

CYTOKINE PROFILE OF INDIVIDUALS WITH TB/HIV CO-INFECTION DURING HIV AND TB TREATMENT

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INTRODUCTION AND PURPOSES

Cytokines are important immunomodulating agents of the immune system. However HIV-infection as well as TB is associated with profound deregulation of the immune system. Cytokine profile during HIV infection is rather well studied. But there is still little data related to the immune status of individuals with TB/HIV co-infection and especially during HIV and TB treatment. The goal of the work was to study the cytokine profile of those patients after the initiation of dual therapy.

METHODS

A prospective study was conducted in a cohort of patients with TB/HIV co-infection at the Moscow Tuberculosis Clinic. All patients were drug-naïve. For the study of cytokine profile (IFN- γ , IL-4, IL-6, IL-10) the blood samples were taken before therapy and at 30, 60, 90 and 150 days after initiation of HIV and TB treatment. CD4+T cell levels and viral loads were measured as blood samples were taken. Patients were divided into two groups according to CD4+T cell count: Group 1 (CD4+ < 200 cells/mm³) and Group 2 (CD4+ > 200 cells/mm³). A statistical analyses was performed using BioStat analysis programme.

RESULTS

• In total 83 patients were enrolled in the study (informed consent obtained from all participants). Afterwards 21 patients were excluded due to non-adherence to the HIV-treatment. The mean age of patients was 35,8 years and 80% of the participants were male.

• Most evident differences in expression of IFN- γ , IL-4, IL-6, IL-10 between Groups 1 and 2 were before therapy. For both groups decrease of pro- and anti-inflammatory cytokines were observed. However, in general lower levels of IL-4, IL-6 and IL-10 were observed for Group 2 before therapy in comparison with Group 1. For IFN- γ levels there were not significant differences between both Groups before or after therapy.

• A difference was marked in the expression of IL-6 levels. For Group 1 (n=38, CD4+ < 200 cells/mm³) the decrease of IL-6 levels was observed on 30 days of HIV/TB treatment. On 60 days of therapy there was an abrupt increase of IL-6 and then the IL-6 levels decreased again (with exception of 2 patients with CD4+ 173 cells/mm³ and 181 cells/mm³). For Group 2 (n=24, CD4+ > 200 cells/mm³) the decrease of IL-6 levels was observed steadily over all period of study.

Table 1. Demographic and clinical characteristics of HIV/TB patients (n=62)

| Characteristics | |
|-----------------------------------|--------------|
| Age (years), median | 35,8 (27÷51) |
| Gender n (%) | |
| Male | 50 (80,6%) |
| Female | 12 (19,4%) |
| Form of tuberculosis n (%) | |
| Disseminated | 22 (35,5%) |
| Pulmonary | 21 (33,9%) |
| Intrathoracic lymph nodes (TITLM) | 18 (29%) |
| Disseminated + TITLM | 1 (1,6%) |
| Positive culture | 33 (53,2%) |

Changes of IL-6 levels during HIV and TB treatment for patients with co-infection TB/HIV

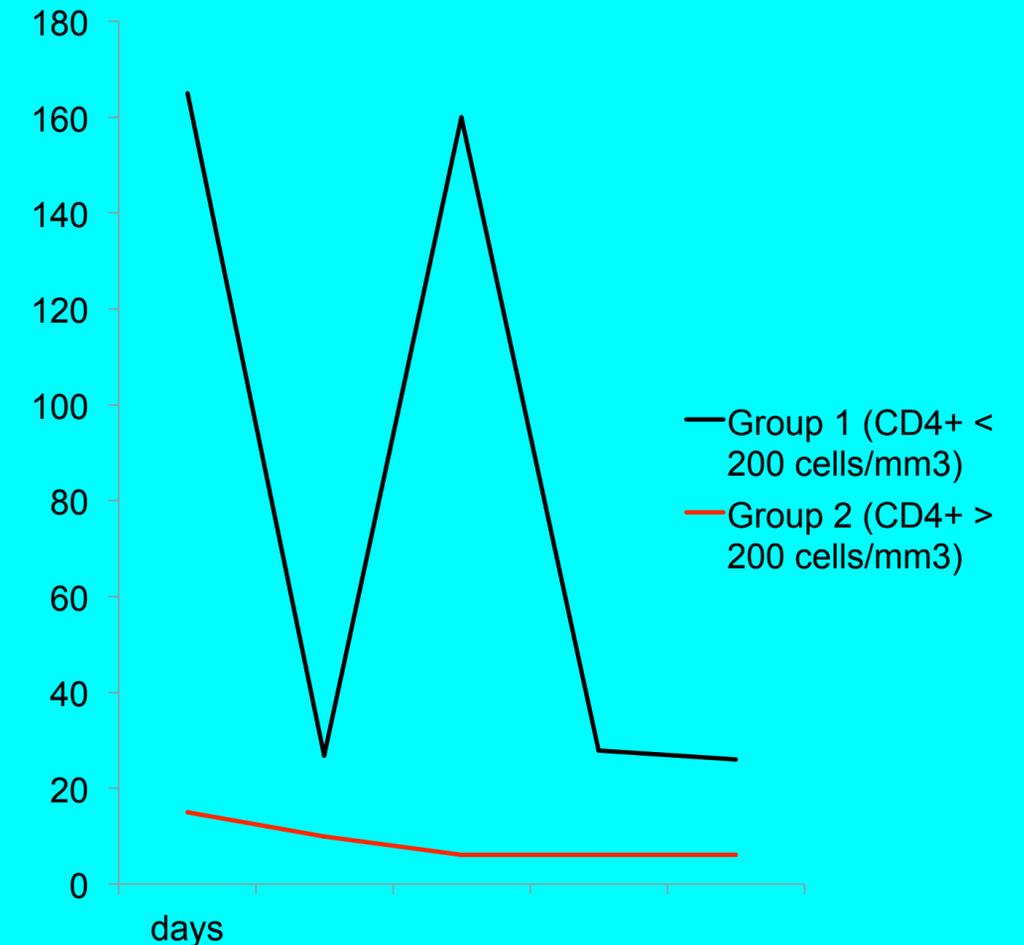


Table 2. Changes of cytokine profiles in HIV/TB patients during HAART and TB treatment

| CD4+cells/mm ³ | IL-4 (pg/ml) | | IL-6 (pg/ml) | | IL-10 (pg/ml) | | IFN- γ (pg/ml) | |
|---------------------------|--------------|-----------|--------------|--------------|---------------|------------|-----------------------|------------|
| | B* | A^ | B | A | B | A | B | A |
| < 200 (n=38) | B* | 7,3(0-50) | B | 25,9 (5-165) | B | 9,1(5-20) | B | 11,5(0-60) |
| | A^ | 1,1(0-10) | A | 26,0 (5-95) | A | 5,2 (0-10) | A | 4,5 (0-55) |
| > 200 (n=24) | B | 5,7(0-18) | B | 6,0 (0-15) | B | 3,1 (0-7) | B | 15,0(0-60) |
| | A | 1,2 (0-5) | A | 6,1(0-15) | A | 4,1 (0-5) | A | 4,2 (0-45) |

B* - before treatment

A^ - after treatment

For all tests P<0.05 was considered significant

CONCLUSIONS

- On the whole independent of their immunosuppression profile all HIV/TB patients were able to recover immune activation after initiation of HAART and anti-TB therapy.
- The patients with severe immunosuppression after initiation of therapy had an immune activation more intense compared with Group 2 (CD4+ > 200 cells/mm³).
- The abrupt increase of IL-6 levels in patients with severe immunosuppression in absence of immune reconstitution inflammatory syndrome (IRIS) suggests a less effective immune reconstitution due to the fact that median CD4+ cell count for Group 1 was <56 cell/mm³.