The mechanism of action of doxofylline is unrelated to HDAC inhibition, PDE inhibition or adenosine receptor antagonism.

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Abstract

Xanthines such as theophylline have been used in the treatment of lung diseases since the early 1900's, but have a major drawback of a very narrow therapeutic window and many drug/drug interactions.

This means that plasma levels have to be measured regularly and can make the use of theophylline problematic.

With the increasing availability of other classes of drugs for the treatment of respiratory diseases, this has limited the use of xanthines, despite their clear clinical benefit in the treatment of patients with asthma and COPD.

Doxofylline is a xanthine molecule having both bronchodilator and anti-inflammatory activity with an improved therapeutic window over conventional xanthines such as theophylline.

However, the mechanistic basis of this improved therapeutic window is not understood.

The present study has investigated some pharmacological activities of doxofylline in comparison with theophylline. Doxofylline does not directly inhibit any of the known HDAC enzymes, and did not inhibit any PDE enzyme subtypes or act as an antagonist at any of the known adenosine receptors, except for PDE2A(1), and adenosine A(2A) and only at the highest tested concentration (10(-4) M).

These results may explain the improved tolerability profile of doxofylline compared with theophylline.

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Comparative study on the efficacy of tiotropium bromide inhalation and oral doxofylline treatment of moderate to severe stable chronic obstructive pulmonary disease.


Abstract

This study compared the efficacy and safety of tiotropium bromide inhalation powder (spiriva) and doxofylline oral tablet (doxofylline) in the treatment of chronic obstructive pulmonary disease (COPD).

A multi-center, randomized, double-blind, double-dummy, parallel-controlled study involved 127 eligible stable moderate to severe COPD patients treated with inhaled tiotropium dry powder (18 µg/day) or oral doxofylline tablets (0.2 g/time, 2 times a day) for 12 and 24 weeks.

Before and after treatment for 12 weeks and 24 weeks, respectively, pulmonary function, 6-min walking distance and dyspnea index were recorded.

The results showed that in both tiotropium group and doxofylline groups, after 12-week treatment, FEV(1), FEV(1)/FVC% and 6-min walk distance were significantly higher than those before the medication, while dyspnea index decreased as compared with that before treatment.

After 24-week treatment, a slight improvement in the measures was observed as compared with that of 12-weeks treatment, but the difference was not statistically significant.

With both 12-week and 24-week treatment, the effect of tiotropium was slightly better than that of doxofylline tablets, with the difference being statistically insignificant.

The major adverse events in the tiotropium group and doxofylline group were observed in 9 cases (9.9%) and 12 cases (12.9%), respectively, and no statistically significant difference was found between them.

We are led to conclude that both tiotropium at 18 µg a day and doxofylline tablets at 0.2 g/day (two times a day) are effective and safe for the treatment of COPD.

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