RESULTS OF CLINICAL TRIALS OF THE DRUG "KAMELIN"

L. Vashvkidze (Л. Вашвкидзе)
W. Torondzhadze (В. Торонджадзе)
"National Centre for Tuberculosis and Lung Diseases".

Research conducted at the National Centre for Tuberculosis and Lung Diseases The study involved:

- Department of Research and Continuing Medical Education;
- Outpatient department;
- Therapeutic Unit;
- Immunology Laboratory;
- Bacteriology Laboratory;
- Other departments and laboratories if necessary.

Study objective:

Evaluation of the efficacy of the drug "Kamelin" in the complex treatment of patients with the refractory form of pulmonary tuberculosis (MDR), and in vitro testing of possible antimicrobial activity
Camellin against mycobacteria.

Tasks of the study:

- Evaluation of clinical and radiological data of patients with refractory pulmonary tuberculosis on Kamelin treatment versus control groups;
- Comparison of the dynamics of immunological indices in the main and control groups;
- Assessment of severity and monitoring of adverse effects of anti-tuberculosis drugs against the background of "Kamelin" treatment
- In vitro study of the effect of 'Kamelin' on the non-specific factor of organismal immuno-resistance - phagocytosis;
- Evaluation of the in vitro antibacterial efficacy of 'Kamelin';
- Assessment of the frequency and nature of adverse events against the background of "Kamelin" treatment

SURVEY STRUCTURE.
Nature of the study:
Open comparative characteristics of the main and control group.

Number of patients and their characteristics:

- The total number of patients studied is 50 (main group - 30; control group - 20).
- *Core group*:

standard anti-tuberculosis therapy + treatment with "Kamelin"

- *Control group:*
  standard anti-tuberculosis therapy, without "Kamelin"
- Anti-tuberculosis therapy carried out in accordance with national guidelines (gaidlinem)
- 'Kamelin' therapy was conducted in accordance with the relevant instructions
- Informed consent was obtained from all patients.

Table 1

Distribution of patients by sex and age:

Groups	n	Gender	n	Age (years)				
				18-25	26-35	36-45	46-55	56-61
Main	**30**	**cob.**	**6**	**1**	**2**	**2**	**1**	**-**
		husbands.	**24**	**2**	**5**	**6**	**9**	**2**
Control	**20**	**cob.**	**9**	**2**	**4**	**2**	**1**	-
		husbands.	**11**	**1**	**5**	**2**	**2**	**1**

SELECTION OF PATIENTS

Inclusion criteria.

- Established refractory pulmonary tuberculosis, with persistent lymphopenia (less than 19%);
- Having written consent from the volunteer for inclusion in the study.

Exclusion criteria:

- Hypersensitivity to the drug Kamelin;
- Patient opt-out of the study;
- Inappropriate patient behaviour.

Test methods

- Clinical-x-ray and standard laboratory examination in dynamics.
- 2-fold immunological testing (before and after Kamelin treatment);

Peripheral blood lymph concentrates (3-10^6), determined:

1. T-lymphocyte count (E-ROK) according to (M. Zondee et al., 1972)
2. Number of T suppressors and T helpers according to M. Shore et al. (1978);
3. Tx/Tc immunoregulatory index (WIR);
4. B lymphocytes, according to M. Zondee et al. (1972);
5. The number of total T cells capable of expressing structural E was calculated;
6. A study of the non-specific immunoreactivity factor-phagocytosis was conducted in neutral lymphocytes isolated from peripheral blood (S. G. Potapova, 1977).
   Killed yeast cells were used as phagocytosis targets. After a 30-minute incubation
   The following parameters of phagocytosis were tested: percentage of neutrophils able to actively capture yeast cells; phagocytic number - mean number of yeast cells
   absorbed by a single neutrophil (LF); phagocytic index (IF).

Study design.

- The results obtained were processed using the method of variational statistics, with estimation of the mathematical mean, mean square error and Student's ratio parameters.

Assessment of the drug's effectiveness

Subjective indicators:
mood, improved sleep, improved appetite, increased energy.
Objective indicators:
Weight gain, reduced intoxication, reduced cough, tendency to normalise T lymphocytes^0 , positive dynamics of laboratory and Ro (X-ray) parameters.
Specific criteria:
Dynamics of resilience parameters.
Assessment of the side effects of the drug:
Comparison of the number of patients with and without side effects; if present, a detailed description of the symptoms of side effects and an assessment of the need to monitor them.

Table 2

Dynamics of clinic-laboratory and roentgenological indices against Kamelin treatment

No.	clinical-laboratory and roentgenological indicators	Main group (30)	Control chart (20)
1	Reduction or elimination of poisoning	30 (100%)	15 (75%)
2	Normalisation of body temperature	20 (66,7%)	7 (35%)
3	Weight gain	28 (93,3%)	10 (50%)
4	Normalisation of lymphocyte count	26 (86,7%)	8 (40%)
5	Sputum conversion	22 (70%)	15 (75%)
6	Reduction or resolution of coughing	12 (40%)	8 (40%)
7	Reduction or disappearance of non-inflammatory phenomena in the lungs	18 (60%)	8 (40%)
8	Positive Rg dynamics	22 (73,3%)	11 (55%)
9	Reduction or disappearance of side effects of anti-tuberculosis therapy	25 (83,3%)	10 (50%)
10	Suspension of treatment due to side effects	3 (10%)	12 (60%)

Side effects caused by *"Kamelin"*
8 (26.7%) - pain and discomfort after injection
3 (10%) - burning and itching
13 (36,7%)

Table 3

Dynamics of immune indices in patients with pulmonary tuberculosis (under treatment)

Groups	n	Limf. T %	Supr. T %	Pom. T %	**T** pom/Tsup	B lymphocytes	TO cells
Before treatment	50	38,1 ± 1,2 P < 0,001	4,9 ± 1,4 P < 0,001	32,6 ± 1,48 P < 0,001	6,7 ± 1,6 P < 0,001	24,3 ± 1,7 P < 0,001	37,5 ± 0,5 P < 0,001
Chemotherapy + immunotherapy (primary)	30	46,9 ± 0,87 P_1 < 0,001 P_3 < 0,1	9,5 ± 0,17 P_1 < 0,001 P_3 < 0,1	37,3 ± 0,5 P_1 < 0,001 P_3 < 0,05	3,9 ± 0,5 P_1 < 0,001 P_3 < 0,1	22,5 ± 0,8 P_1 < 0,001 P_3 < 0,1	31,6 ± 0,11 P_1 < 0,001 P_3 < 0,05
Chemotherapy only (control)	20	44,6 ± 11 P_2 < 0,001	7,9 ± 0,86 P_2 < 0,01	35,9 ± 0,38 P_2 < 0,01	4,93 ± 0,93 P_2 < 0,01	21,6 ± 0,41 P_2 < 0,01	33,4 ± 0,73 P_2 < 0,01
Healthy	25	52,5 ± 1,7	12,3 ± 3,1	41,9 ± 3,0	3,4 ± 1,7	19,1 ± 1,33	38,4 ± 1,77

CONCLUSIONS

- Before treatment, markedly reduced number and imbalance of cells Immunoregulatory compared to healthy people, increased number of cells B lymphocytes and To cells.
- After "anti-tuberculosis + Kamelin" therapy, the number of immunoregulatory cells increases, they approach normal levels, the imbalance is evened out; there is a decrease in the B-lymphocyte levels (but above noma).
- Against the background of anti-tuberculosis therapy without Kamelin, there was a statistically insignificant improvement in the indicated resistance parameters (no).

Table 4.

Functional activity of neutrophils in the treatment of severe forms of tuberculosis

groups	n	LF%	Absorption function	
			LF	LF
Before treatment	50	37,4 ± 21 P < 0,001	2,04 ± 0,2 P < 0,001	1,3 ± 0,18 P < 0,001
Chemotherapy + immunotherapy (main)	30	64,2 ± 1,2 P_1 < 0,001 P_3 < 0.001	3,8 ± 0,16 P_1 < 0,001 P_3 < 0.001	2,6 ± 0,23 P_1 < 0,001 P_3 < 0,01
Chemotherapy only (control)	20	48,1 ± 1,6 P_2 < 0,01	2,21 ± 0,38 P_2 < 0,05	1,6 ± 0,27 P_2 < 0,05
Healthy	25	66,8 ± 1,7	3,5 ± 0,008	2,4 ± 0,35

- *CONCLUSIONS*

- In vitro studies showed inhibition of neutrophil phagocytic function prior to treatment;
- Against the backdrop of the "anti-tuberculosis + Kamelin" therapy, a significant trend towards correction of the non-specific indices of immunity and normalisation of phagocyte action capacity.
- Against the background of anti-tuberculosis therapy without Kamelin, there was also a statistically insignificant positive dynamic.

- The national drug 'Kamelin' is an effective and safe immunotherapeutic agent for the comprehensive treatment of severe forms of tuberculosis that occur against a background of immunosuppression.
- The use of Kamelin together with anti-tuberculosis chemotherapy already in the first course of treatment improves the subjective state of patients: reduced intoxication, improved appetite, weight gain, tendency to normalise body temperature.
- After completing the full 'Kamelin' course, compared to the control group (the group with no "Kamelin"), a significant improvement in immune parameters (quantitative and functional), which is an unconditional indicator of a drug's immunotherapeutic efficacy.

- The use of "Kamelin" significantly reduces the side effects of anti-tuberculosis chemotherapy, the process of monitoring them is facilitated, practically the possibility of reducing the intensity of chemotherapy.
- The use of 'Kamelin' increases the efficacy of basic chemotherapy, the cessation of germ carriage is achieved and roentgenomorphological dynamics are improved.
- Thus, the results obtained make it possible to recommend 'Kamelinu' for use in the clinic as an immunotherapeutic drug in the comprehensive (pathogenetic) treatment of tuberculosis.