Critical Review Form
Therapy

PGY-1

HYPERLINK "http://pmid.us/34158778"Jahanian F, Khatir IG, Ahidashti HA, Amirifard S. The Effect of Intravenous Magnesium Sulphate as an Adjuvant in the Treatment of Acute Exacerbations of COPD in the Emergency Department: A Double-Blind Randomized Clinical Trial. Ethiop J Health Sci. 2021 Mar;31(2):267-274.

Objectives: **"to evaluate the effect of intravenous magnesium sulphate as an adjuvant in the treatment of AECOPD [acute exacerbations of COPD] in the ED." (p. 268)**

Methods: **This double-blind, single-center, randomized controlled trial was conducted in the ED of Imam Khomeini Hospital in Iran between September 2016 and February 2018. Patients with known history of moderate COPD (FEV1/FVC < 70%, FEV1 between 30 and 50) with either shortness of breath or increase in severity of shortness of breath, cough, and sputum volume. Exclusion criteria were presence of "diseases that mimic the clinical features of COPD," need for tracheal intubation or noninvasive ventilation on admission to the ED, history of cardiac disease, inability to cooperate or undergo spirometry, reduced level of consciousness, use of IV magnesium sulfate in the past 24 hours, systolic blood pressure < 100 mmHg, use of medications that contain magnesium, presence of hyperkalemia or hypocalcemia with ECG abnormalities, and respiratory rate < 16.**

Patients were randomized in a 1:1 fashion to receive either magnesium sulfate (2 g in 100 mL of saline) or normal saline alone, over 30 minutes, in addition to standard treatment (inhaled salbutamol and ipratropium and IV hydrocortisone). Spirometry (FEV1) was performed on all patients prior to the intervention (T1), 45 minutes after the intervention (T2), and 6 hours after the intervention (T3). Respiratory rate (RR), pulse rate (PR), O2 saturation (SPO2), and Borg dyspnea scale scores were also measured at these time intervals.

Seventy-two consecutive patients with AECOPD who presented to the ED during the study period were evaluated for inclusion. Eight did not meet inclusion criteria and 4 declined to participate, leaving 60 patients in the final analysis, with 30 randomized to each group. The mean ages in the intervention and control group were 63 and 66 years, respectively, and 83.3% and 70% were female.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis?**	
1.	Were patients randomized?	Yes. Patients were randomized to intervention and control groups with equal sample size.

2.	Was allocation concealed? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group?	Presumably yes. "Randomization was done using a sealed envelope technique with a computer-generated random numbering system with the help of a nurse who was blinded to the study groups." (p. 268) While not specifically stated, it is assumed that the envelopes were opaque. This should be sufficient to maintain allocation concealment.
3.	Were patients analyzed in the groups to which they were randomized?	Yes. The authors do not specify that an intention to treat analysis was performed. They also make no mention of crossover between groups, although it appears that all patients received the treatment to which they were allocated.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Patients were similar with respect to age, current cigarette use, proportion of patients with disease duration < 5 years, and being "concurrently on medical treatment." Patients were also similar with respect to baseline mean FEV1, Borg score, respiratory rate, pulse rate, and oxygen saturation.
B.	**Did experimental and control groups retain a similar prognosis after the study started?**	
1.	Were patients aware of group allocation?	No. "All drugs were prepared in syringes in the same size, color, volume, and shape. The syringes were labeled as A or B by a pharmacist and were administered by a nurse, using a peripheral venous catheter. Also, patients were unaware of the type of medication they were receiving." (p. 269)
2.	Were clinicians aware of group allocation?	Presumably no. While not specifically mentioned, it seems likely that nurse administering the treatment were not aware whether A or B was magnesium or placebo.
3.	Were outcome assessors aware of group allocation?	Presumably no. While not specifically mentioned, it seems likely that outcome assessors were not aware of group allocation.
4.	Was follow-up complete?	Yes. There were no patients lost to follow-up.
II.	**What are the results ?**	
1.	How large was the treatment effect?	• FEV1 and SPO2 increased significantly at T2 and T3 in both group ($p < 0.001$) while Borg scores, RR, and PR decreased significantly ($p < 0.001$) in both groups. Treatment group did not have a significant effect on any of these outcomes, with p-values ranging from 0.22 to 0.89.
2.	How precise was the estimate of the treatment effect?	See above.

III.	**How can I apply the results to patient care?**	
1.	Were the study patients similar to my patient?	No. This study was conducted in Iran, with the potential for cultural and ethnic differences impacting treatment effect. Additionally, alternate medications were primarily used in the management of these patients (e.g. hydrocortisone) which could also impact outcomes (external validity).
2.	Were all clinically important outcomes considered?	No. The authors measured surrogate outcomes, including FEV1 and vital sign measurements, and did not measure more patient-centered outcomes, such as need for hospitalization, ICU admission, intubation, length of ED or hospital stay, and patient satisfaction.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain. While this study did not demonstrate any benefit with regards to RR, SPO2, FEV1, PR, or Borg scores, this was a single-center study conducted in Iran using somewhat different meds from those typically used in the US. These results will need to be validated in additional settings using more patient-centered outcomes.

Limitations:

1. **While the authors did conduct a sample size calculation, they do not support their presumed effect size of 0.2 with any prior evidence from the literature.**
2. **No primary outcome was specified. The outcomes measured were primarily surrogate outcomes rather than patient-centered outcomes.**
3. **This study was conducted at a single center in Iran and will need to be validate in additional sites (external validity).**

Bottom Line:

This single-center, randomized controlled trial from Iran found that the administration of IV magnesium sulfate (2 grams) acute exacerbations of COPD did not significant improve FEV1, RR, PR, SPO2, or Borg scores at 45 minutes or 6 hours when compared to placebo.