Combination treatment with inhaled corticosteroids and long-acting β₂-agonists decreases exacerbations and improves quality of life in patients with COPD; however; a potential concern is an increased risk of pneumonia. Although the TORCH and INSPIRE studies have shown the risk of pneumonia to increase with fluticasone/salmeterol versus placebo and tiotropium, there has been no direct comparison of fixed combinations of inhaled corticosteroids/long-acting β₂-agonists.

The PATHOS study compared the occurrences of pneumonia and pneumonia-related events in patients with COPD treated with either fluticasone/salmeterol (Seretide) or budesonide/formoterol (Symbicort). This was an observational retrospective cohort study matched for propensity score comparing 2734 patients in each group. Two thousand one hundred and fifteen patients (39%) had at least one diagnosis of pneumonia during the study period. Compared with the budesonide/formoterol group, the rate of pneumonia and the rate of admission to hospital related to pneumonia were 73% and 74% higher in the fluticasone/salmeterol treatment group, giving a rate ratio of 1.73 and 1.74, respectively. When comparing fluticasone/salmeterol with budesonide/formoterol, the pneumonia event rate per 100 patient years was 11.0 versus 6.4. There were 97 deaths from pneumonia in the fluticasone/salmeterol group compared with 52 deaths in the budesonide/formoterol group, corresponding to a 76% increase in mortality. Furthermore, there was no dose–response relation with regard to risk of pneumonia with the two treatments, indicating that differences were due to the class of inhaled corticosteroids/long-acting β₂-agonists and not the dose.

This study shows that the risks of pneumonia and pneumonia-related events are higher with fluticasone/salmeterol than with budesonide/formoterol in patients with COPD. This represents an intraclass difference between fixed combinations of inhaled corticosteroids/long-acting β₂-agonists. Such differences may be related to differences in the immunosuppressant potencies between budesonide and fluticasone. Long-term randomised controlled trials would be beneficial to assess the extent of such intraclass differences put in context with the benefits of such regimens in preventing exacerbations.


Avais Jabbar
Correspondence to Dr Avais Jabbar, Department of General Medicine, Northampton General Hospital NHS Trust, Northampton NN1 5BD, UK; ajabbar1@mhs.net