Cochrane for Clinicians

Putting Evidence Into Practice

Addition of Magnesium Sulfate for Acute COPD Exacerbations

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Clinical Question

Is magnesium sulfate an effective addition to usual care for adults with chronic obstructive pulmonary disease (COPD) exacerbations?

Evidence-Based Answer

Adding intravenous magnesium to standard care for adults with COPD exacerbations may decrease hospital admissions and the length of hospitalization. Seven people with COPD exacerbations would need to be treated with intravenous magnesium to prevent one admission. Patients treated with intravenous magnesium who require hospitalization have a decreased length of stay (mean difference = 2.7 days). There is insufficient evidence about the frequency and severity of adverse events.[1] (Strength of Recommendation: A, consistent, good-quality patient-oriented evidence.)

Practice Pointers

Acute exacerbations of COPD are common, with 7% to 33% of patients being hospitalized for severe exacerbations per year, depending on their baseline severity of illness.[2] The authors of the Cochrane review sought to determine the effectiveness and safety of nebulized and intravenous magnesium sulfate in treating COPD exacerbations in terms of hospitalization rate and other factors.

This Cochrane review included 762 patients in 11 randomized controlled trials conducted in Iran, New Zealand, Nepal, Turkey, the United Kingdom, Tunisia, and the United States.[1] The trials investigated magnesium, administered via intravenous or nebulized routes, in addition to standard therapies in adults 35 years and older with acute COPD exacerbations in emergency department settings. Seven studies investigated intravenous magnesium sulfate plus standard care vs. placebo plus standard care. Three studies examined nebulized magnesium sulfate plus standard care vs. placebo plus standard care. One study investigated nebulized magnesium sulfate plus intravenous magnesium sulfate vs. nebulized ipratropium bromide plus intravenous saline. The trials described weight-based magnesium sulfate dosing of 40 mg per kg of body weight, up to a maximum dose of 2 g administered by infusion over 20 minutes.

The primary outcomes were hospital admission, the need for noninvasive ventilation or assisted ventilation, intensive care unit admission, and serious adverse events. Secondary outcomes included the length of hospital stay, mortality, other adverse events, lung function, blood gas measurements, and dyspnea score, as measured by the dyspnea severity score and the Borg dyspnea scale. Lower scores on the dyspnea severity and Borg scales indicate less severe dyspnea. Although it is unclear what a minimal clinically significant difference on the dyspnea severity scale would be, a minimal clinically significant difference on the Borg scale is only a one-unit difference.[3]

This review showed that fewer patients receiving intravenous magnesium sulfate plus standard treatment vs. standard treatment alone were hospitalized (number needed to treat [NNT] = 7; 95% CI, 3 to 32) and that their length of hospital stay was shorter (mean difference = −2.7 days; 95% CI, −0.66 to −4.73). Patients receiving intravenous magnesium sulfate had a slightly lower dyspnea score (standardized mean difference = −1.4; 95% CI, −1.83 to −0.96). There was no significant difference in the need for noninvasive ventilation; no serious adverse events were reported in either group. Patients who received nebulized magnesium sulfate plus standard treatment experienced no improvement in hospitalization or intensive care unit admission rates, compared with standard treatment alone, and there was no difference in the use of noninvasive ventilation, length of hospital stay, or dyspnea score. Serious adverse events were not assessed in those studies.

Patients who received nebulized plus intravenous magnesium sulfate compared with nebulized ipratropium bromide, both in addition to standard treatment, experienced no difference in length of hospital stay or rates of hospitalization, endotracheal intubation, or serious adverse events.

International guidelines recognize the effectiveness of intravenous magnesium sulfate as a second- or third-line agent for treating severe asthma exacerbations.[4] However, U.S. and international guidelines do not include intravenous magnesium sulfate for the management of severe COPD exacerbations.[5,6]

These are summaries of reviews from the Cochrane Library.

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CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 342.

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The findings of this Cochrane review suggest that family physicians should be prepared to discuss the role of intravenous magnesium sulfate as an adjunctive therapy for severe COPD exacerbations that do not respond to initial treatments.

The practice recommendations in this activity are available at https://www.cochrane.org/CD013506.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army, the U.S. Department of Defense, or the U.S. government.

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Aspirin Use and the Risk of Mortality in Patients With Hypertension

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Patient perspective by John James

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Clinical Question

Does the use of aspirin decrease the risk of all-cause or cardiovascular mortality in patients with hypertension?

Evidence-Based Answer

The use of aspirin for primary prevention likely decreases the risk of all cardiovascular events (number needed to treat [NNT] = 175) but does not modify all-cause or cardiovascular mortality and increases the risk of major bleeding (number needed to harm [NNH] = 175) in patients with hypertension.[1]

Practice Pointers

Cardiovascular disease (CVD) is the leading cause of mortality worldwide, causing 17.9 million deaths (32% of the total) in 2019.[2] Hypertension is a significant risk factor in the progression of morbidity and increases all-cause mortality.[3] The authors of this review sought to determine the value of taking aspirin as the primary prevention of all-cause and cardiovascular mortality in patients with hypertension.

This Cochrane review included six single- or double-blinded randomized controlled trials (published between 1996 and 2019) involving 61,015 participants who were 30 to 85 years of age.[1] Inclusion criteria were a systolic blood pressure of 140 mm Hg or greater or a diastolic blood pressure of 90 mm Hg or greater. The treatment durations were between three months and five years. Primary outcomes were all-cause and cardiovascular mortality. Secondary outcomes were nonfatal cardiovascular events and major bleeding events. Major bleeding was defined as hemorrhagic stroke or blood loss involving a decrease in hemoglobin greater than 2 g per dL (20 g per L).

Aspirin in daily dosages of 75 mg, 81 mg, or 100 mg (three studies; n = 35,794) did not improve all-cause mortality (odds ratio [OR] = 0.97; 95% CI, 0.87 to 1.08) or cardiovascular mortality (OR = 0.98; 95% CI, 0.82 to 1.17) compared with placebo. Aspirin decreased the risk of nonfatal cardiovascular events (OR = 0.63; 95% CI, 0.45 to 0.87; NNT = 37) and all cardiovascular events (OR = 0.86; 95% CI, 0.77 to 0.96; NNT = 175). However, aspirin increased the risk of major bleeding events (OR = 1.77; 95% CI, 1.34 to 2.32; NNH = 175). The outcome of increased risk of major bleeding events was derived from evidence rated as high certainty on the GRADE rating system.

The U.S. Preventive Services Task Force (USPSTF) recommends that adults 40 to 59 years of age with a 10% or greater 10-year CVD risk make individual decisions when considering the initiation of low-dose aspirin for the primary prevention of CVD because evidence indicates that the net benefit of aspirin use in this group is small.[4] People not at increased risk of bleeding who are willing to take low-dose aspirin daily are

SUMMARY TABLE

Outcomes of Aspirin Use and the Risk of Mortality in Patients With Hypertension

Outcomes (mean follow-up in years)	Probable outcome with placebo (per 1,000 patients-years)	Probable outcome with aspirin (per 1,000 patients-years)	Number needed to treat or harm	Participants (studies)	Certainty of evidence
Total mortality (3.8)	40.1 deaths	38.8 deaths	Not applicable	35,794 (3)	Low
Cardiovascular mortality (3.8)	13.7 deaths	13.4 deaths	Not applicable	35,794 (3)	Low
Nonfatal cardiovascular events (4.4)	77.0 events	49.7 events	37	2,540 (1)	Low
All cardiovascular events (3.8)	42.8 events	37.1 events	175	35,794 (3)	Low
Major bleeding (3.8)	7.7 events	13.4 events	175	21,330 (2)	High

more likely to benefit (Grade C recommendation). The USPSTF recommends against initiating low-dose aspirin for the primary prevention of CVD in adults 60 years or older (Grade D recommendation).[4] The American College of Cardiology and American Heart Association recommend that low-dose aspirin be considered for the primary prevention of atherosclerotic CVD in certain adults at higher risk who are between 40 and 70 years of age and not at increased risk of bleeding. However, aspirin should not be administered on a routine basis for the primary prevention of atherosclerotic CVD among adults older than 70 years or among adults at any age who are at increased risk of bleeding.[5] Guideline-directed management of hypertension is an effective way to decrease a patient's overall atherosclerotic CVD risk score.

Patient Perspective

Most of us know someone who has had a heart attack. Taking a simple and cheap medication such as aspirin seems inviting to prevent a heart attack, until the risk of gastrointestinal bleeding tempers any excitement. This appears to be an area in which shared decision-making is essential. Perhaps the patient wants to take aspirin because close relatives have had heart attacks. The accompanying table seems to be a good starting point for a shared decision between physician and patient about taking low-dose aspirin. It's unclear if the studies included in the review involved coated aspirin or if this affects the gastrointestinal bleeding risk. Even though no one has experienced a heart attack in my household, my spouse chooses to take a coated, low-dose aspirin every other day.

Editor's Note: The NNT and NNH reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

The practice recommendations in this activity are available at https://www.cochrane.org/CD003186.

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