The effect and mechanism analysis of valaciclovir on herpes zoster in elderly patients

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Valaciclovir
Herpes zoster
Tumor necrosis factor
Up-regulated expression

ABSTRACT

Objective: To explore the effect and mechanism of valaciclovir on herpes zoster in elderly patients. Methods: 80 cases patients received valaciclovir treatments in our hospital were analyzed in this part. The expression of TNF-α, NF-κB, CD4 and CD8 were detected by Western Blotting. Results: The content of TNF-α, NF-κB, CD4 and CD8 was increased greatly in patients after drug treatments with statistical differences. Conclusion: Up-regulated expression of TNF-α, NF-κB, CD4 and CD8 is involved in the pathogenesis of herpes zoster and valaciclovir therapy mainly through normalizing those abnormal expressions of proteins.

1. Introduction

Herpes zoster is a common viral skin disease in clinical, which is easily suffered by crowds with low immunity, such as the elderly and children[1-3]. The symptom of herpes zoster for the elderly patients is long course of disease and high proportion of incidence rate of residual neuralgia. Timely diagnosis and treatment are needed. Valaciclovir is the antiviral drug in clinical for treating chicken pox and herpes zoster infection. With good water solubility, it can rapidly translate into acyclovir in vivo[4-6]. CD4 cell is the important immune cell in vivo, which is the important molecule to maintain body immunity system function. The reduction of CD4 level of patient will cause serious randomly infected diseases[7-10]. This thesis has studied the effect analysis of valaciclovir to patients with herpes zoster and the participation mechanism of cytokines, which has provided reference for clinical treatment.

2. Materials and methods

2.1. General data

80 cases elderly patients who received valaciclovir treatments in our hospital were analyzed, including 34 male patients and 46 female patients with average age of (62.0±11.9) years old. The expression of TNF-α, NF-κB, CD4 and CD8 in serum was analyzed before and after treatment.

2.2. Reagent and method

Primary antibodies are all purchased from American Abcam Company; IgG-HRP with HRP sign/second antibodies of HRP-IgG are purchased from Beijing Zhongshan Gold Bridge Biotechnology Co., Ltd.; PVDF membrane is purchased from American Amersham Company; electrophoresis tank, electrophoresis apparatus and protein transfer system are purchased from American ABI Company; the other reagents are market-sold analytically pure. Western blotting is adopted to detect the expression of TNF-α, NF-κB, CD4 and CD8 in serum of patients in all groups.

2.3. Protein expression detected by western blotting and ELISA method

Extract the total protein after patient's serum is centrifuged, take protein quantification by BCA method and take 10% SDS-PAGE electrophoretic analysis and then adopt semidry method to transfer the membrane and seal the cellulose membrane by 5.0% skim milk. Then crossbreed the cellulose membrane with primary antibodies and rinse with sterile phosphate buffer for three times and take color developing and photographing after reaction of horseradish peroxidase sign second antibody under room temperature. ELISA operation shall be taken by completely following the kit instructions. GAPDH is the relative quantitative analysis of β-actin for taking

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Tel: 13464842977.
Fund: Changsha Medicine and Health Scientific Research Planning Program (B2010-035).
protein.

2.4. Gene mRNA expression detected by PCR

The extraction and reverse transcription of mRNA shall be operated by strictly following the instructions: add the following substances in centrifuge tube with nuclear-free enzyme in sequence: 5× BU-Script buffer 4 µL; dNTP mix (10 mM) 1 µL; 10 pmol/µL Oligo (dT)18 1 µL; 20 U/µL RNase Inhibitor 1 µL; 200 U/µL BU-Script; RT (reverse transcriptase) 1 µL; 1 µg/µL total RNA: 2 µL; add RNase-free H2O to 20 µL. Take RT after vortex mixing: 1) 30 °C, 10 min; 2) 42 °C, 60 min; 3) 99 °C, 5 min; 4) 4 °C, 5 min. Polymerase China Reaction system includes the following components: Taq DNA Polymerase mixture 12.5 µL; primer sense (20 nmol/L) 0.75 µL; primer anti-sense (20 nmol/L) 0.75 µL; cDNA 1 µL; add DEPC water to 25 µL. Use 2% AGE to test the product and take analysis by image analysis system. Primer sequence is: CD4: Forward 5'-GACGACCAGTGGGGAGAGTA-3', Reverse 5'-GTCATTGAGCCGACCTAA-3'; CD8: Forward 5'-AAAGACAGCTCCTCCTCGAAGGT-3', Reverse 5'-TGACCAAATCCCCATTTACGC-3'; GAPDH Forward: 5'-AACGACCCCTTCATTGAC-3' reverse: 5'-TCCACGACATACTCAGCAC-3'.

2.5. Data statistics and analysis

Data statistics shall be finished by SPSS20.0 statistical software. Measurement data shall be analyzed by one-way ANOVA and expressed by average ± standard deviation and enumeration data are detected by chi-square test. Difference between groups P<0.05 is considered of significant statistical difference.

3. Results

3.1. TNF-α expression of herpes zoster patients after valaciclovir treatment detected by ELISA method

It is discovered in this thesis that the serum TNF-α level of patients with herpes zoster virus is significantly lower than control group, which is of significant statistical difference; while TNF-α after drug therapy has been significantly recovered, which has significant statistical difference compared with that before treatment. See Figure 1.

3.2. NF-κB Gene mRNA expression of herpes zoster patients after valaciclovir treatment detected by PCR method

It is discovered in the thesis that serum NF-κB gene level of patients with herpes zoster virus is significantly lower than control group, which is of significant statistical difference; while NF-κB after drug therapy has been significantly recovered, which has significant statistical difference compared with that before therapy. See Figure 2.

3.3. CD4/CD8 protein expression correlation analysis of herpes zoster after Valaciclovir treatment

It is discovered in this thesis that serum CD4/CD8 level of patients with herpes zoster virus is significantly lower than control group, which is of significant statistical difference; while CD4/CD8 after drug therapy has been significantly recovered, which has significant statistical difference compared with that before therapy (P<0.01). See Figure 3 A-C.
4. Discussion

Herpes zoster is a viral skin disease manifesting clustering vesicle and neuralgia in clinical, which is mainly caused by chicken pox-herpes zoster virus. Nucleoside drugs are the main therapeutic for herpes zoster in clinical, but the exact molecule mechanism is still unknown. Through research on effect analysis and mechanism in patients with herpes zoster after Valaciclovir treatment, it is discovered in the thesis that the expression of serum TNF-α, NF-κB, CD4 and CD8 protein for the patients with herpes zoster virus after treatment are significantly enhanced compared with that before treatment, which has significant statistical difference with that before treatment. Therefore, up-regulated expression of TNF-α, NF-κB, CD4 and CD8 is involved in the pathogenesis of herpes zoster and valaciclovir therapy mainly through normalizing those abnormal expressions of proteins.

TNF-α has the physiological effect of killing tumor cells, enhancing phagocytic ability of neutrophil and promoting cell proliferation and differentiation and anti-infection. It is discovered in the research on Ying heat clearing and superificies-relieving mixture’s dynamic expression influence to influenza virus infection on mice PB Th1/2 cytokines that cytokines TNF-α in model group has been significantly enhanced compared with that in control group, which has expressed that Ying heat clearing and superificies-relieving mixture exerts the function of recovering body anti-infectious immunity balance and enhancing body immunity through regulating cytokines level[11]. It is proved in the research on different baseline CD4 level and anti-virus effect that anti-virus treatment under higher CD4 condition is more beneficial for the reconstruction of patient’s immunity and has better treatment effect[12]. It is also discovered in the analysis of correlation research on T cell subset and viral load for patients with herpes zoster virus that the patient’s clinical features, T cell subset and PB viral load exist correlation and the cell immunity of patients in serious condition has been restricted and viral load is relatively higher[13]. It is also discovered in the correlation analysis on human-infected H7N9 avian influenza virus load and CD4 lymphocyte that viral load has significant correlation with CD4 lymphocyte in illness condition variation progress, and the variation trend is detected to have important significance to clinical pathological change.

Therefore, up-regulated expression of TNF-α, NF-κB, CD4 and CD8 is involved in the pathogenesis of herpes zoster and valaciclovir therapy mainly through normalizing those abnormal expressions of proteins.

References


