehabilitative treatment of the frequently ill children presenting with chronic infectious foci in the nasopharynx). Voprosy kurortolohii, fizioterapii i lechebnoi fizicheskoi kultury. 2014;2:33–37.
2. Maiorov RV, Chereshneva MV, Verzilin SD, et al. Effektivnost primeneniia immunokorrigiruiushchikh preparatov dlia profilaktiki respiratornykh infektsii i ikh oslozhnenii u chasto boleiushchikh detei mladshego shkolnogo vozrasta (Efficiency of some immunomodulatory drugs for prevention of respiratory infections and their complications in young schoolchildren with recurrent respiratory infections). Meditsinskaia immunolohia. 2013;15(3):255–262. doi: 10.15789/1563–0625–2013–3–255–262.
3. Kryvopustov SP. Antybiotykorezystentnist u pediatrii. Rol fitoterapii z dovedenoiu efektyvnistiu (Antibioticresistance in pediatrics. The role of phytotherapy with proven efficacy). Medical Nature. 2017;2(22):25–27.
4. Lemko IS, Lemko OI. Speleo– ta haloaerozolterapiia na Zakarpatti – stanovlennia, sohodennia, perspektyvy (Speleo– and haloerosoltherapy of Transcarpathia – formation, present, prospects). Aktualnyie voprosy kurortolohii, fizioterapii i meditsinskoi reabilitatsii: Trudy. Tom XXIV. Yalta, Crimea. 2013;132–138.
5. Lemko OI, Vantyukh NV, Lukaschuk SV. Mozhlyvosti zastosuvannia fizychnykh i preformovanykh likuvalnykh faktoriv v imunoreabilitatsii ditei, yaki strazhdaiut na retsydyvuiuchi bronkhity (Possibilities of nonmedicamental immunorehabilitation of children, suffering from recurrent bronchitis). Zbirnyk naukovykh prats spivrobitnykiv NMAPO imeni P.L. Shupyka. 2016;26:44–50.
6. Lukashchuk SV, Lemko OI. Chasti ta retsydyvuiuchi respiratorni infektsii u ditei: suchasnyi stan problemy (ohliad literatury) (Frequent and recurrent respiratory infections in children: modern state of problem (literature review)). Problemy klinichnoi pediatrii. 2016;3–4:66–71.
7. Lukashchuk SV, Lemko OI. Pryntsypy vedennia ditei iz chastymy ta retsydyvuiuchymy zakhvoriuvanniamy dykhalnykh shliakhiv (ohliad literatury) (The principles of treatment in children with frequent and recurrent respiratory diseases (literature review)). Sovremennaia pediatriia. 2016;79(7):48–52. doi: 10.15574/SP.2016.79.48.
8. Marushko YuV, Movchan OS, Marushko TV. Funktsionuvannia systemy mistsevoho imunitetu ta yii osoblyvosti v ditey, yaki chasto khvoriiut na respiratorni infektsii (Functioning of the system of local immunity and its features in children who often suffer from respiratory infections). Ukrainskii medichnii chasopis. 2014;99(1):41–44.

ISSN 2307-3373

11. Оцінка деяких показників імунітету у дітей з рецидивуючим бронхітом / О.І. Лемко, Н.В. Вантюх, С.В. Лукащук, Т.І. Кополовець, М.І. Попадинець. Збірник наукових праць співробітників КМАПО імені П.Л. Шупика. Випуск 24, книга 3. Київ, 2015. С. 280–285.

12. Патент на винахід 109307 Україна, (51) МПК (2016.01) A61M 16/00. Спосіб відновлювального лікування часто хворіючих дітей та дітей хворих на рецидивуючий бронхіт / Лемко О.І., Лемко І.С.; заявник и патентовласник Державна установа «Науково–практичний медичний центр «Реабілітація» міністерства охорони здоров'я України». № u 2016 00972; заявл. 08.02.2016; опубл. 25.08.2016, Бюл. № 16, 2016р.

13. Щербак И.Б. Бион 3 Кид в комплексной ммунореабилитации часто болеющих детей. Український медичний часопис. 2014. № 2. С. 78–81.

14. Юлиш Е.И., Ярошенко С.Я. Часто болеющие дети и тактика педиатра. Здоровье ребенка. 2013. № 6 (49). С. 70–76.

15. Endre L. Theoretical basis and clinical benefits of dry salt inhalation therapy. Orv. Hetil. 2015. Vol. 156, № 41. P. 1643–1652. doi: 10.1556/650.2015.30267.

16. Immunomodulatory effect of pleuran (β–glucan from Pleurotus ostreatus) in children with recurrent respiratory tract infections / M. Jesenak, J. Majtan, Z. Rennerova et al. International Immunopharmacology. 2013. Vol. 15, № 2. P. 395–399. doi: 10.1016/j.intimp.2012.11.020.

17. Lemko I., Lukaschuk S. The usage of haloaerosoltherapy in the rehabilitational treatment of children with recurrent bronchitis. Balneo Research Journal. 2015. Vol.6, № 2. P. 60–64. doi:10.12680/balneo.2015.1087.

18. Neutrophils regulate the lung inflammatory response via γδ T cell infiltration in an experimental mouse model of human metapneumovirus infection / N.R. Cheemarla, MD. R. Baños–Lara, S. Naidu et al. J. Leukoc. Biol. 2017. Vol. 101, № 6. P. 1383–1392. doi:10.1189/jlb.4A1216–519RR.

19. Recurrent respiratory tract infections in children – analysis of immunological examinations / A. Raniszewska, E. Górska, I. Kotu a et al. Cent. Eur. J. Immunol. 2015. Vol. 40, № 2. P. 167–173. doi: 10.5114/ceji.2015.52830.

20. Riley, D.S. Efficacy and Tolerability of High–dose Pelargonium Extract in Patients With the Common Cold / D.S. Riley, V.G. Lizogub, A. Zimmermann et al. Altern. Ther. Health Med. 2018. № 2 (24). С. 16–26.

21. Verhagen L.M., de Groot R. Recurrent, protracted and persistent lower respiratory tract infection: A neglected clinical entity. J. Infect. 2015. Vol. 71, № 1. P. 106–111. doi: 10.1016/j.jinf.2015.04.011.

9. Moiseenko RO, Dudina OO, Hoyda NH. Analiz stanu zakhvoriuvanosti ta poshyrenosti zakhvoriuvan u ditei v ukraini za period 2011–2015 roky (Analysis of incidence and prevalence of diseases among children in Ukraine for the 2011–2015 period). Sovremennaia pediatriia. 2017;82(2):17–27. doi: 10.15574/SP.2017.82.17.

10. Mukvich OM, Omelchenko LI. Profilaktyka rekurentnykh hostrykh respiratornykh infektsii u ditei shkilnoho viku (Prevention of recurrent acute respiratory infections in school–age children). Dytiachyi likar. 2013;27(6):65–70.

11. Lemko OI, Vantyukh NV, Lukashchuk SV, et al. Otsinka deiakykh pokaznykiv imunitetu u ditey z retsydyvuiuchym bronkhitom (Evaluating some parameters of the immune system in children with recurrent bronchitis). Zbirnyk naukovykh prats spivrobitnykiv NMAPO imeni P.L. Shupyka. 2015;24(3):280–285.

12. Lemko OI, Lemko IS. Sposib vidnovliuvalnoho likuvannia chasto khvoriiuchykh ditei ta ditei khvorykh na retsydyvuiuchyi bronkhit (Method of recovery treatment of frequently ill children and children with recurrent bronchitis). The patent of Ukraine 109 307 (51) of the IPC (2016.01) A61M 16/00. № u 2016 00972, 2016.

13. Shcherbak YB. Bion Z Kid v kompleksnoy immunoreabilitatsii chasto boleiushchikh detei (Bion Z Kid in complex mnourehabilitation of often ill children). Ukrainskyi medichnyi chasopys. 2014;2:78–81.

14. Yulysh EY, Yaroshenko SYa. Chasto boleiushchiie deti i taktika pediatra (Sickly children and pediatrician's approach). Zdorovie rebenka. 2013;49(6):70–76.

15. Endre L. Theoretical basis and clinical benefits of dry salt inhalation therapy. Orv. Hetil. 2015;156(41):1643–1652. doi: 10.1556/650.2015.30267.

16. Jesenak M, Majtan J, Rennerova Z, et al. Immunomodulatory effect of pleuran (b–glucan from Pleurotus ostreatus) in children with recurrent respiratory tract infections. International Immunopharmacology. 2013;15(2):395–399. doi: 10.1016/j.intimp.2012.11.020.

17. Lemko I, Lukaschuk S. The usage of haloaerosoltherapy in the rehabilitational treatment of children with recurrent bronchitis. Balneo Research Journal. 2015;6(2):60–64. doi:10.12680/balneo.2015.1087.

18. Cheemarla NR, Baños–Lara MDR, Naidu S, Guerrero–Plata A. Neutrophils regulate the lung inflammatory response via γδ T cell infiltration in an experimental mouse model of human metapneumovirus infection. J. Leukoc. Biol. 2017;101(6):1383–1392. doi:10.1189/jlb.4A1216–519RR.

19. Raniszewska A, Górska E, Kotu a I, et al. Recurrent respiratory tract infections in children – analysis of immunological examinations. Cent. Eur. J. Immunol. 2015;40(2):167–173. doi: 10.5114/ceji.2015.52830.

20. Riley DS, Lizogub VG, Zimmermann A, et al. Efficacy and Tolerability of High–dose Pelargonium Extract in Patients With the Common Cold. Altern. Ther. Health Med. 2018;2(24):16–26.

21. Verhagen LM, de Groot R. Recurrent, protracted and persistent lower respiratory tract infection: A neglected clinical entity. J. Infect. 2015;71(1):106–111. doi: 10.1016/j.jinf.2015.04.011.

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