Functional disability and antibody response to influenza vaccine in elderly patients in a Dutch nursing home

E J Remarque, H J M Cools, T J Boere, R J van der Klis, N Masurel, G J Ligthart

Section of Gerontology, Department of Pathology, Leiden University Hospital, Building 1 P3-Q, PO Box 9600, 2300 RC Leiden, Netherlands E J Remarque, research fellow T J Boere, medical student R J van der Klis, research technician G J Ligthart, senior investigator

Section of Dutch Nursing Home Medicine, Department of General Practice, Leiden University, PO Box 2088, 2301 RC Leiden H J M Cools, professor

WHO National Influenza Centre for the Netherlands, Department of Virology, Erasmus University Rotterdam, PO Box 1738, 3000 DR Rotterdam, Netherlands N Masurel, professor

Correspondence to: Dr Remarque.

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Serological studies have yielded conflicting results about the antibody response to influenza vaccines in elderly people¹—hence the association of advanced age with declined protection is in question. Differences in subjects' state of health may be one reason for the divergent findings.¹² We therefore investigated the influence of chronic disease, drug treatment, and functional disability on the immune response to influenza vaccine in elderly people.

Subjects, methods, and results

Influenza vaccine was offered to all of the patients in one nursing home in Delft, the Netherlands, who were not terminally ill. A total of 175 patients gave their informed consent and were included in the study. Their mean age was 82 (SD 7), and 133 patients were women. The study was approved by the medical faculty ethics committee. Activities of daily living, illness, and drug treatment at the time of vaccination were recorded from multidisciplinary patient files. Activities of daily living were assessed according to the questionnaire of Katz *et al*^p (six items), with higher scores indicating greater dependency (bottom third 0-6, middle third 7-9, and top third 10-12 points). The mean score was 8 (3).

The vaccine for the 1990-1 season (Influvac whole virus, Solvay-Duphar, the Netherlands) contained A/ Taiwan/1/86 (H1N1) and A/Guizhou/54/89 (H3N2), both with 15 µg haemagglutinin, and B/Beijing/1/87 and B/Yamagata/16/88, both with 10 µg haemagglutinin. The vaccine was given intramuscularly in the deltoid region. A blood sample was taken just before vaccination and a mean of 21 days (range 19-23) later. Titres of IgG antibody against the vaccine strains were determined by enzyme linked immunosorbent assay (ELISA) as described previously.4 To obtain normality, antibody titres were \log_2 transformed for analysis. Postvaccination titres were analysed by forward stepwise multiple regression with prevaccination titre, Katz score, age, sex, ward (psychogeriatric or medical), vaccination against influenza in the previous two years, illness, and drug treatment as explanatory

variables. Explanatory variables that were significant for at least one of the influenza strains were included in the final regression model.

Katz score was inversely correlated with postvaccination titre for all strains (table 1). After vaccination patients with Katz scores in the top third had about half the antibody titre of patients with Katz scores in the bottom third. Prevaccination titres correlated with postvaccination titres for all strains under investigation. Men had higher postvaccination titres, but this was significant only for the A/Guizhou strain. Patients with cardiovascular or pulmonary disease had lower postvaccination titres for B/Beijing. Titres of influenza specific IgG increased significantly in all patients, but they were not optimal in functionally disabled patients.

Comment

Although the increase in antibody titres was not optimal in functionally disabled patients, this should not be a reason for not vaccinating them as the rise that does occur indicates a reduced susceptibility to influenza.⁵ Because functionally disabled elderly patients have decreased immune responses to influenza vaccine, the risk of influenza infections is expected to be higher. These patients have poor health and therefore the risk of secondary complications is probably higher. Thus, in the event of an influenza A epidemic, these patients could receive antiviral chemoprophylaxis.

The association between functional disability and lower immune responses to influenza vaccine is in agreement with Gross *et al*, who used the chronic health evaluation scale.² In elderly patients with long term illness they found a lower immune response only to an antigenically new vaccine strain,² whereas we consistently found correlations between Katz score and all of the vaccine strains investigated.

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- Beyer WEP, Palache AM, Baljet M, Masurel N. Antibody induction by influenza vaccines in the elderly: a review of the literature. *Vaccine* 1989;7:385-94.
- 2 Gross PA, Quinnan GV, Weksler ME, Setia U, Douglas RG. Relation of chronic disease and immune response to influenza vaccine in the elderly. *Vaccine* 1980:7:301-8.
- Katz S, Downs TD, Cash HR, Grotz RC. Progress in the development of the index of ADL. Gerontologist 1970;10:20-30.
 Remarque EJ, van Beek WCA, Ligthart GJ, Borst RJA, Nagelkerken L,
- 4 Remarque EJ, van Beek WCA, Ligthart GJ, Borst RJA, Nagelkerken L, Palache AM, et al. Improvement of the immunoglobulin subclass response to influenza vaccine in elderly nursing-home residents by the use of high-dose vaccines. Vaccine 1993;11:649-54.
- 5 Potter CW, Oxford JS. Determinants of immunity to influenza in man. Br Med Bull 1979;35:69-75.

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Table 1—Effects of significant explanatory variables* on postvaccination titre in 175 elderly patients (stepwise multiple regression analysis)†

Explanatory variable	Effect on postvaccination titre			
	A/Taiwan	A/Guizhou	B/Beijing	B/Yamagata
Prevaccination titre	1.58 (1.47 to 1.71)	1.50 (1.40 to 1.61)	1.66 (1.55 to 1.78)	1.69 (1.56 to 1.82)
Katz score	0.94 (0.90 to 0.97)	0.94 (0.90 to 0.97)	0.94 (0.91 to 0.98)	0.95 (0.91 to 0.98)
Male sex	1.27 (0.97 to 1.66)	1.33 (1.02 to 1.72)	1.17 (0.93 to 1.48)	1.19 (0.95 to 1.49)
Cardiovascular and pulmonary disease	1.09 (0.85 to 1.41)	0.84 (0.66 to 1.08)	0.79 (0.63 to 0.996)	0.85 (0.68 to 1.07)
Previous influenza vaccination	0-81 (0-65 to 1-01)	0.81 (0.66 to 1.01)	0.89 (0.73 to 1.09)	0.93 (0.76 to 1.14)

*Expressed as 2^β of estimate from regression analysis, where β is estimate. Figures in parentheses are 95% confidence intervals. †Regression model was: IgG day 21=constant×pe^{loglog day} 0×ke^{Kat} ^{score}×ge^{male sex}×cpe^{cardiovascular} ^{and} ^{pulmonary} disease×pve^{previous} ^{vacchation} where pe=effect of prevaccination titre, ke=effect of Katz score, ge=effect of sex, cpe=effect of cardiovascular and pulmonary disease, and pve=effect of previous vaccination given in table 1. Male sex, cardiovascular and pulmonary disease, and previous vaccination were dummy variables coded as 1 for presence and 0 for absence.