



Journal Club Presentation

(Critical Care Rotation)
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Done By:

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Outlines:



Article:



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Chronic obstructive pulmonary disease

ORIGINAL ARTICLE

Use of nebulised magnesium sulphate as an adjuvant in the treatment of acute exacerbations of COPD in adults: a randomised double-blind placebo-controlled trial

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Background:

- COPD refers to a group of lung diseases that block airflow and make breathing difficult.
- Emphysema and chronic bronchitis are the two most common conditions that make up COPD.
- Airflow may not be fully reversible, but aggressive and associated with abnormal inflammatory response.
- Most cases of COPD are the result of exposure to noxious stimuli, most often cigarette smoke.

Cont. Background:

- **The Burden of Obstructive Lung Disease (BOLD) study found a global prevalence of 10.1%.**
- **It is the fifth leading cause of death in high-income countries and the sixth leading cause of death in low- and middle-income countries, accounting for 4.9 % of total deaths.**

The prevalence of chronic obstructive pulmonary disease in Saudi Arabia: Where do we stand?

Mohammed Al Ghobain

comprising 14.2% of the study population.

- In BREATHE study by GSK, the prevalence rate in Saudi Arabia is as high as 2.4 %in the population aged 40 years and above.

Cont. Background:

- In the airways, magnesium is a bronchodilator through various mechanisms.
- IV/Nebulized MgSO₄ in asthma
- IV MgSO₄ in AECOPD.

Showed an enhanced bronchodilator response in severe exacerbations asthma.

- Improved symptoms
- Reduced hospital length of stay
- Increased PEF
- Increased FEV1

Only 6 placebo-controlled trials involving IV and nebulized Mg in AE or stable settings of COPD:

- **3 were only in an abstract form.**
- **One randomized double blinded placebo controlled trial with IV Mg of 22 subjects showed:**
 1. Significant reduction in lung hyperinflation.
 2. Increased respiratory muscle strength.

Cont.

- Randomized study, one group received Terbutaline + Ipratropium and the other received Terbutaline + one bolus only of IV Mg, showed no significant difference.

- Nebulized Mg in stable showed significant incr

BUT..

- It wasn't randomized
- Not double-blinded.
- Only 18 patients were studied.

Is there a role for adjuvant nebulized magnesium treatment in the management of acute exacerbations of chronic obstructive pulmonary disease?

- **P:** Patients with AECOPD.
- **I:** Adjuvant magnesium treatment administered via nebulizer.
- **C:** Placebo.
- **O:** Management of AECOPD.

Method:



- **Participants**



- **Study Protocol**



- **Randomization and Masking**



- **Statistical Analysis**

1) Participants:

Inclusion criteria

Age \geq 35

Diagnosis of COPD

FEV₁/FVC < 70%

FEV₁ \leq 50%

Exclusion criteria

Patients required intubation or NIV

Patients unable to perform spirometry

Evidence of Pneumothorax

Hypotension or any serious condition or pregnancy

2) Study protocol:

- Patients with AECOPD presented to ED between 2008-2011 in two university hospitals in New Zealand

- Potential subjects were clinically assessed and received standard treatment.

- 2.5 mg Salbutamol
- 500 µg Ipratopium.
- 40 mg Prednisone.

- Subjects with $FEV_1 \leq 50\%$ after 20 minutes administration of standard treatment were enrolled in the trial.

- After randomization, patients received:

-2.5 mg Salbutamol + 2.5 ml isotonic $MgSO_4$
-2.5 mg Salbutamol + 2.5 ml isotonic NS.

- FEV_1 recorded.

Randomization and Masking:

- Patients were randomly allocated in a double-blind fashion.
- block randomization performed with a block size of 8 using computer-generated random sequence.
- It was administered by a third party, participants and investigators were unaware of treatments allocation.
- Hospital pharmacy pre-prepared identical syringes containing the placebo and the study drug.

4) Statistical Analysis:

- Analysis was by intention-to-treat.
- Primary outcome was FEV₁ at 90 min.
- Secondary outcomes were:
 - 1) FEV₁ at 30 and 60 mins
 - 2) Hospital admission.
 - 3) Episodes of NIV
 - 4) Admission to ICU.

Table 1 Baseline characteristics of patient group

| | Placebo (N=61) | Magnesium (N=48) |
|---|-----------------------|-----------------------|
| Mean (SD) age, years | 69.5 (11.9) | 73.2 (9.8) |
| Female sex, n (%) | 30 (49.2) | 21 (43.8) |
| Current smokers, n (%) | 22/56 (39.3) | 18/45 (40.0) |
| Mean (SD) amount smoked, pack-years | 45.0 (30.7) (N=55) | 41.3 (21.3) (N=42) |
| Never smoker, n (%) | 2/56 (3.6) | 1/45 (2.2) |
| Long term oral steroid use, n (%) | 6/56 (10.7) | 5/45 (11.1) |
| Inhaled corticosteroid, n (%) | 44/56 (78.6) | 37/45 (82.2) |
| Home nebuliser, n (%) | 17/56 (30.4) | 11/45 (24.4) |
| Home oxygen, n (%) | 10/56 (17.9) | 8/45 (17.8) |
| Diuretic use, n (%) | 12/61 (19.7) | 13/48 (27.1) |
| Hospital admission in last year | 1.3 (N=55) | 1.0 (N=45) |
| Mean (SD) presentation FEV ₁ , l | 0.72 (0.25) | 0.69 (0.26) |
| Mean (SD) presentation FEV ₁ , % predicted | 29.7 (9.2) | 28.2 (9.3) |
| Mean (SD) baseline FEV ₁ , l | 0.74 (0.28) | 0.74 (0.28) |
| Serum magnesium level (mmol/l) | 0.78 (0.10) (N=42) | 0.81 (0.08) (N=36) |

FEV₁, forced expiratory volume in 1 s.

Results:

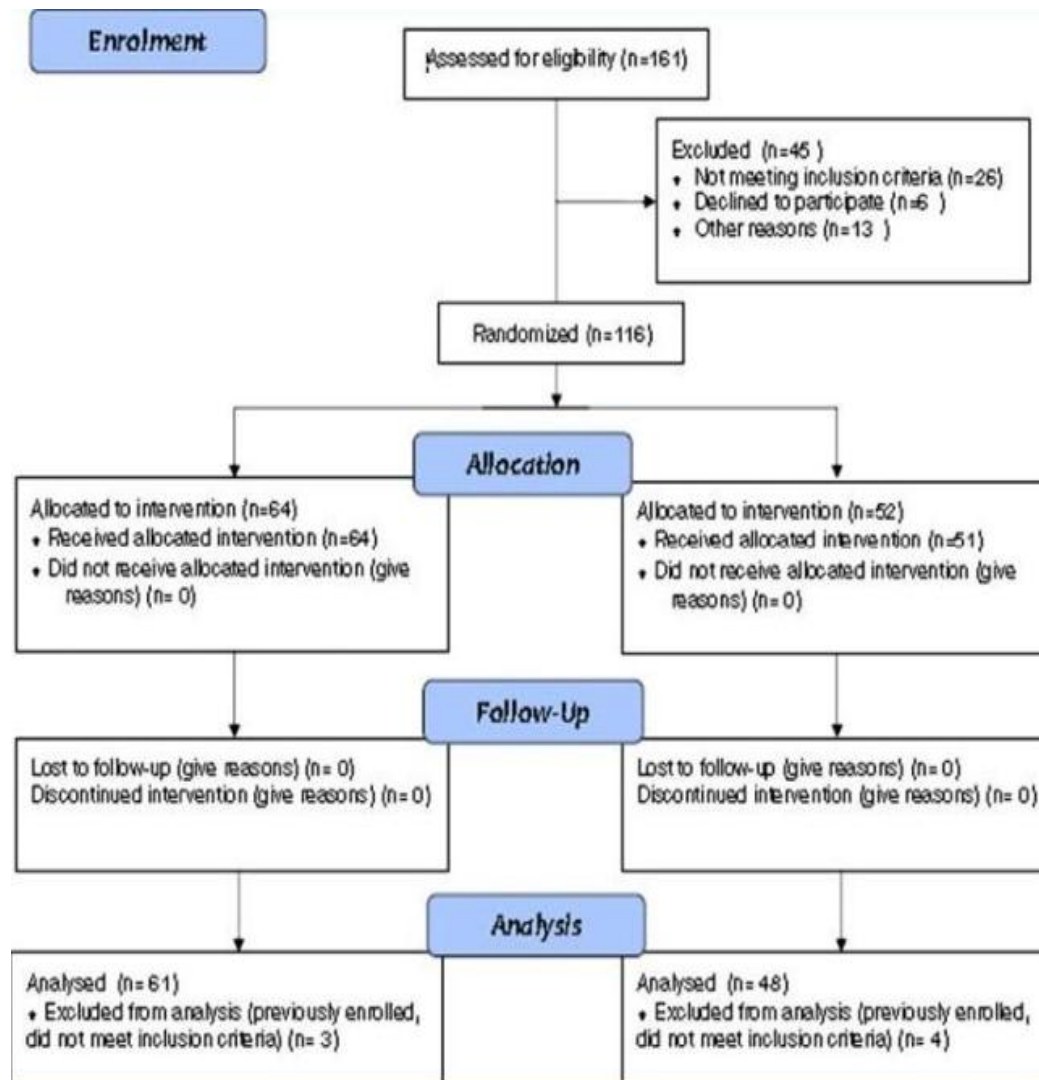


Table 2 Serial forced expiratory volume in 1 s (FEV₁) in patients receiving nebulised magnesium or placebo

| | Mean (SD) |
|--------------------------|-------------|
| FEV ₁ Time 0 | |
| Magnesium (N=48) | 0.74 (0.28) |
| Placebo (N=61) | 0.74 (0.28) |
| All (N=109) | 0.74 (0.28) |
| FEV ₁ Time 30 | |
| Magnesium (N=48) | 0.74 (0.29) |
| Placebo (N=61) | 0.79 (0.29) |
| All (N=109) | 0.76 (0.29) |
| FEV ₁ Time 60 | |
| Magnesium (N=48) | 0.76 (0.31) |
| Placebo (N=61) | 0.81 (0.31) |
| FEV ₁ Time 90 | |
| Magnesium (N=47) | 0.78 (0.33) |
| Placebo (N=61) | 0.81 (0.30) |
| All (N=108) | 0.79 (0.31) |

Head points:

- **Relation of Mg in COPD in this study to other studies.**
- **Considerations of the findings here in relation to Asthma literature.**
- **Route of administration.**
- **Patients group.**
- **Association between serum Mg and COPD.**

Author's Conclusion:

- This trial has shown no evidence of efficacy of single or repeated nebulized Mg as an adjunct to nebulized salbutamol in AECOPD.
- The priority for further investigation of magnesium in AECOPD should be with the intravenous route of administration.

strengths

Randomized

Double blind

**Important clinical
outcome**

No sig AE reported

**General inclusion
criteria**

**Clear and well
oriented**

weaknesses

Not Multinational

**No specific mention
of possible AE**

Drug interactions

Safety issues

Cost issues

**Weak statistical
analysis**

Thank you
for
listening..

Questions?

