Assessment of immunomodulating effects of alkylglycerols in healthy volunteers.

Clinical Study, Moscow 1997

Juri Reznikov M.D., Ph.D.

Head of Laboratory of Clinical Immunology Central Clinical Hospital.
Medical Centre of the Administration of the President of the Russian Federation - Moscow, Russia.

Marcin Krotkiewski M.D., Ph.D.

Department of Rehabilitation Medicine, University of Gothenburg - Gothenburg, Sweden

Assessment of immunomodulating effects of alkylglycerols in healthy volunteers.

Clinical Study, Moscow 1997

Juri Reznikov M.D., Ph.D.

Head of Laboratory of Clinical Immunology Central Clinical Hospital.
Medical Centre of the Administration of the President of the Russian Federation - Moscow, Russia.

Marcin Krotkiewski M.D., Ph.D.

Department of Rehabilitation Medicine, University of Gothenburg - Gothenburg, Sweden

Introduction

Alkylglycerols have been described as immunological stimulators and used in treatment and / or prevention of cancer as well as prevention of myelosuppressive effects of cancer radiotherapy, preventing the leucopenia and thrombocytopenia following this kind of treatment.
More specifically, it has been shown that alkylglycerols activate haemopoesis, enhance phagocytic and tumoricidal activity of neutrophils and macrophages / monocytes by activating production of reactive oxygen species in these cells, promote antitumour activity of NK-cells, elevate IgM and IgG levels in serum, inhibits expression of adhesive molecules on endothelial cells and last but not least - induce apoptosis of tumour cells (1,2,3,4,5,6,7)
The aim of the proposed pilot study is to further elucidate the possible mechanism of action of alkylglycerols by investigating their effects on the immune system in healthy volunteers.

Methods

Subjects

twenty-four healthy volunteers - men and women - were randomly divided into two groups. All volunteers have been subjected to usual medical examination. Neither medical examination nor medical history revealed any cardiovascular, kidney, pulmonary or infection diseases. Blood formula and serum biochemistry (AST, ALT, cholesterol, glucose) were normal. All participants were free from any medical treatment during the last 2 months preceding the tests.

Study design

A cross-over, double-blind placebo-controlled study design was used. The overall study design was approved by the Ethical Committee of the Central Clinical Hospital of the Medical Center of the Presidents Administration of Russian Federation.

All the participants signed a written informed consent in which all the main points of the study design as well as any possible side effects were mentioned.

Double-blind were done according to usual rules, i.e. both ***Alkymer*** and ***Placebo*** capsules had the same appearance and were packed in coded boxes.

Only the monitor of the study knew the actual contents of each box. Both the participants and a person distributing the boxes did not know it.

The course of treatment by ***Alkymer*** or ***Placebo*** took 15 days (2 capsules 3 times daily, i.e., 6 capsules / day). The course for group **A** included: 15 days wash-out, ***Alkymer***, 30 days wash-out, ***Placebo***. 30 days wash-out. The course for group **B** included: 15 days wash-out, ***Placebo***, 30 days wash-out, ***Alkymer***, 30 days wash-out. Blood sampling and immunological tests were done at the beginning and by the end of each treatment period (in sum - 6 samplings). The overall study design is depicted on the following scheme:

GROUP A (12 INDIVIDUALS, No. No. 1-12)

15 days	15 days	30 days		15 days	30 days	
*———	*———	*———		*———	*———	
Wash-out	***Alkymer***	**Wash-out**	.....	***Placebo***	**Wash-out**	.....
1	**2**	**3**		**4**	**5**	**6**

GROUP B (12 INDIVIDUALS, No. No. 16-27)

15 days	15 days	30 days		15 days	30 days	
*———	*———	*———		*———	*———	
Wash-out	***Placebo***	**Wash-out**	.....	***Alkymer***	**Wash-out**	.....
1	**2**	**3**		**4**	**5**	**6**

*= Blood sampling (6 times)

Immunological tests performed

1. Leukocyte count (Coulter Counter)
2. Lymphocyte count (Coulter Counter)
3. CD4+ and CD8+ lymphocytes, CD4/CD8 ratio, CD56+/CD16+ cells (direct immunofluorescence on Becton-Dickinson FACSCalibur flow cytometer)
4. B- and T-lymphocyte count (CD19, CD3 - FACSCalibur)
5. T-lymphocyte proliferative response to ConA (^{3}H-thymidine uptake, in cpm/cell)
6. PMA-induced chemiluminescence (LKB 1251 Luminometer)
7. Serum IgA, IgM, IgG (Behring Nephelometer Analyser)
8. Concentration of kappa- and lambda- immunoglobulin light chains in serum (RID, Behring)

9. Acute phase proteins: alpha-1-antitripsin, alpha-2-macroglobulin, CRP, alpha-1-acid glycoprotein (Behring Nephelometer Analyser, RID, Behring)
10. complement components: C4, C3c, C3-activator (Behring Nephelometer Analyser)

Statistics

Statistical calculations have been made by means of nonparametric Wilcoxon test for matched pairs.

In the calculations tables the following abbreviations have been used.

Alc before - ***Alkymer*** treatment preceding (before) ***Placebo*** treatment - group **A.**

Alc after - ***Alkymer*** treatment following ***Placebo*** treatment - group **B.**

Pla before - ***Placebo*** treatment preceding (before) ***Alkymer*** treatment.

Pla after - ***Placebo*** treatment following ***Alkymer*** treatment - group **A.**

Leuk before - Absolute count of leukocytes at the base-line.

Leuk aa - Absolute count of leukocytes at the end of ***Alkymer*** treatment (after).

Leuk ap - Absolute count of leukocytes by the end of (after) ***Placebo*** treatment.

Leuk aw - Absolute count of leukocytes by the end of (after) wash-out period.

Lym - Percent of lymphocytes.

Lyma - Absolute count of lymphocytes.

T - T-lymphocytes.

B - B-lymphocytes.

Ma - Mitogenic activity (T-lymphocytes proliferative response to Con A).

Fag - PMA-induced chemiluminescence of leukocytes.

R 48 - CD4 / CD8 ratio.

NK - CD56+ / CD16 + cells, C3c, C4, C3-act - complement components.

AAT - Alpha-1-acid glycoprotein.

A 2 M - Alpha-2-macroglobulin, kappa and lamb - concentration of kappa and lambda light chains.

Results

Five participants have been excluded because of different family reasons (2) and accidental infections (3). All other participants completed the study. No side-effects have been observed throughout the treatment (inclusively wash-out) periods. No changes have been noted in blood pressure, general routine blood chemistry (liver-tests, blood glucose, haemoglobin concentration and body weight).