Available online at www.sciencedirect.com
ScienceDirect
Autoimmunity Reviews 6 (2007) 543 – 546
AUTOIMMUNITY REVIEWS
www.elsevier.com/locate/autrev

Influenza vaccination of patients with systemic lupus erythematosus: Safety and immunogenecity issues

Mahmoud Abu-Shakra *, Joseph Press, Dan Buskila, Shaul Sukenik

Rheumatic Diseases Unit, Department of Medicine, Soroka Medical Center and Ben-Gurion University, Beer-Sheva, Israel

Received 12 October 2006; accepted 5 December 2006
Available online 9 January 2007

Abstract

The influenza vaccine is highly efficacious in the general population; however there have been concerns about the safety, and immunogenecity of the vaccine in patients with SLE. Several studies have suggested that the immune response of patients with SLE to influenza vaccine is significantly lower than the general population, mainly in patients with age ≥50 years and those treated with prednisone.

The vaccine is safe for patients with SLE and it does not affect the clinical manifestations of SLE including renal features, disease activity, or the requirement for steroids or cytotoxic drugs. However, the vaccine may trigger the generation of autoantibodies which is usually short term and is not associated with clinical significance.

Keywords: SLE; Influenza; Vaccination; Autoantibodies; SLEDAI

Contents

Systemic lupus erythematosus (SLE) is a chronic inflammatory multisystem disease with distinct clinical and laboratory features. The disease is characterized by a variable clinical course. While in some patients the disease may be mild affecting only one organ systems,

Abbreviations: SLE, Systemic Lupus erythematosus; GMT, geometric mean titers; HI, hemagglutination inhibition; SLEDAI, SLE disease activity index SLEDAI; aCL, anticardiolipin.

* Corresponding author. Medicine D, Soroka Medical Center, P.O.B. 151, Beer-Sheva, Israel. Fax: +972 8 6272836.
E-mail address: mahmoud@bgumail.bgu.ac.il (M. Abu-Shakra).

1568-9972/$ - see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.autrev.2006.12.004

in others it is manifested by severe central nervous system, renal and other vital organs involvement. The medical management of SLE includes the use of nonsteroidal anti-inflammatory and anti-malarial drugs for the cutaneous and articular features of the disease and corticosteroids and cytotoxic agents for the severe forms of the disease.

The association between infections and SLE is of great interest. Infections may trigger autoimmunity and possibly have a pathogenic role in the development and exacerbation of SLE [1]. In addition, infections contribute significantly to the mortality and morbidity of patients with systemic lupus erythematosus (SLE). A high proportion of SLE patients, particularly those with active disease, develop major infection that requires intravenous antibiotic therapy and hospitalization. Mortality studies have identified infections as one of the primary causes of mortality among patients with SLE. In one study, infection was the primary cause of death in 32% of 124 deaths and it contributed to death in other 10% of the patients [2]. Infections in SLE patients are caused by common bacterial and by opportunistic infections. Lungs and urinary tract infections are the most common site of major infection in SLE.

The frequency of influenza infection among patients with SLE has not been estimated. While prevention of influenza infections may reduce the risk of development of pneumonia, there has been concern that influenza vaccine may trigger flare of SLE [3]. In this paper we review the safety and efficacy of influenza vaccine in patients with SLE.

1. The vaccine

The influenza vaccine is composed of two inactivated influenza A and one influenza B viruses. The virus is constantly changing, therefore each year the WHO recommends for the composition of the inactivated vaccine intended for use the following winter. Influenza A is mainly of the H3N2 and of the H1N1. Influenza B activity is usually sporadic and various influenza B viruses are antigenically related to influenza B/Beijing subtypes.

Trivalent inactivated vaccines containing the antigens of 2 influenza A and 1 influenza B antigens are given in doses of 15 micrograms of each haemagglutinin. The immune response against the vaccine is measured by hemagglutination inhibition (HI) test. At least a 4-fold rise in the HI titer after immunization or seroconversion indicates an immune the vaccine. HI titers $\geq$ 1:40 are defined as protective against infection with influenza virus [4,5].

2. Efficacy of the vaccine

The influenza vaccine is highly efficacious in the general population. The WHO report on influenza vaccine indicates that vaccine containing influenza A/Sydney/5/97 (H3N2) induced postimmunization HI antibodies at titers $\geq$ 1:40 in 89% of adults, influenza A/Beijing262/95 stimulated HI antibodies in 66% and vaccines containing B/Harbin/07/97 stimulated post-immunization protective antibodies in the sera of 97% of adults [6].

Several studies have suggested that the immune response of patients with SLE to influenza vaccine is significantly lower than the general population. In 1976, with the threat of a swine influenza epidemic, 109 SLE patients at various centers were immunized with the influenza A/New Jersey/76 (Hsw1N1) and A/Victoria3/75 (H3N2) strains [7–11]. Four centers reported the HI titers and geometric mean titers (GMT) before and after immunization of SLE patients and control groups [7–10]. Two studies reported a significantly lower response postimmunization. In one study [8], 47% of 19 SLE patients had seroconversion following immunization compared with 94% in age-matched group. As well, the GMTs to A/Victoria before vaccination were significantly low or undetectable in the SLE patients. In the second study [10], 48% of the SLE patients and 62% of the controls had 4-fold increase in antibody titers and there was a trend suggesting higher postimmunization titers in the control group. A third study [9], did not detect significant difference in the mean antibody response to A/Voctoria/3/75 between SLE patients and controls, however, the control group had a higher baseline mean antibody titer and higher postvaccination GMTs to A/New Jersey /8/76. The fourth study [7] included only 11 patients with SLE and did not identify a difference between the immune response of the SLE patients and controls.

In a recent study [12], 24 SLE patients received the split virion, inactivated vaccine of A/Beijing/262/95 (H1N1), A/Sydney/05/97 (H3N2), and B/Harbin/07/94. Before vaccination, the percentage of SLE patients with protective levels of HI antibodies and the GMT of HI antibodies were similar to those of age matched healthy women. However, the number of patients with SLE who responded to the vaccine was lower than expected in the general population. Only 58%, 63%, and 38% of the SLE patients responded to A/Beijing/262/95, A/Sydney/05/97, and B/Harbin/07/94 respectively. In addition there was a trend toward a lower response in patients with age $\geq$ 50 years, prednisone dosage $\geq$ 10 mg and use of azathioprine. Similar observation was reported by