Response to diphtheria booster vaccination in healthy adults: vaccine trial

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The diphtheria epidemic in eastern Europe and the worldwide increase in diphtheria morbidity have sparked discussion on whether people in western Europe are adequately protected. In western Europe, the effectiveness of long term protection afforded by immunisation programmes is under debate.

In Belgium, the national immunisation programme against diphtheria was introduced in 1959. Vaccination was recommended for all infants, and a catch up programme for children up to the age of 15 years was also instituted. The programme comprises four doses of toxoid, given at age 3, 4, 5, and 15 months. The vaccine is a combination of diphtheria, pertussis, and tetanus toxins, and 95% of children are covered. We evaluated the effectiveness of the current recommended adult booster immunisation of a single, low dose diphtheria vaccine.

Subjects, methods, and results

Altogether 176 volunteers were recruited from the employees of a company in Flanders in 1997. We focused on recruiting subjects aged 33-50 years as they had been the first to be vaccinated in the national programme and we expected to find a high proportion of subjects who were susceptible to infection in this group. After being screened and answering questions about previous vaccinations, subjects gave a blood sample and received an intramuscular dose of vaccine in the deltoid region (T edivax pro adulto (> 4 IU of diphtheria toxin and > 40 IU of tetanus toxin); Smith-Kline Beecham Biologicals, Belgium). A follow up programme was instituted. The programme comprises four doses of toxoid, given at age 3, 4, 5, and 15 months. The vaccine is a combination of diphtheria, pertussis, and tetanus toxins, and 95% of children are covered. We evaluated the effectiveness of the current recommended adult booster immunisation of a single, low dose diphtheria vaccine.

Antitoxin titres of < 0.01 IU/ml (class 1) indicate susceptibility to diphtheria, whereas titres ≥0.1 IU/ml (class 3) afford protection. At titres between ≥0.01 IU/ml and < 0.1 IU/ml (class 2), protection is of limited duration.

Statistical analysis was performed with SPSS for Windows 9.0. Differences in age and weight in the groups were compared by analysis of variance and t test; the χ2 test was used to compare gender differences.

The study population comprised 96 men and 80 women with a mean (SD) age of 41.2 (4.2) years. As a result of the booster vaccination, 76% obtained protection (class 3), 5% had limited protection (class 2), and 19% remained susceptible (class 1) (table). Age was the only significant factor determining the serological class before booster vaccination (F = 5.383, df = 2, P < 0.005) and after it (F = 7.377, df = 2, P < 0.001). Weight and sex seemed to have no effect. All subjects whose titres were in class 2 before the booster achieved class 3 status afterwards. Nine (13%) subjects in class 1 moved to class 2 and 27 (39%) to class 3 after the booster; the rest stayed in class 1 (48%). The 42 subjects who remained in classes 1 or 2 after booster vaccination were significantly older than the subjects who moved from class 1 or 2 to class 3 (43.3 (4.1) years vs 41.1 (4.3) years; t = 2.579, df = 98, P < 0.05).

Comment

The single adult diphtheria booster is insufficient to obtain adequate protection. In published reports, at least 70% of the adults who receive a booster dose of diphtheria toxoid achieve protection; in our study, 76% did: this means that 24% of our subjects did not respond adequately, whereas 42% of those who are not protected beforehand do not obtain full protection.

Age is a main determinant of long term protection against diphtheria induced by vaccination. However, the antitoxin titres achieved by some of the younger people who had been vaccinated in childhood were not satisfactory. Because of this, public health recommendations based on age cannot be formulated.

Contributors: AV undertook statistical analysis, and wrote the paper. PVD designed and coordinated this study and edited the paper. EJ carried out the blood sampling and data collection. HJ was responsible for the laboratory analysis. PVD is guarantor.

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Age and antitoxin titre class before and after booster immunisation against diphtheria. Values are numbers (percentages) of subjects

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>No of subjects</th>
<th>Before booster</th>
<th>After booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>79</td>
<td>Class 1 (21 (31))</td>
<td>Class 2 (18 (28))</td>
</tr>
<tr>
<td>40-44</td>
<td>56</td>
<td>25 (38)</td>
<td>5 (16)</td>
</tr>
<tr>
<td>≥45</td>
<td>41</td>
<td>23 (33)</td>
<td>8 (26)</td>
</tr>
<tr>
<td>Total</td>
<td>176</td>
<td>69 (39)</td>
<td>31 (18)</td>
</tr>
</tbody>
</table>

Class 1=susceptibility to infection; class 2=limited protection; class 3=protection.