LETTERS TO THE EDITOR

Effects of Anticholinergics and β -agonists in COPD

To the Editor:—In a meta-analysis, Dr. Saltpeter and her colleagues reported an association between maintenance use of inhaled β 2-agonists for COPD and increased risk of respiratory death.¹ This result is highly dependent on a single multicenter study of Calverley et al.,^{2,3} which compared therapeutic outcomes and adverse events in 1,022 patients with COPD who were randomized to receive treatment for 12 months with formoterol, budesonide, the combination of these 2 inhaled drugs, or placebo. The numbers of deaths in these four treatment groups were 14, 6, 5, and 5, respectively.³ Calverley et al. reported that “most of the deaths were events related to COPD and only a few were related to cardiovascular events.” However, no notable increase in other respiratory adverse events was associated with formoterol used alone or in combination with budesonide compared to the other 2 treatment regimens. If formoterol caused or contributed to excess respiratory deaths in this study, the mechanism might have been an idiosyncratic reaction, heretofore unrecognized, that may not occur in patients who receive formoterol in combination with budesonide. The idiosyncratic reaction might not be shared by other β 2-agonists. Thus, additional information regarding the underlying disease severity and the timing and apparent cause of death during the study by Calverley et al. would be of considerable interest.

Calverley et al.⁴ have also recently published a multicenter study that reported outcomes for 1,465 COPD patients who received either salmeterol, fluticasone, the combination of

the 2, or placebo for 12 months. Perhaps because deaths were not reported as an adverse outcome in this study, it was not included in the meta-analysis performed by Saltpeter and colleagues. If available, information on deaths during this study would also be of interest.

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