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This series is coordinated by Sumi Sexton, MD, Associate Deputy Editor.

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Single-Dose Dexamethasone an Option for Acute Adult Asthma

Clinical Question

Is a single dose of dexamethasone as effective as five days of prednisone for acute exacerbations of asthma?

Bottom Line

A single dose of 12-mg dexamethasone, which has a longer duration of action than prednisone, is almost as effective as five days of 60-mg prednisone for the prevention of relapse in adults with acute asthma treated in an emergency department. It is a reasonable option for treatment in the emergency department, given its fewer adverse effects. In this study, patients who received the single dose also took placebo for four days. Further research is needed to determine whether patients are comfortable with taking just a single dose. (Level of Evidence = 2b)

Synopsis

These investigators enrolled 465 adults younger than 56 years who presented with acute asthma to an emergency department and required at least one treatment with a beta agonist. The patients were randomly assigned, using concealed allocation, to receive treatment with prednisone, 60 mg daily, for five days or a single dose of dexamethasone, 12 mg, followed by four days of placebo. Treatment was started in the emergency department. Of the 465 persons initially enrolled, 376 could be evaluated; 16 were admitted before leaving the emergency department and 73 could not be contacted (more in the

dexamethasone group). Over the subsequent two weeks, 12.1% of the dexamethasone group and 9.8% of the prednisone group had a relapse that required additional treatment (difference = 2.3%; 95% confidence interval, -4.1% to 8.6%). This difference did not meet the researchers' threshold for noninferiority of 8%, meaning that treatment with dexamethasone was slightly less effective. The hospitalization rate was low (3%) and did not differ between treatment groups. Adverse effects were more common in the prednisone group.

Study design: Randomized controlled trial (double-blinded)

Funding source: Foundation

Allocation: Concealed

Setting: Emergency department

Reference: *Rehrer MW, Liu B, Rodriguez M, Lam J, Alter HJ.*

A randomized controlled noninferiority trial of single dose of oral dexamethasone versus 5 days of oral prednisone in acute adult asthma. *Ann Emerg Med.* 2016;68(5):608-613.

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Detrimental Effect of Tight Glucose Control on CV Mortality Persists Over Nine Years

Clinical Question

What is the long-term effect of intensive blood glucose control in patients with type 2 diabetes mellitus?

Bottom Line

The initial Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, which compared standard treatment with intensive control, found that despite good intentions, cardiovascular (CV) and overall mortality are significantly higher when blood glucose levels are lower. This study, which followed patients for an additional five years, found that patients in the intensive treatment group continued to maintain lower A1C levels than patients in the standard care group; they also continued to be at increased risk of death from a CV event. (Level of Evidence = 2b)

Synopsis

This report is a follow-up of patients who were enrolled in the ACCORD study, which randomly assigned patients with type 2 diabetes and a high risk of CV outcomes to

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receive usual care or treatment aimed at intensive control of blood glucose. After the 3.7-year study, patients were followed for an additional five years to determine the long-term effect of their initial treatment. The patients were no longer on a protocol, and their treatment goals were at the discretion of their clinician, but A1C levels were still lower overall in the patients who had been in the intensive-care group. The investigators did a thorough job of keeping track of the patients, following up with 98% of them (n = 8,601) who did not experience a primary outcome or death during the original trial. Over this additional time, intensive glucose lowering did not increase or decrease the primary composite outcome of nonfatal myocardial infarction, nonfatal stroke, CV death, death from any other cause, or overall mortality. The increased CV mortality rate seen with intensive control during the active treatment stage decreased in the subsequent years but was still higher than in the group initially treated with standard treatment (hazard ratio = 1.20; 95% confidence interval, 1.03 to 1.39; $P = .02$).

Study design: Cohort (prospective)

Funding source: Government

Setting: Outpatient (any)

Reference: ACCORD Study Group. *Nine-year effects of 3.7 years of intensive glycemic control on cardiovascular outcomes.* *Diabetes Care.* 2016;39(5):701-708.

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Antipsychotics Worsen Symptoms in Patients with Delirium Who Receive Palliative Care

Clinical Question

Do antipsychotic drugs improve symptoms of distress associated with delirium in patients receiving palliative care?

Bottom Line

For hospitalized patients with acute delirium and symptoms of distress who are receiving palliative care, the use of risperidone (Risperdal) or haloperidol at conservative oral doses worsens symptoms and may shorten overall survival. (Level of Evidence = 1b)

Synopsis

These researchers enrolled 247 hospitalized patients who were receiving palliative care and had delirium-related symptoms of distress. Patients were randomized, using

concealed allocation, to receive oral risperidone, haloperidol, or placebo for 72 hours for the management of these symptoms. There were slightly more than 80 patients in each of the three arms. The initial dosage for risperidone and haloperidol was 1 mg, with maintenance dosages of 0.5 mg every 12 hours titrated to a maximum dosage of 4 mg per day. Patients older than 65 years received half this dosage. All patients also received nonpharmacologic measures for delirium treatment, such as vision and/or hearing aids and frequent reorientation, as well as treatment for reversible precipitants of delirium. Subcutaneous midazolam was given as needed for patients who required immediate intervention for safety or distress.

Delirium symptom scores were obtained every eight hours using the three items on the Nursing Delirium Screening Scale that are considered measures of distress (inappropriate behavior, inappropriate communication, and illusions/hallucinations). Each item was scored from 0 to 2, based on the presence and intensity of the symptom, for a total score of 0 to 6. The primary outcome was the average of the last two delirium symptom scores on day 3 of treatment. The three study groups had similar delirium symptom scores at baseline. The mean age in each group was 75 years, and almost 90% of patients had cancer. Analysis was by intention to treat.

Overall, patients who received haloperidol and patients who received risperidone had significantly higher delirium symptom scores at day 3, compared with those who received placebo, by an average of 0.48 and 0.24, respectively. Both intervention groups also required more rescue midazolam than did the placebo group. Finally, the haloperidol group was noted to have decreased overall survival compared with the placebo group (hazard ratio = 1.73; 95% confidence interval, 1.20 to 2.50; $P = .003$). The authors suggest that this may be due to prolonged delirium or longer exposure to antipsychotics. Survival was also decreased in the risperidone group, although this did not reach statistical significance.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Inpatient (ward only)

Reference: Agar MR, Lawlor PG, Quinn S, et al. *Efficacy of oral risperidone, haloperidol, or placebo for symptoms of delirium among patients in palliative care: a randomized clinical trial.* *JAMA Intern Med.* 2017;177(1):34-42.

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