DOI: 10.5455/msm.2017.29.14-16

Received: 23 January 2017; Accepted: 15 March 2017

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ORIGINAL PAPER

Mater Sociomed. 2017 Mar; 29(1): 14-16

T-lymphocyte Subsets as a Prognostic Factor in a Clinical Course of Chickenpox

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ABSTRACT

Objective: To investigate possible prognostic values of CD4+, CD8+ T-lymphocytes, CD4/CD8 ratio to clinical course of chickenpox in immunocompetent hosts. **Materials and methods:** We performed a prospective study which included 69 immunocompetent patients with chickenpox who were admitted to Clinic for infectious disease, Clinical Center University of Sarajevo, in a 18 month period. All patients were divided into two groups depending on clinical presentation on admission. Patients with mild clinical form were dedicated to „outpatient“ group, and patients with moderate, severe or life-threatening clinical forms were dedicated to „hospitalized“ group. Also 30 healthy volunteers are included in study as a control group. We analyzed values of CD4+, CD8+ percentage, CD4/CD8 ratio with comparison to clinical course of chickenpox. All specimens were taken in acute phase of illness. **Results:** Values of CD4+ percentage were significantly declined in a group of hospitalized patients, compared to group of outpatients and control group. Values of CD8+ percentage were higher in a group of hospitalized patients, while CD4/CD8 values were lower in comparison to a group of outpatients and control group. **Conclusion:** We found significant correlation between these parameters and clinical course of chickenpox.

Keywords: Chickenpox, T-lymphocyte, prognostic factors.

1. INTRODUCTION

Varicella zoster virus (VZV) is one of the most prevalent viruses which affects the human race (1). Primary infection known as chickenpox, mostly occurs in childhood, with mild clinical course in immunocompetent hosts, but it can cause significant morbidity in healthy adults with life threatening forms in immunocompromised persons. VZV establishes latency in sensory ganglia,

and can be reactivated years later as herpes zoster. Circulating VZV-specific antibody can prevent primary infection but innate and cellular responses are more important in its severity and duration (2). Clinical studies suggest that T cell immunity plays a key role in the protection against VZV primary infection. Few studies found significant depression of CD4+ T lymphocytes, augmentation of CD8+ T-lymphocytes and changes in CD4/CD8 ratio but none of them were compared to clinical course of illness (3, 4).

2. MATERIALS AND METHODS

We performed a prospective clinical study which included 69 immunocompetent persons with confirmed chickenpox in a period July 2014 - January 2016. Patients were divided into two groups: group with mild clinical presentation who were treated as outpatients, and group with moderate, severe or life-threatening clinical presentation which were hospitalized. Study also included 30 healthy volunteers with age and sex similar to the other groups. The study was approved from Ethics Committee of Clinical Center University of Sarajevo. We checked general characteristics such as age, sex, complications, clinical course of illness, percentage values of CD4+, CD8+ T-lymphocytes and CD4/CD8 ratio. Values for CD4+, CD8+ T-lymphocyte percentage and CD4/CD8 ratio was obtained using FACS Canto, BD Biosciences flow cytometer and BD Multitest™ 6-color TBNK immunofluorescent test. Statistical analysis was performed using SPSS software version 16 (SPSS, Inc., Chicago, USA). Values with normal distribution were expressed as mean±standard deviation. To compare mean values for variables without normal distribution Chi-square test was used. One-way ANOVA test was used for statistical evaluation of more than three groups. Correlation of monitored variables is determined by Pearsons test. To determine influence of these variables to a clinical presentation we used logical regression

Graph 1. Clinical presentation of the illness

Graph 2. CD4+ percentage values in the groups

(backward method). P-values less than 0.05 were considered statistically significant.

3. RESULTS

Mean age in outpatient group was 28.47 years with standard deviation (SD) 10.3 while in the other group was 24.57 (SD=14.14), with no statistically significant difference between groups ($p>0.05$). Females were dominant in outpatients group (65%:35%), while males were in higher number in other group (71%:29%). Chi-squared test found statistically significant difference between these two groups ($p<0.05$). The number of complications vary from zero to four per patient, and all were presented in a hospitalized patients. Clinical presentation vary from mild to life-threatening. Mean value of CD4+ percentage for outpatient group was 44.06 (SD 11.48) and for a group of hospitalised patients it was 28.20 (SD=12.70). Mean value for a control group was 44.26 (SD 6.69). One-way ANOVA test found statistically significant difference between group of hospitalised patients and outpatients, as well as hospitalised patients and control group ($p<0.0001$). There were no statistically significant difference between outpatients and control group ($p>0.05$).

Values for percentage of CD8+ T-lymphocytes were as follows: outpatients 30.15 (SD=9.46); hospitalised patients 38.34 (SD=15.52); control group 28.40 (SD=7.34).

One-way ANOVA test found statistically significant difference between group of hospitalised patients and outpatients, as well as hospitalised patients and control group ($p<0.0001$). There were no statistically significant difference between outpatients and control group ($p>0.05$).

CD4/CD8 ratio was 1.74 (0.40-8.10) in group of outpatients, 1.05 (0.10-3.60) in group of hospitalised patients and 1.73

Graph 3. CD8+ percentage values for all groups

Graph 4. CD4/CD8 ratio values for the groups

(0.80-3.70) in a control group. One-way ANOVA test found statistically significant difference between group of hospitalised patients and outpatients, as well as hospitalised patients and control group ($p=0.006$). There were no statistically significant difference between outpatients and control group ($p>0.05$). Using Pearson's correlation factor we have found very strong negative correlation between CD4+ percentage value and clinical presentation ($r=0.61$, $p<0.0001$); strong positive correlation between CD8+ percentage value and clinical picture and also weak negative correlation between CD4/CD8 ratio and clinical presentation. In addition we performed regression analysis to determine which of mentioned parameters have the strongest influence to clinical presenta-

Graph 5. Correlation of CD4+ percentage values and clinical presentation

tion. Values of CD4+ percentage have a very strong influence as a prognostic factor to clinical presentation and possible severity of clinical picture (beta coefficient = 0.56, $p<0.0001$).

4. DISCUSSION

Results of our study correlate with other studies regarding age and sex of the patients, where most of them with complications were males, age 21-40, primary because of pre-existing medical conditions (5). Several studies suggest that cellular immunity has a key role in control of VZV primary infection (6, 7). Patients with primary agamaglobulinaemia develop mild clinical form, while patients with deficiency of cellular immunity develop severe and life-threatening forms of chickenpox (8). So far, there is no prognostic marker for a severity of clinical picture and outcome of the disease, which can be measured in short time and predict further development of the illness. In our study we tried to investigate if values of CD4+ and CD8+ T-lymphocytes percentage, so as CD4/CD8 ratio, can be considered as relevant prognostic factors for clinical course of chickenpox. We measured values of these parameters from blood samples taken from the patients in acute phase of disease, 24 - 72h after development of the rash, and correlate with presented complications and severity of clinical picture. Values of CD4+ T-lymphocytes mostly decrease in acute phase of all viral infection, so as VZV, with recovery during the time. For significant number of diseases it can be strong prognostic factor for possible coinfections and complications in clinical course (3, 9, 10). In our study decrease of CD4+ percentage was very significant, compared to the group with mild clinical form and control group. These values had strong correlation with developed complications and clinical form. Also CD8+ percentage value increased in acute phase of illness among hospitalized patients with presented complications. Early studies suggest similar dynamic of these subsets of T-lymphocytes (11). Significant difference between these patients and outpatients, so as control group, was confirmed with ANOVA test. CD4/CD8 ratio is very important in follow-up of some viral diseases and other medical conditions (12, 13). We found significant decrease in values of CD4/CD8 in hospitalized patients, while values in group of outpatients and controls were almost the same. Further comparison using regression analysis found values of CD4+ percentage of T-lymphocytes as a strong predictive factor for clinical course of the disease. Also values of CD8+ T-lymphocyte percentage were in a strong correlation with clinical pictures.

5. CONCLUSION

According to the results of our study, we can consider values of CD4+ and CD8+ T-lymphocyte subsets as strong predictive factor for a clinical course of chickenpox in immunocompetent patients. Values of CD4+ T-lymphocytes have the strongest influence, while CD4/CD8 ratio stays as

a prognostic factor, but not so strong like in other viral diseases, such as HIV.

• Conflict of interest: none declared.

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