Influenza Vaccination: Reduction in Hospitalizations and Death Rates among Members of “Maccabi Healthcare Services” during the 2000–2001 Influenza Season

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Abstract

Background: Upper respiratory tract illnesses have been associated with an increased risk of morbidity and mortality.

Objective: To assess the influence of vaccination against influenza on the risk of hospitalization in internal medicine and geriatric wards, and the risk of death from all causes during the 2000–2001 influenza season.

Methods: A historical cohort study was conducted using computerized general practitioner records on patients aged 65 years and above, members of “Maccabi Healthcare Services” – the second largest health maintenance organization in Israel with 1.6 million members. The patients were divided into high and low risk groups corresponding to coexisting conditions, and were studied. Administrative and clinical data were used to evaluate outcomes.

Results: Of the 84,613 subjects in the cohort 42.8% were immunized. At baseline, vaccinated subjects were sicker and had higher rates of coexisting conditions than unvaccinated subjects. Vaccination against influenza was associated with a 30% reduction in hospitalization rates and 70% in mortality rates in the high risk group. The NNT (number needed to treat) measured to prevent one hospitalization was 53.2 (28.2 in the high risk group and 100.4 in the low risk group). When referring to length of hospitalization, one vaccine was needed to prevent 3.3 days of hospitalization among the high risk group. Analyses according to age and the presence or absence of major medical conditions at baseline revealed similar findings across all subgroups.

Conclusions: In the elderly, vaccination against influenza is associated with a reduction in both the total risk of hospitalization and in the risk of death from all causes during the influenza season. These findings compel the rationale to increase compliance with recommendations for annual influenza vaccination among the elderly.
Statistical analysis
Analyses were conducted in subgroups according to age (65–74, 75–84, and 85 years or older) and risk. High risk was defined by one of the following coexisting conditions: heart disease, lung disease, diabetes or endocrine disorders, renal disease, stroke or dementia, vasculitis or rheumatologic disease, or cancer. Low risk was defined by the absence of any of these conditions.

Gender proportions and prevalence rates were compared using the chi-square test corrected for continuity, while mean ages were compared using the standard Student t-test. Significance values and 95% confidence intervals were calculated using Compare2 version 1.11 (copyright JH Abramson 2000–2002).

The summer months (June through September) after the influenza season were selected as a control period. We assessed the effect of vaccination on the risk of hospitalization during these months, a period during which influenza was not circulating and at a time when the vaccination was expected to provide minimal benefit.

Results
There were 84,613 subjects in the cohort. The crude compliance rate with influenza vaccination was 42.8%. At baseline, vaccinated subjects presented a significantly (P < 0.001) higher prevalence rate of coexisting conditions (Table 1).

During the influenza season, there were 2,380 and 3,585 hospitalizations and 238 and 872 deaths among high risk vaccinated and unvaccinated subjects respectively, presenting a reduction of 30% in hospitalization rates (relative risk 0.70, 95% confidence interval 0.67–0.73) and 71.2% in death rates (RR 0.29, 95%CI 0.25–0.33). There were 276 and 807 hospitalizations and 31 and 180 deaths among low risk vaccinated and unvaccinated subjects respectively, yielding a reduction of 22% in hospitalization rates (RR 0.78, 95%CI 0.68–0.89) and 60.6% in death rates (RR 0.39, 95%CI 0.27–0.58). (Table 2)

Estimates of vaccine effectiveness were similar among the age subgroups (Table 3). The number needed to treat (i.e., vaccinate) to prevent one hospitalization was 53.2 (28.2 in the high risk group and 100.4 in the low risk group). When referring to length of hospitalization, one vaccine is needed to prevent 1 day of hospitalization among the high risk group.

During the summer following the influenza season, which was chosen as a control period, high risk vaccinated subjects had similar hospitalization rates compared to controls (6.7% vs. 7.1%) (RR 0.94, 95%CI 0.89–1.00), while among the low risk group there were substantial differences (2.8% vs. 3.42%) (RR 0.83, 95%CI 0.71–0.97).

Discussion
Several previous observational studies suggested vaccination-associated reductions of 20–40% in the risk of hospitalization for pneumonia or influenza [5–14]. Nichol and co-workers [4] reported a 29–32% reduction in the risk of hospitalization for pneumonia or influenza, basing the results on one of the largest cohorts ever used to evaluate the effectiveness of the vaccine. Some observational studies reported vaccination-associated reductions of 30–50% in the risk of death from any cause [15–18]. Nichol et al. [4] reported a 48–50% reduction in the risk of death from all causes.

In our study, influenza vaccination in high risk elderly persons was associated with substantial reductions in the risk of hospitalization for any reason in internal medicine and geriatric wards, and death from all causes during the 2000–2001 influenza season, at rates similar to those reported previously. However, we were not able to estimate the effectiveness of vaccine among members of the low risk group due to a selection bias. Moreover, some of the benefits attributed to influenza vaccination may be due to pneumococcal vaccination. Pneumococcal vaccinations are usually given only once and may be effective for 6 to 10 years. However, pneumococcal vaccination has not been shown consistently to reduce the risk of hospitalization for pneumonia [19].

RR = relative risk
CI = confidence interval

Table 1. Baseline characteristics of subjects in the cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vaccinated subjects</th>
<th>Unvaccinated subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>36,569</td>
<td>48,044</td>
</tr>
<tr>
<td>Age group (yrs) (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–74</td>
<td>60.8</td>
<td>60.1</td>
</tr>
<tr>
<td>75–84</td>
<td>32.2</td>
<td>29.2</td>
</tr>
<tr>
<td>≥85</td>
<td>7.0</td>
<td>10.7</td>
</tr>
<tr>
<td>Mean age ± SD</td>
<td>74.3 ± 7.2</td>
<td>74 ± 6.4</td>
</tr>
</tbody>
</table>

Table 2. Outcome during the influenza season among vaccinated and unvaccinated subjects in high and low risk groups

<table>
<thead>
<tr>
<th>Outcome</th>
<th>High risk group</th>
<th>Low risk group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vaccinated</td>
<td>Unvaccinated</td>
</tr>
<tr>
<td></td>
<td>(n=2,380)</td>
<td>(n=3,585)</td>
</tr>
<tr>
<td>Hospitalization rate</td>
<td>8.25%</td>
<td>11.8%</td>
</tr>
<tr>
<td>Death rate</td>
<td>0.82% (n=238)</td>
<td>2.7% (n=872)</td>
</tr>
</tbody>
</table>

Table 3. Relative risk (and 95%CI) in outcome measures during the influenza season among vaccinated and unvaccinated subjects in high and low risk groups corresponding to age subgroups

<table>
<thead>
<tr>
<th>Outcome</th>
<th>High risk age subgroups</th>
<th>Low risk age subgroups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6–74</td>
<td>75–84</td>
</tr>
<tr>
<td>Reduction in hospitalization rates (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>68.7</td>
<td>71.2</td>
<td>64.8</td>
</tr>
<tr>
<td>Reduction in death rates (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.71</td>
<td>0.76</td>
<td>0.70</td>
</tr>
<tr>
<td>(0.64–0.79)</td>
<td>(0.70–0.82)</td>
<td>(0.65–0.76)</td>
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</table>
The findings of our study support the aim of increasing compliance with recommendations for annual influenza vaccination among the elderly.

References

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The Falklands War: two bald men fighting over a comb.

Gore Vidal (1925– ), American writer and critic, most of whose fiction deals satirically with history and politics.

Capsule

Compugen discovers antisense RNA

Compugen Ltd. announced, at the Molecular Medicine Marketplace conference, the discovery that the transcription of antisense RNAs from the human genome, a phenomenon usually regarded as extremely rare, is surprisingly a fairly common occurrence. Until recently, only tens of genes were believed to have an antisense partner, but Compugen’s scientists have identified at least 1,600 sense/antisense pairs, or 3,200 genes, demonstrating that this phenomenon is far more widespread than previously believed.

‘Our knowledge of natural human antisense transcription sets the stage for new understanding of gene regulation, including double-stranded RNA-mediated gene-silencing pathways such as RNAI. This information on antisense transcription will also provide significant advantages in the design and analysis of functional genomic experiments, as well as for target discovery, protein pathways and antisense drug design,’ stated Compugen.

In the paper being published in Nature Biotechnology, Compugen’s scientists report using their LEADS platform and an ‘Antisensor’ algorithm, designed specifically for detecting genes on opposite DNA strands, to identify 2,667 genomic loci with evidence of transcriptional units on both strands from the 40,000 genes identified in the August 2001 draft human genome sequence and the human expressed sequences (82,289 mRNAs and 3,733,145 ESTs). The experimental work was carried out in Compugen’s laboratories in Tel Aviv, Israel, and the design of the ‘Antisensor’ at Compugen’s facilities in Jamesburg, New Jersey.