Available online at www.sciencedirect.com
ScienceDirect
Comparative Immunology, Microbiology and Infectious Diseases 32 (2009) 9–19
COMPARATIVE IMMUNOLOGY MICROBIOLOGY & INFECTIOUS DISEASES
www.elsevier.com/locate/cimid

Ovine anti-rabies antibody production and evaluation

EL-Rashdy M. Redwan [a,*], Ali Fahmy [b], Amr EL Hanafy [c], Nawal Abd EL-Baky [a], Sobhy M.A. Sallam [d]

[a] *Antibody Laboratory, Protein Research Department, Genetic Engineering and Biotechnology Research Institute, Mubarak City for Scientific Research and Technology Applications, New Borg EL Arab 21934, Alexandria, Egypt*
[b] *VACSERA, Giza, Cairo, Egypt*
[c] *Nucleic Acid Department, Genetic Engineering and Biotechnology Research Institute, Mubarak City for Scientific Research and Technology Applications, New Borg EL Arab 21934, Alexandria, Egypt*
[d] *Faculty of Agriculture, Alexandria University, Egypt*

Accepted 3 November 2007

Abstract

In view of the disadvantages of human and equine rabies immunoglobulin still there is urgent needs for safe and cost-control anti-rabies immunoglobulins especially for person who have been severely exposed (categories III) to the virus. Our attempt to produce a less immunogenic and cheaper anti-rabies immunoglobulin affordable for those people living in developing countries, has been harnessed the ovine as a bioreactor instead the horse. The animals have been intramuscular immunized, and the plasma processed with 5% caprylic acid to yield IgG with purity of 95%. Moreover, antibody apparently indicated that the titer and neutralizing indexes were harmonized, especially at higher antibody dilution. The results showed that three immunized sheep were produced about 7000 IU of purified anti-rabies antibody. Sheep's IgG has low immunogenic effect than human and horse antibodies when injected into the mouse. Pure concentrated ovine antibody may serve as a possible alternative to currently available anti-rabies human or equine immunoglobulin.

Keywords: Ovine; Rabies; Anti-rabies; Purified antibody; Neutralization; Immunogenicity

* Corresponding author. Tel.: +20 34593420; fax: +20 34593423.
E-mail address: redwan1961@yahoo.com (E.-R.M. Redwan).

0147-9571/$ – see front matter
doi:10.1016/j.cimid.2007.11.004

Résumé

En raison des inconvénients des immunoglobulines rabiques d'origine humaine et équine, il existe un besoin urgent d'immunoglobulines antirabiques plus sûres et moins chères notamment pour les personnes qui ont été exposées très sévèrement au virus (catégorie 3). Notre tentative de produire une immunoglobuline antirabique moins immunogène et meilleur marché a utilisé le mouton comme animal bioréacteur plutôt que le cheval Les animaux ont été immunisés par voie intramusculaire et le plasma traité avec de l'acide caprylique à 5%, pour récolter les immunoglobulines avec une pureté de 95%.

En outre, les titres et les index neutralisant ont été harmonisés. Les résultats ont prouvé que trois moutons immunisés ont produit environ 7000 unités d'anticorps antirabiques purifiés. Les immunoglobulines de mouton déclenchent une réaction immunogénique moins élevée que les anticorps humains et équins chez la souris. Les anticorps obtenus chez le mouton purifiés et concentrés pourraient servir d'alternative possible à l'utilisation des anticorps humains et équins.

Mots clés : Ovine ; La rage ; l'Antirage ; A purifié l'anticorps ; La neutralization ; Immunogenicity

1. Introduction

Rabies is still a serious public health problem in the developing and developed countries, especially in Asia. It is believed that at least 50,000–60,000 human deaths due to rabies each year, and more than 10 million people are reported to receive post-exposure prophylaxis (PEP) every year throughout the world [1]. The combination of local treatment of the wound, passive immunization with rabies immunoglobulins and vaccination is recommended for all sever (category III) exposure to rabies. The use of homologous immunoglobulins for human post-exposure treatment virtually eliminated the risk of anaphylaxis and serum sickness associated with heterologous serum products [1]. In 1965, approximately 16% of persons treated with anti-rabies serum of equine origin were reported to have developed serum sickness, among person over 15 years of age, the incidence was 46% [2]. In past few years, purified equine immunoglobulins have become available, and in recent studies, the incidence of serum sickness among recipients was reported to be <1–6.2% [3–6]. This high incidence of allergic effects may be due to high levels of IgG_T in horse serum [3]. To avoid such reactions, human rabies immunoglobulin (HRIG) preparations have been developed and used for post-exposure treatment in most industrialized countries. HRIG is well tolerated, but it is expensive and available in only limited quantities at developed countries. However, the most common disadvantages of HRIG are the cost and/or blood borne infectious diseases [7,8].

Alternative sources to human and equine anti-rabies for treatment of rabies should be considered and will include human monoclonal antibodies, human recombinant antibodies, and ovine [1,9]. The ovine serum has been preferred as a source for therapeutic immunoglobulin; (1) because it is widely available, inexpensive, and lack IgG_T [3], (2) because of recent successes in producing Digibind Fab to treat cardiac glycoside [10]. The use of Digibind in the USA has been estimated at about 2500 treatments per year