Serological response to influenza vaccination and nutritional and functional status of patients in geriatric medical long-term care

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Abstract

Introduction: in the UK the Department of Health recommends influenza vaccination for elderly people resident in institutional care. However, the efficacy of vaccination may be reduced in very frail elderly people with functional impairment, undernutrition and multiple pathologies. Nutritional and functional status is claimed to affect vaccine responses in healthy elderly subjects. We wished to determine if a relationship could be seen between nutritional and functional status and seroconversion in patients receiving long-term care.

Methods: all patients in geriatric medical long-term care were offered vaccine. Consenting patients had pre- and post-vaccine serology measured using single radial haemolysis. Anthropometry was measured to enable body mass index (BMI) to be calculated. Functional independence was assessed using the 20-point Barthel index.

Results: of 260 patients who received influenza vaccine, 137 (36 male, 101 female) consented to venesection for serology and thus form the study population. Mean age was 82 years (SD 7.9). The median Barthel score was 3/20 and the mean BMI was 21.6 (SD 4.6, range 13–36.2). Antibodies to influenza A were undetectable both pre- and post-vaccination in 63/137 patients. In 49 patients the antibody titre rose after vaccination and 25 had detectable antibody titres pre-vaccination which failed to rise post-vaccine. There were no significant associations between post-vaccination influenza antibody responses and BMI, Barthel score or age.

Conclusion: frail elderly patients in geriatric medical long-term care had a poor antibody response to influenza vaccination. Within this group, serological responses could not be predicted by nutritional or functional status.

Keywords: aged, body mass index, long-term care, influenza vaccine, serology

Introduction

Influenza vaccination is recommended by the Department of Health in the UK for frail elderly patients in institutional care [1]. However, the efficacy of vaccination in this group has been questioned. Trials on elderly patients (mainly nursing home residents) in the USA report low seroconversion rates at around 25% [2–4]. Residents of geriatric long-term-care wards in the UK are very frail and dependent [5]. Up to 50% of these patients are undernourished [6], chronic illness is common and many have impaired functional capacity; all of which are associated with impaired immune function [7–9].

Improved nutritional status is associated with an enhanced antibody response to influenza vaccination [10]. We wished to determine whether nutritional status is related to serological response to influenza A and B virus vaccines in frail, institutionalized elderly patients.

Patients and methods

We studied prospectively 268 elderly long-term-care patients, resident in three National Health Service (NHS) sites (11 wards) in the south of Glasgow during the winter of 1994–95. All these patients had been designated as requiring ongoing NHS care and all were
taking part in a larger study of the effects of influenza vaccination of health care workers on the mortality of geriatric long-term-care patients throughout Glasgow [11]. As a separate pre-specified study, we examined serological responses to influenza vaccine in a sub-group of participating geriatric medical long-term-care sites. The study was approved by the Greater Glasgow Health Board Care of the Elderly Unit ethics committee.

Serology
All patients were offered influenza vaccine in October 1994. Consenting patients had 10 ml of clotted blood taken for baseline serology before immunization and a further sample taken 6 weeks after vaccination. Serum antibodies for influenza A and B were measured using single radial haemolysis (SRH). A rise in antibody titre to influenza vaccine was considered significant at or above a twofold increase in haemolysis zone [12].

Nutritional and functional status
During that 6-week period, consenting patients had weight measured in night clothes using Seca portable scales (coefficient of variation 0.3%), and heel–shin length measured in centimetres by two trained observers who were blinded to serology results. Predicted height and body mass index (BMI) were then calculated using standard equations [13, 14]. Nutritional status was defined by percentiles of BMI which were taken from Burr's percentile categories for elderly people [15]. Functional independence was recorded using the 20-point Barthel activities of daily living index.

Statistics
Statistical analysis was performed using the SPSS computer software package. BMI percentiles and serological responses were grouped and compared by \( \chi^2 \) analysis and ANOVA. Correlation coefficients and multiple regression analysis was performed considering vaccine response, BMI, Barthel total score and age. Results were accepted as statistically significant at the 5% level of probability.

Results
Of 268 patients (200 women) offered vaccine, 260 accepted. A total of 137 consented to venepuncture on two occasions and thus have baseline and final serology for consideration. The mean age of the vaccinated population was 83 years. The patient group who consented to venepuncture for serology were significantly less dependent, better nourished and had less deaths at the end of follow-up surveillance (5 months post-vaccine) than those who refused (Table 1).

The following results refer to the 137 patients who consented to both venepuncture and anthropometry. The mean age of this group was 82 years (range 59–101). The median Barthel score was 3/20.

Nutritional status
The mean BMI of the study group was 21.6 (SD 4.6, range 13–36.2): 46.5% of patients were below the 25th percentile and 14% below the 5th. This is similar to findings in previous studies of the nutritional status of elderly patients receiving long-term care [6, 16].

Serological response to vaccination
The serum antibody response measured by SRH to influenza vaccination is shown in Table 2. Patients were divided into three groups according to their antibody responses to vaccine for influenza A and B. Serum antibodies to influenza A were undetectable both before and after vaccination in 63 (45.9%) of the 137 patients; a further 25 (18.2%) had detectable antibody levels pre-vaccination with no rise after vaccination. Only 49 (35.7%) had a rise after receiving vaccine. Similar results were found for influenza B.

Table 1. Comparison of Barthel scores, body mass index (BMI) and deaths at the end of 5-month follow-up, in those consenting to vena puncture for serology and those not consenting

<table>
<thead>
<tr>
<th>Value, by venesection decision</th>
<th>Consented (n = 137)</th>
<th>Refused (n = 131)</th>
<th>Total (n = 268)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (and SD)</td>
<td>82 (8)</td>
<td>85 (8)</td>
<td>83 (8)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>56/101</td>
<td>32/99</td>
<td>68/200</td>
</tr>
<tr>
<td>Mean BMI (SD)</td>
<td>21.2 (4.4)</td>
<td>19.8 (4.8)</td>
<td>21 (4.7)</td>
</tr>
<tr>
<td>Mean total Barthel score (SD)</td>
<td>4.7 (4.5)</td>
<td>3.6 (3.8)</td>
<td>4.2 (4.1)</td>
</tr>
<tr>
<td>No. of deaths at the end of follow-up</td>
<td>10</td>
<td>27*</td>
<td>37</td>
</tr>
</tbody>
</table>

*Levene’s test for equality of variance \( P = 0.438, 95\% CI \) for difference −2.691 to −0.191

*Mann–Whitney U test \( P = 0.0024.\)

*\( \chi^2 = 9.97152, P = 0.0015.\)
with 30 (21.5%) of the 137 subjects having a rise in antibody levels to influenza B after vaccination. Of these 30, only 12 also had a rise in antibody titre to influenza A. Overall, 66 out of 137 (48.2%) had a rise in antibody titres to either influenza A or B.

Those with detectable baseline titres to influenza A, but no post-vaccine increase, had a higher mean BMI (ANOVA $F=3.12$, $P<0.05$).

There were no other significant differences in mean Barthel scores or BMI.

Figure 1 shows the scatter of serological response to influenza A vaccine at 6 weeks by BMI. There was no relationship between the BMI of the patients and the post-vaccine titre. The linear correlation coefficient was $R=0.02$, $P=0.81$.

Those patients who had detectable post-vaccine titres by SRH to influenza A and B were compared with those who had no detectable titres post-vaccine using multiple regression analysis. None of the factors considered (total Barthel score, age and BMI) had any significant association with influenza A (multiple $R=0.15$, $F=0.68$, $P=0.61$), or influenza B titres (multiple $R=0.11$, $F=0.36$, $P=0.83$).

Discussion
Patients resident in NHS geriatric long-term care in the UK are a very frail and disabled group, with a high mortality rate (50% per annum). They are frequently undernourished, with many pathologies and multiple medication usage [5]. Approximately 50% of the patients in the study were undernourished (BMI <25th percentile) compared with a age–sex-matched population [15]. We have measured nutritional status by anthropometry and have not considered other supposed markers of nutritional status, such as serum albumin concentration. In sick patients, biochemical markers reflect illness rather than nutritional status [17], and these were inappropriate for this study. The level of undernutrition is similar to other studies of nutritional status on similar groups of patients [6, 16].

We have used SRH as the method for quantifying antibody response. This has a higher sensitivity and specificity than complement-fixation tests or haemagglutinin inhibition [12]. Seroconversion rates were low in the study population, with 37.5% having antibodies to influenza A, 21.5% to influenza B and only 12 subjects (11.4%) having antibodies to both. This confirms previous studies in similar patient groups [3, 4]. If it were possible to predict which of these patients were likely to seroconvert, this could have practical implications, such as targeting vaccination to those likely to respond or considering additional means of protection against influenza infection if

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**Table 2. Serum antibody levels to influenza A and B and age, body mass index (BMI) and Barthel score**

<table>
<thead>
<tr>
<th></th>
<th>Number (%)</th>
<th>Mean value (and SD)</th>
<th>$F$</th>
<th>$P$</th>
<th>$95%$ CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Influenza A titre</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre- and post-vaccine = 0</td>
<td>63 (45.9)</td>
<td>82.3 (7.9)</td>
<td>4.6 (4.5)</td>
<td>21.0 (4.8)</td>
<td></td>
</tr>
<tr>
<td>Post-vaccine &gt; baseline</td>
<td>49 (35.8)</td>
<td>82.7 (8.3)</td>
<td>5.1 (4.5)</td>
<td>20.4 (3.7)</td>
<td></td>
</tr>
<tr>
<td>Post-vaccine ≤ elevated baseline</td>
<td>25 (18.2)</td>
<td>80.8 (7.1)</td>
<td>4.2 (3.1)</td>
<td>23.1 (4.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Statistics</strong></td>
<td></td>
<td></td>
<td>$F=0.61$</td>
<td>$P=0.45$</td>
<td>$F=3.12$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$P=0.55$</td>
<td>$P=0.05$</td>
<td>$P&lt;0.05$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95% CI $-2.2$ to 1.2$</td>
<td>95% CI $-1.1$ to 2.2$</td>
<td></td>
</tr>
<tr>
<td><strong>Influenza B titre</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre- and post-vaccine = 0</td>
<td>85 (62.0)</td>
<td>85.0 (8.0)</td>
<td>4.7 (4.0)</td>
<td>21.2 (3.9)</td>
<td></td>
</tr>
<tr>
<td>Post-vaccine &gt; baseline</td>
<td>30 (21.9)</td>
<td>81.2 (8.0)</td>
<td>4.8 (5.1)</td>
<td>20.9 (4.4)</td>
<td></td>
</tr>
<tr>
<td>Post-vaccine ≤ elevated baseline</td>
<td>22 (16.1)</td>
<td>81.4 (7.1)</td>
<td>4.5 (4.2)</td>
<td>21.6 (6.2)</td>
<td></td>
</tr>
<tr>
<td><strong>Statistics</strong></td>
<td></td>
<td></td>
<td>$F=0.17$</td>
<td>$F=0.05$</td>
<td>$F=0.14$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$P=0.92$</td>
<td>$P=0.97$</td>
<td>$P=0.87$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95% CI $-1.9$ to 2.2$</td>
<td>95% CI $-1.5$ to 2.0$</td>
<td></td>
</tr>
</tbody>
</table>

$^{a}$ANOVA has been used for the other characteristics.

$^{b}$95% confidence intervals for equality of means $t$test.

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**Figure 1.** Relationship between body mass index (BMI) and post-vaccine titre to influenza A using single radial haemolysis.
seroconversion was unlikely. This could have implications for vaccination policy, as asymptomatic influenza infection is prevalent in hospital staff and vaccination of staff may prove to be a more efficient way to reduce patient mortality [11, 18, 19]. Unfortunately, we have been unable to demonstrate a simple clinical means of predicting those likely to seroconvert since in our population there was no clear relationship between BMI, Barthel score, age and seroconversion.

There was a significantly higher BMI value in those patients with elevated baseline titres to influenza A but no post-vaccine response. Antibody titres which are high at baseline could represent previous exposure to influenza infection, previous vaccination or both. SRH can detect antibodies present for up to 12 months, and 90% of the patients with high baseline serology had been resident in long-term care long enough to have been vaccinated in one or more previous years. As the uptake of influenza vaccine in the unit has been over of 95% for the previous 3 years, the higher baseline antibody titres may represent the effect of repeated immune stimulation. This group has survived in hospital long-term care for several years and appear to be fitter and better nourished.

In contrast, those patients of the original cohort who did not consent to venesection had a greater mortality at 5 months than the study population. This group were more frail than the study population, as reflected by an increased dependency and greater undernourishment. As both groups were vaccinated, this increase in deaths is most likely a further reflection of their increased frailty. It may be that in many of the open non-randomized studies of elderly patients being offered influenza vaccine in nursing homes, those who consent to study participation are a less frail group than those who do not and that differences in mortality seen in such studies cannot be attributed solely to vaccine effect [20–22].

The lack of an association between BMI or Barthel score with serological response to vaccination is in contrast to that reported elsewhere. A randomized trial of nutritional supplementation in community-dwelling elderly subjects reported improvements in nutritional status in addition to better seroconversion rates and higher post-vaccine titres in the group given supplements [10]. Likewise, an association between functional independence and improved serological response to vaccination was reported in residents vaccinated in a nursing home in the Netherlands [9]. In both of these studies the patients were less frail and the seroconversion rates higher than in our patient group. Clinical effects of vaccination in healthier elderly people does show benefits in terms of reductions in documented flu-like illnesses, pneumonia and hospitalization in addition to high overall seroconversion rates [23–25]. Vaccination of our frail elderly patients was not associated with any reduction in mortality—perhaps due to poor serological responses [11].

Conclusion

Influenza vaccination of patients in NHS geriatric medical long-term care in Glasgow was associated with a rise in serum antibody levels to influenza A in only 35.7% of patients. There was no relationship between BMI or 20-point Barthel activities of daily living score and serological response. Within this group of frail elderly patients, serological response to vaccination could not be predicted by nutritional or functional status.

Key points

- Elderly residents of long-term-care wards were highly physically dependent, with a median Barthel score of 3/20. They were also frequently under-nourished (46.5% below the 25th percentile for BMI).
- It was common for subjects not to seroconvert after influenza vaccination (35.7% showed a serological response for influenza A and 21.5% for influenza B).
- Seroconversion to influenza vaccine could not be predicted by BMI or Barthel activities of daily living score.

Acknowledgement

This study was supported by the Greater Glasgow Care for the Elderly Unit. Medeva plc provided the influenza vaccine.

References

BMI and influenza vaccine response


Received 29 December 1997; accepted 9 February 1998

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Grandfather walks his grandchild to put it to sleep. © Sally and Richard Greenhill.