Tiotropium improved lung function more than did ipratropium in chronic obstructive pulmonary disease


QUESTION
In patients with stable chronic obstructive pulmonary disease (COPD), what is the long-term effectiveness and safety of tiotropium compared with those of ipratropium?

DESIGN
Randomized (allocation concealed\*), blinded (patient and outcome assessor),* controlled trial with 13 weeks of follow-up.

SETTING
14 centers in the Netherlands.

PATIENTS
288 patients ≥ 40 years of age (mean age 64 y, 83% men) who were current or past smokers with a diagnosis of COPD and stable airways obstruction, an FEV1 < 65% of the predicted normal rate, and a ratio of FEV1 to forced vital capacity (FVC) of < 70%. Exclusion criteria included a history of asthma, allergic rhinitis, or atopy; a recent history of myocardial infarction, heart failure, or cardiac arrhythmia requiring drug treatment; upper respiratory tract infection in the past 6 weeks; and hypersensitivity to anticholinergic drugs. 90% completed all tests.

INTERVENTION
191 patients were assigned to tiotropium, 18 µg once daily, delivered by a dry-powder inhaler system; and 97 were assigned to ipratropium, 40 µg 4 times daily, delivered by a metered-dose inhaler. Each group also received placebo doses of the other treatment.

MAIN OUTCOME MEASURES
Lung function, peak expiratory flow (PEF), use of concomitant salbutamol, and adverse effects.

MAIN RESULTS
Trough, peak, and mean FEV1 response and trough and mean FVC response showed greater improvement with tiotropium than with ipratropium (Table). Morning and evening PEF was consistently better with tiotropium (P < 0.05). Use of concomitant salbutamol was lower in the tiotropium group (P < 0.05). The groups did not differ for adverse effects.

CONCLUSIONS
In patients with chronic obstructive pulmonary disease, tiotropium improved lung function more than did ipratropium. The safety profiles of the 2 drugs were similar.

*See Glossary.
†Information provided by the author.

Tiotropium vs ipratropium at 13 weeks in chronic obstructive pulmonary disease (lung function improvement, in liters, compared with baseline at start of study)‡

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Tiotropium</th>
<th>Ipratropium</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 trough</td>
<td>0.16</td>
<td>0.03</td>
<td>0.13 (0.08 to 0.18)</td>
</tr>
<tr>
<td>FEV1 peak (at 50 d)</td>
<td>0.38</td>
<td>0.30</td>
<td>0.08 (0.02 to 0.15)</td>
</tr>
<tr>
<td>FEV1 mean (over 6 h)</td>
<td>0.26</td>
<td>0.18</td>
<td>0.08 (0.03 to 0.13)</td>
</tr>
<tr>
<td>FVC trough</td>
<td>0.39</td>
<td>0.18</td>
<td>0.21 (0.10 to 0.32)</td>
</tr>
<tr>
<td>FVC mean (at 50 d)</td>
<td>0.62</td>
<td>0.45</td>
<td>0.17 (0.50 to 0.29)</td>
</tr>
</tbody>
</table>

‡FVC = forced vital capacity.

The study by van Noord and colleagues provides important data, showing the superiority of tiotropium (18 µg once/d) over the usual dose of ipratropium (40 µg 4 times/d). Patients were permitted to use many of their own usual medications (including methylxanthines, inhaled steroids, and oral steroids up to 10 mg of prednisone/d) during the course of the trial, showing the effectiveness of tiotropium in a meaningful clinical context. Tiotropium, not yet approved for use in the United States, appears to have great potential in the long-term maintenance therapy of COPD.

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References