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General non-specific adaptive reactions and expresiveness of endogenous intoxication in pulmonary tuberculosis

Objective was the comparative analysis of general nonspecific adaptive reactions (RANG) and the expresiveness of endogenous intoxication in various forms of pulmonary infiltrative tuberculosis.

Materials and methods. RANG structure, intoxication indices and plasma level of circulating immune complexes were assessed at 374 new pulmonary infiltrative TB cases.

Results and discussion. Standard treatment enhanced RANG structure only in limited forms of pulmonary TB. Despite of concludent diminishing of intoxication indices in both groups, the high level of circulating immune complexes at the end of intensive treatment phase, demonstrated the insuficient immune adaptive and desinstoxication activity of the standard regimen.

Conclusions. The standard TB treatment demonstrated an unsuficient immune restoring action, necessitating the association of immune adaptive drugs.

Key words

Tuberculosis, adaptive reactions, immune reactivity.

Aquired immunity plays the major role in the immune resistance against infection with *M. tuberculosis*. Although, the degree of endogenous intoxication determines the clinical manifestations, morphopathological aspects and treatment outcome of persons who encountered this pathogen [4].

Aim — comparative analysis of general nonspecific adaptive reactions (GNAR) and the expresiveness of endogenous intoxication in various forms of pulmonary infiltrative tuberculosis according the severity of radiological extenssion.

Materials and methods

A retrospective, selective and descriptive analysis of a total number of 374 new pulmonary infiltrative TB cases, with 18—70 age old, distributed in 2 groups: group 1 — 129 patients with extensive infiltrates (caseous pneumonia and lobitis) and group 2 — 125 patients with limited infiltrates was performed. Mathematic indices were calculated accroding formulas: *immune reactivity leucocyte index*

$ILI = L + CP + E + B/MIE + NT + NN + NS + E;$

with acronymes: MIE — mielocyte, CP — plasmatic cells, NT — young neutrophyles, NN —nonsegmented neutrophyles, NS — segmented neutrophyles, L — limphocytes, M — monocytes, E — eosinophyles, B — basophyles; N = 0.46;

Adaptive index (IA):

$IA = L / NS + 2NN + 3NT + MIE;\ N = 0.49;$

Intoxication leucocyte index Ya. Kalf-Kalif:

$ILIK = (4MIE + 3NT + 2NN + NS) + (CP+1)/ /(L + M) \times (E + 1);\ N = 0.62 \pm 0.083.$

Intoxication leucocyte index V.K. Ostrovski:

$ILIo = (CP + NT + NN + NS)/(L + M + E + B);\ N = 1.6 \pm 0.3.$

Intoxication leucocyte index Vasiliev

$IHI_v = ILI_k \cdot K_l \cdot K_{vsh};$

where ILI_k — Intoxication leucocyte indix Ya. Kalf-Kalif; K_l — coeficient calculated to the leucocyte quantity; K_{vsh} — coeficient calculated to the ESR rate; N = 0.61 ± 0.3. Circulating immune complexes where analised according the method Ghinda S. et al.

Table 1. **GNAR structure under the ethiologic treatment (%, M ± m)**

GNAR reactions	1	2	1	2
	Extenssive TB (group 1, n = 129)		Limited TB (group 2, n = 125)	
Stres	35.29 ± 8.87	23.53 ± 7.45	31.43 ± 8.01	14.29 ± 6.09*
Entrainment	47.06 ± 8.12	41.18 ± 8.23	48.57 ± 8.12	40.01 ± 8.52
Latent activation	11.76 ± 5.56	26.47 ± 8.46	11.43 ± 5.01	34.29 ± 8.26*
High activation	5.71 ± 4.78	8.82 ± 5.62	2.86 ± 2.90	5.71 ± 4.04
Hyperactivation	0	0	5.71 ± 4.04	5.71 ± 4.04

Note. Statistic difference between indices before (1) and at the end of intenssive phase of the treatment (2).

(2008). Immune reactivity results where compared with a sample group of 50 health individuals.

Results and discussion

Assessing the distribution of the patients in groups, it was established their homogenous distribution in age groups and sex (75.1 ± 3.80) % vs (76.80 ± 3.77) % males and (24.80 ± 3.80) % vs (23.20 ± 3.77) % females) with age 41.8 years vs 37.2 years, that confirmed the comparability of assessed groups. Evaluating GNAR it was established that in both groups before the initiation of standardised treatment prevaled the reactions «Stress» and «Entrainment reactivity». So, in group 1 (35.29 ± 8.87) % of patients had the reaction type «Stres» and (47.06 ± 8.12) % of them «Entrainment reactivity», but in the group 2 was appreciated at (31.43 ± 8.01) % of patients the reaction type «Stres» si at (48.57 ± 8.12) % of them reaction type «Entrainment reactivity». The frequence of the reaction «Latent activation» and «High activation» had a minor rate in both groups, that demonstrates the low degree of adaptability of the patients with active TB process. So, in group 1 «Latent activation» achived the (11.76 ± 5.56) % rate and «High activation» — (5.71 ± 4.78) %.

At the end of intensive phase of antituberculosis treatment, the GNAR dynamics showed an optimal trend in both groups, but the concludent difference was appreciated only for «Stress» reactivity in the group 2. So, at the end of intensive phase of the treatment, it was assessed that the frequence of «Stress» reactivity reduced statisticaly concludent to (23.53 ± 7.45) % rate, and «Entrainment reactivity» reduced to (41.18 ± 8.23) % rate. This restructuring was due to the encreased number of patients that developed «Latent reactivity» and «High reactivity» under the specific treatment. Optimal concludent dynamic was established in the group of patients with limited forms of TB (group 2), where was appreciated the diminished rate of «Stress» reactivity (14.29 ± 6.09; $p < 0.01$), slightly diminished the «Entrainment reactivity» ((40.01 ± ± 8.52) %), and concludent encreased rate of «Latent reactivity» ((34.29 ± 8.26) %; $p < 0.01$). It was established a slightly encreasing of «High reactivity» ((5.71 ± 4.04) %) and «Hyper reactivity» ((5.71 ± 4.04) %) state. Kalf-Kalif index was increased in group 1, and non-significantly disturbed in group 2, in comparison with the sample group ($t = 2.5$; $p < 0.05$). At the end of the treatment, diminished statistically only in the group 1 ($t = 4.08$; $p < 0.001$), being at an inferior level in both groups than in sample group ($t = 4.47$; $p < 0.001$). Ostrovski index was increased in both groups, but the statistical threshold was achieved only in the group 1 ($t = 3.1$; $p < 0.01$). At the end of the treatment, the index reduced in both groups, but more evident in the group 1 ($t = 5.77$; $p < 0.001$ and $t = 3.77$; $p < 0.001$ for the group 2). Vasiliev index before treatment in both groups was increased in comparison with the sample groups ($t = 5.1$; $p < 0.001$ for group 1 si $t = 3.0$; $p < 0.01$ for group 2). At the end of intensive phase the index reduced but more evident in the group 1 ($t = 5.27$; $p < 0.001$ and $t = 3.39$; $p < 0.01$ for group 2). So, the mathematic intoxication indexes showed high disturbances and more evident dynamics in the group 1. Immune reactivity index in the group 1 was more diminished than in the sample group ($t = 13.4$; $p < 0.001$) also in comparison with the group 2 ($t = 3.52$; $p < 0.01$). After the treatment the index encreased in both groups at the same level ($t = 5.5$; $p < 0.001$ pentru grupul 1 and $t = 5.7$; $p < 0.001$ for group 2), remaining at the inferior level in the group 1 in comparision with the group 2 ($t = 3.17$; $p < 0.01$). Adaptive index was reduced in both groups in comparision with the sample ($t = 17.9$; $p < 0.001$ group 1 and $t = 8.94$; $p < 0.001$ group 2), being more disturbed in the group 1 than in the group 2 ($t = 4.75$; $p < 0.001$). At the end of intensive phase of the treatment the adaption index encreased at the same level in both groups, remaining at a lower level in the group 1 ($t = 4.07$; $p < 0.001$). Presented data, demonstrated the reduced immune reactivity, and a diminished adaptive immunity in the group 1, that were assessed as features of severe evolution of pumonary extenssive infiltrative TB.

Table 2. **Dynamics of endogenous intoxication indexes (%, M ± m)**

Indexes	Sample, n = 50	Group 1, n = 129		Group 2, n = 125	
		1	2	1	2
IKK u. c.	0.9 ± 0.04	1.4 ± 0.20*	0.5 ± 0.08#*	0.7 ± 0.12	0.5 ± 0.07*
I Ostrovschi u. c.	1.6 ± 0.3	2.7 ± 0.18*	1.6 ± 0.09#	1.7 ± 0.11	1.2 ± 0.07#
I Vasiliev u. c.	0.6 ± 0.03	2.4 ± 0.35*	0.5 ± 0.08#	1.2 ± 0.2*	0.5 ± 0.07#
ILI u. c.	0.6 ± 0.01	0.3 ± 0.02*	0.5 ± 0.03#	0.4 ± 0.1*	0.6 ± 0.04#*
IA u. c.	0.6 ± 0.01	0.2 ± 0.02*	0.4 ± 0.03#	0.4 ± 0.02*	0.6 ± 0.04#*
		Group 1, n = 48		Group 2, n = 21	
PEG-2.5 % udo	11.2 ± 0.74	48.1 ± 4.00*	33.9 ± 2.58#	29.8 ± 4.14*	16.5 ± 1.70#*
PEG-4.2 % udo	29.9 ± 1.57	83.8 ± 6.12*	63.6 ± 2.74#	66.4 ± 4.59*	47.3 ± 4.09#*
PEG-8.0 % udo	282 ± 10.7	542 ± 33.6*	445 ± 17.7#	353 ± 24.9*	269 ± 22.5#*

Note. *Statistically significant difference in comparison with those for a sound sample; diferent statistically significant between group (1) and group (2) intensive treatment; * statistically significant difference between group 1 and group 2.

One of the used biomarkers of endogenous intoxication was the plasma level of circulating immune complexes of 3 molecular weight. So, the quantity of CIC with high molecular weight (PEG-2.5 %), presenting a low toxicity was higher in both groups than in sample group, but more evident in the group 1 ($t = 9.1$; $p < 0.001$ and $t = 4.4$; $p < 0.01$ group 2). At the end of the treatment, the level reduced in both groups similary ($p < 0.01$), although remained higher in the group 1 ($t = 5.63$; $p < 0.001$). The quantity of CIC with medium molecular weight (PEG-4.2 %), presenting a medium toxicity was higher in both groups than in sample group, but more evident in the group 1 ($t = 8.5$; $p < 0.001$ and $t = 7.5$; $p < 0.01$ group 2). At the end of the treatment, the level reduced similary in both groups ($p < 0.01$), although remained at a higher level in the group 1 than in the group 2 ($t = 3.31$; $p < 0.001$). Consecutively, the quantity of CIC with low molecular weight (PEG-8 %), presenting a high toxicity was higher in both groups than in sample group, but more evident in the group 1 ($t = 7.4$; $p < 0.001$ and $t = 2.6$; $p < 0.01$ for group 2). At the end of the treatment, the level reduced similary in both groups ($p < 0.05$), although remained at a higher level in the group 1 than in the group 2 ($t = 6.15$; $p < 0.001$). By this way it was appreciated that despite of concludent diminishing of intoxication mathematic indexes in both groups, the high remained level of circulating immune complexes (with low, mediu and high molecular weight) at the end of the intensive treatment phase demonstrated the more expressed endogenous intoxication in the group of patients with extenssive forms of pulmonary TB.

Conclusions

1. At the start of standard TB treatment, it was assessed a similar rate of «Stress» , «Entrainment», «Latent reactivity» and «High reactivity» in both groups without any difference between the groups of patients with extensive and limited forms of pulmonary TB. The ethiologic treatment determined a statistical diminishing action in the group of patients with limited forms of TB through the diminishing the rate of «Stres» reaction and increasing of the frequence of «Latent activity».

2. Intoxication indices were concludent encreased and showed a more evident dynimics in the group with extensive TB. Immunereactivity and adaptive indices were statisticaly diminished before starting the treatment in both groups, and complete immune restoring in the groups with limited forms of TB. This fact demonstrated necessity ofthe association of immune adaptive drugs to standard TB treatment.

3. Although the endogenous intoxication indexes restored at the end of the treatment, the remaining high concentration of immune circulating complexes demonstrated a higher expressiveness of endogenous intoxication in extesnive forms of pulmonary TB.

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Загальні адаптивні реакції і вираженість ендогенної інтоксикації у хворих на туберкульоз легень

Мета роботи — порівняльний аналіз загальних неспецифічних адаптивних реакцій і інтоксикаційних показників у хворих на інфільтративний туберкульоз легень.

Матеріали та методи. Імунологічні показники і загальні адаптивні реакції були проаналізовані у 374 пацієнтів з інфільтративним туберкульозом легень.

Результати та обговорення. Показано ефективність протитуберкульозного впливу на структуру адаптивних реакцій у хворих з лімітованими процесами. Незважаючи на зменшення інтоксикаційних показників в обох групах, високий рівень імунних циркулюючих комплексів у момент завершення інтенсивної фази хіміотерапії показує недостатню імуноадаптивну і дезінтоксикаційну ефективність стандартного протитуберкульозного лікування.

Висновки. Стандартне протитуберкульозне лікування демонструє недостатню ефективність імунного відновлення, вимагаючи асоційованих імуноадаптивних препаратів.

Ключові слова: туберкульоз, стрес, адаптивні відповіді, BioR.

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Общие адаптивные реакции и выраженность эндогенной интоксикации у больных туберкулезом легких

Цель работы — сравнительный анализ общих неспецифических адаптивных реакций и интоксикационных показателей у больных инфильтративным туберкулезом легких.

Материалы и методы. Иммунологические показатели и общие адаптивные реакции были проанализированы у 374 пациентов с инфильтративным туберкулезом легких.

Результаты и обсуждение. Показана эффективность противотуберкулезного воздействия на структуру адаптивных реакций у больных с лимитированными процессами. Несмотря на уменьшение интоксикационных показателей в обеих группах, высокий уровень иммунных циркулирующих комплексов в момент завершения интенсивной фазы химиотерапии показывает недостаточную иммуноадаптивную и дезинтоксикационную эффективность стандартного противотуберкулезного лечения.

Выводы. Стандартное противотуберкулезное лечение демонстрирует недостаточную эффективность иммунного восстановления, требуя ассоциированных иммуноадаптивных препаратов.

Ключевые слова: туберкулез, стресс, адаптивные ответы, BioR.

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