Efficacy of Purified Vero Cell Rabies Vaccine (PVRV) under the Zagreb Regimen in Iran

Pooneh Rahimi 1*, Mohammad Reza Shirzadi 2, Firoozeh Farahatj 3, Vida Fallahian 4, Jamal Sharifian 2, Nader Howaizi 3, Mansour Shamsipour 5, Rouhollah Vahabpour 1

1 Department of Hepatitis and AIDS, Pasteur Institute of Iran, Tehran, Iran
2 Center of Disease Control (CDC), Ministry of Health, Tehran, Iran
3 WHO Collaborating Center for Reference and Research on Rabies, Pasteur Institute of Iran, Tehran, Iran
4 Department of Vaccination, Rabies post-exposure prophylaxis, Pasteur Institute of Iran, Tehran, Iran
5 School of Public Health and Institute of Public Health Research, Tehran University of Medical Sciences, Tehran, Iran

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Abstract:
Introduction: Despite the effective pre- and post-exposure treatments, at least 60,000 deaths from rabies occur worldwide every year. Post-exposure treatment is considered as one of the most significant measures for preventing human deaths in exposed individuals. The 2-1-1 rabies post-exposure treatment schedule known as Zagreb regimen is an abbreviated immunization plan in which a tissue culture rabies vaccine is administered intramuscularly at two sites on day 0 and at one site on days 7 and 21. Objectives: In this study the efficacy of rabies vaccine administration under Zagreb regimen in an Iranian group of patients attending Pasteur Institute of Iran was evaluated. Methods: Rabies neutralizing antibody titer was measured in 75 serum samples collected from 25 volunteers receiving post exposure treatment by rapid fluorescent focus inhibition test (RFFIT), and ELISA. Results: All patients were negative for rabies antibody in both ELISA and FRRIT tests on day 0. A satisfactory rabies virus antibody response with the titer of ≥0.5 IU/ml was detected in all patients on day 21 and two weeks after the completion of vaccination (day 35). Conclusions: Rabies immunization with rabies Vero-cell vaccine (PVRV) under the 2-1-1 schedule (Zagreb regimen) could result in an adequate immune response without any adverse effect. However a more comprehensive comparative study is underway to confirm these findings. Vac Res, 2014, 1 (1): 25 - 27

Keywords: Zagreb regimen, PVRV, Rabies vaccines, Post-exposure prophylaxis.

INTRODUCTION

Human rabies is a viral encephalitis caused by RNA viruses belonging to the family Rhabdoviridae, genus Lyssavirus with high mortality that is usually transmitted by the bite or scratch of a rabid animal to humans [1]. Treatment of the exposed person depends on the appraisal of the risk of infection and consists of no treatment for category I, vaccine alone for category II and immediate treatment of category III by vaccination therapy with rabies immunoglobulin [2]. There are two main post-exposure prophylaxis protocols with intramuscular (IM) administration of cell culture rabies vaccines recommended by WHO [2, 3]. The Essen protocol is the gold standard for immunization consisting of 5 single doses of vaccine injected intramuscularly over a 28-day period and the Zagreb regimen known as 2-1-1 protocol is administered over a 21-day duration with two doses at two separate

*Corresponding Author: Pooneh Rahimi
Department of Hepatitis and AIDS, Pasteur Institute of Iran, No. 69, Pasteur Ave, Tehran, Iran, 1316943551.
Email: Prahimi@pasteur.ac.ir
Tel: +98 21 64112204 Fax: +98 21 66969291
sites on D0, followed by single doses on days 7 and 21 [4].

Human diploid cell culture vaccine (HDCV) was used throughout the country prior to 1992, but was replaced by rabies vero-cell vaccine (Aventis Pasteur, France) under the Essen 5- dose regimen for both pre- and post exposure immunization [5, 6, 7]. Post exposure vaccination using ESSEN regimen has been very successful in reducing the number of human deaths due to rabies however, simplifying the procedure could save time and money and consequently result in better patient compliance especially for those living in remote areas. The 2-1-1 regimen needing only 3 visits to the health centers seems a more acceptable alternative both economically and time-wise. This study was undertaken to assess the antibody level raised in patient volunteers immunized with 2-1-1 schedule.

MATERIALS AND METHODS

Patients. Participants were 25 healthy volunteers with animal bites of the second category who were under treatment in the Department of Vaccine, Rabies Treatment and Prophylaxis, Pasteur Institute of Iran. According to the Helsinki Declaration, the aim of the project and the blood sampling procedures were explained to the patients and the consent form was signed by each volunteer.

This study was approved by the Ethical Committees of Pasteur Institute of Iran, and the committee of Rabies Control, Ministry of Health, Treatment and Medical Education of Iran. Patients were between 18-60 years old and immune-competent, had no history of rabies vaccination, were not taking immune-suppressives or Choloroquine, had not been immunized with other killed or live vaccines within the last 3 weeks of rabies vaccination, and did not have any acute febrile disease. Three blood samples were taken on days 0, 21 and 35.

Assessment of post-immunization immune response. Rabies neutralizing antibody titer was measured using the rapid fluorescent focus inhibition test (RFFIT) as described by WHO [8, 9] using international reference sera as control. Briefly, The BSR cells (a clone of baby hamster ovary cells) were grown and used in the test as described previously [9]. Sera were diluted at 1:3 in the sera-virus mixture was incubated at 37°C for 6-8 h after opening with or without rabies immunoglobulin. The onset of clinical symptoms in human rabies invariably results in death, but prompt and appropriate post-exposure prophylaxis prevents the fatalities [2]. Selection of an appropriate regimen for post-exposure treatment from the several approved by WHO is a decision made by individual countries. The efficacy of an immunization protocol is judged by the presence of neutralizing antibody in the sera of the vaccinees to the level of >0.5 IU/ml by day 14 as recommended by WHO [2, 10]. Essen immunization which is the gold standard of rabies post-exposure treatment (PET) consists of 5 intramuscular injection of 0.1 ml out of an 0.5 ml PVRV vial which has to be used within 6-8 h after opening with or without rabies immunoglobulin. The cost of the vaccine, coupled with expenditures incurred for travelling, visits to the clinics and other ser-
vices over a period of 28 days make this protocol a costly one. It has been estimated that the cost of PET in Asia and Africa accounts for 83% of the total budget allocated for rabies control [11]. Zagreb regimen is a shortened version of Essen treatment, reducing the number of injections, visits and duration of the treatment, making it economically more acceptable. Clinical trials and epidemiological studies have demonstrated the efficacy of Zagreb protocol [8, 10, 12].

All patients were negative for anti-rabies antibody prior to treatment (D0) but subsequently showed significant increase in anti-rabies antibody on day 21 (Table 1). In a study conducted in China using locally produced PVRV administered under the 2-1-1 regimen similar anti-body levels were reported [8]. Furthermore, Liu et al. [8] did not observe a significant difference in antibody level between subjects undergoing vaccination under Essen protocol with those of Zagreb method.

In line with the WHO recommendations, antibody titers of ≥0.5 IU/ml was considered indicative of seroconversion and in this study, this value was almost 3 times higher, therefore seroconversion was 100% by day 21. In conclusion, this study showed that rabies vaccination with PVRV under the 2-1-1 schedule (Zagreb regimen) could result in satisfactorily seroconversion without any adverse effect.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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