

Dexamethasone for pneumonia

Steroids down-regulate genes responsible for the production of pro-inflammatory cytokines and up-regulate genes responsible for producing anti-inflammatory cytokines. In patients with pneumonia they could promote quicker resolution of the pulmonary and systemic inflammatory response. Researchers in the Netherlands, publishing in the *Lancet*, have shown that adding dexamethasone to the treatment of patients with community-acquired pneumonia leads to earlier improvement and hospital discharge.

The two-centre trial included 304 patients (mean age 64, 57% men) with community-acquired pneumonia who were randomised to i.v. dexamethasone 5 mg daily, or placebo, for 4 days after starting antibiotic treatment. About half of the patients had severe pneumonia. The median length of hospital stay was 6.5 days (dexamethasone) vs 7.5 days (placebo), a significant difference. Hyperglycaemia occurred in 44% vs 23%. In-hospital mortality was 5% in each group and 30-day mortality 6% vs 7%. Levels of C-reactive protein and interleukin-6 fell more quickly on dexamethasone. Steroid treatment may promote earlier recovery in patients with community-acquired pneumonia. *Lancet* commentators suggest that future trials should assess the value of giving steroids for longer periods to promote full resolution.

Increased mortality with tiotropium mist inhaler

A meta-analysis of 17 trials showed an increased risk of major cardiovascular events with the use of inhaled anticholinergics. Now a systematic review and meta-analysis of five placebo-controlled trials (6522 patients) has shown an increased risk of death associated with use of a tiotropium mist inhaler (Respimat Soft Mist Inhaler) among patients with chronic obstructive pulmonary disease (COPD).

Overall, use of either a 5 µg dose or a 10 µg dose of inhaled tiotropium was associated with a 52% increase in risk of death (2.4% vs 1.7%). The 5 µg dose (the usual dose) was associated with a 46% increase in risk and the 10 µg dose with a 2.15-fold increase. The numbers-needed-to-treat were 110 (5 or 10 µg), 124 (5 µg), and 50 (10 µg). An editorialist suggests that the powder inhaler (Handihaler) may be safer. A trial comparing the two inhalers is in progress. The tiotropium mist inhaler may be associated with increased mortality in patients with COPD. The research was published in the *BMJ*.

Placebo effects in patients with asthma

Asthma is a good subject for the study of placebo effects because short-term responses can be measured easily. Researchers in the USA have studied lung function and

subjective responses after a variety of active and non-active interventions.

The study, published in the *New England Journal of Medicine* included 46 patients with mild-to-moderate asthma and an FEV1 response to inhaled salbutamol, and 39 completed the course of investigations. There were four interventions: inhaled salbutamol (albuterol), inhaled placebo, sham acupuncture, or control (no intervention). Using a block design, each subject received a different one of these interventions in random order on each of four visits with an interval of 307 days between visits. This procedure was repeated twice to a total of 12 visits per subject (three blocks, each of four visits). The average increase in FEV1 was 20% with salbutamol and around 7% with the placebo inhaler, sham acupuncture, or control groups. Subjective responses were assessed by asking subjects to assess their own improvement on a scale of 0–10 (0 = no improvement, 10 = complete improvement). The average subjective improvement was 50% (salbutamol), 45% (placebo inhaler), 46% (sham acupuncture), and 21% (controls). All three interventions were followed by significantly greater subjective improvement than in the control group. The placebo interventions had no objective effect but subjectively assessed responses were similar with active (salbutamol) treatment and the two placebo treatments and all three were superior to no treatment (controls).

Beta-blockers in COPD

Beta-blockers have been regarded as contraindicated in chronic obstructive pulmonary disease (COPD) because of the risk of inducing bronchospasm. Now a study of Scottish data, published in the *BMJ*, has shown that beta-blocker treatment may be beneficial.

The retrospective cohort study included 5977 patients with COPD. Beta-blocker use was associated with a 22% reduction in all-cause mortality overall and reduced mortality at all severities of COPD as judged by stage of treatment. Compared with patients who were treated only with inhaled short-acting β-agonists or antimuscarinics, increasing intensity of treatment was associated with a 57% reduction in overall mortality and the addition of a beta-blocker increased this reduction to 72%. Beta-blockers did not reduce pulmonary function when given with a long-acting β-agonist or a long-acting antimuscarinic.

Why beta-blockers should have this effect is unclear. Many patients with COPD also have coronary disease and beta-blockers are beneficial for patients with coronary disease but that does not explain all of the benefit in COPD. It is suggested that in COPD long-term beta-blocker treatment may be bronchoprotective, anti-inflammatory, and mucus-resolving. Prospective trials are needed before beta-blocker therapy can be accepted as standard in COPD.