Global Magnesium COVID-19 Project

Announcing Meeting #10

Wednesday, February 24, 2021

1 pm ET USA 10 am Pacific time USA noon Mexico/ North Dakota, USA 7 pm Germany, France, Italy

Guitti Pourdowlat

Inhalation of magnesium sulfate in hospitalized COVID-19 patients

Power Point presentation. Much discussion, not recorded, concluded this pilot project was very well designed, accomplished, with very promising results.

Click to proceed to sound presentation

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Magnesium Sulfate inhalation in hospitalized COVID-19 patients

GUITTI POURDOWLAT

PULMONOLOGIST

NRITLD

asthma

Mg sulfate can cause bronchodilation in asthmatic patients by various mechanisms, including

- by inhibition of calcium influx into the cytosol,
- prevention of acetylcholine secretion,
- inhibition of histamine release;
- and finally, by enhancement of β2-receptor affinity, increases bronchodilator effect of β2-agonists

Magnesium Sulfate: A Potential Adjuvant Treatment on COVID-19

Parichehr Pooransari1, Guitti Pourdowlat2*

- Mg sulfate can be used both systemically and by inhalation, but nebulizer route has potential effect on rapid onset of action on respiratory system and reduced incidence of systemic side effects .

- Such as excessive muscle relaxation
- Hypotension
- bradycardia

Magnesium sulfate for persistent pulmonary hypertension of the newborn

Ho JJ, Rasa G , 18 July 2007

- **Magnesium sulfate** is a potent **vasodilator** and hence has the potential to reduce the high **pulmonary** arterial pressures associated with PPHN. If **magnesium sulfate** were found to be effective in the treatment of PPHN, this could be a cost effective and potentially life-saving therapy.
- Parenteral MgSO4 is easy to administer and monitor during treatment. When MgSO4 is used, systemic hypotension can be adequately controlled with ionotropes.
-

- low Mg level is associated with increased inflammatory response.
- in vitro studies showed that short-term exposure to Mg sulfate without affecting on viability and function of phagocytes, diminished cytokine gene and protein expression, and consequently could reduce production of **TNF-α** and **IL-6** from neonatal monocytes (5). Moreover, Mg sulfate can reduce the level of **interleukin 1β**, that is a potent proinflammatory cytokine
- neutralized Mg ions can convert THP-1- derived macrophages to the M2 phenotype (antiinflammatory macrophages), thereby reduce the production of inflammatory cytokines and enhance the secretion of anti-inflammatory cytokines
-

systemic or local Mg deficiency predicts platelet-dependent thrombosis. Stefano Iotti et all

- chronic Mg deficiency might create a favorable microenvironment for the virus to promote thromboembolism
- systemic or local Mg deficiency predicts platelet-dependent thrombosis.

- we know that

  one of the ethology of hypoxemia in covid-19 patients is microvscular thrombosis.

- Mg may reduce platelet aggregation and microthrombosis in the pulmonary microvasculature

So

Inhalation of Mg sulfate may affect this phenomenon locally and improve microcirculation in the lung

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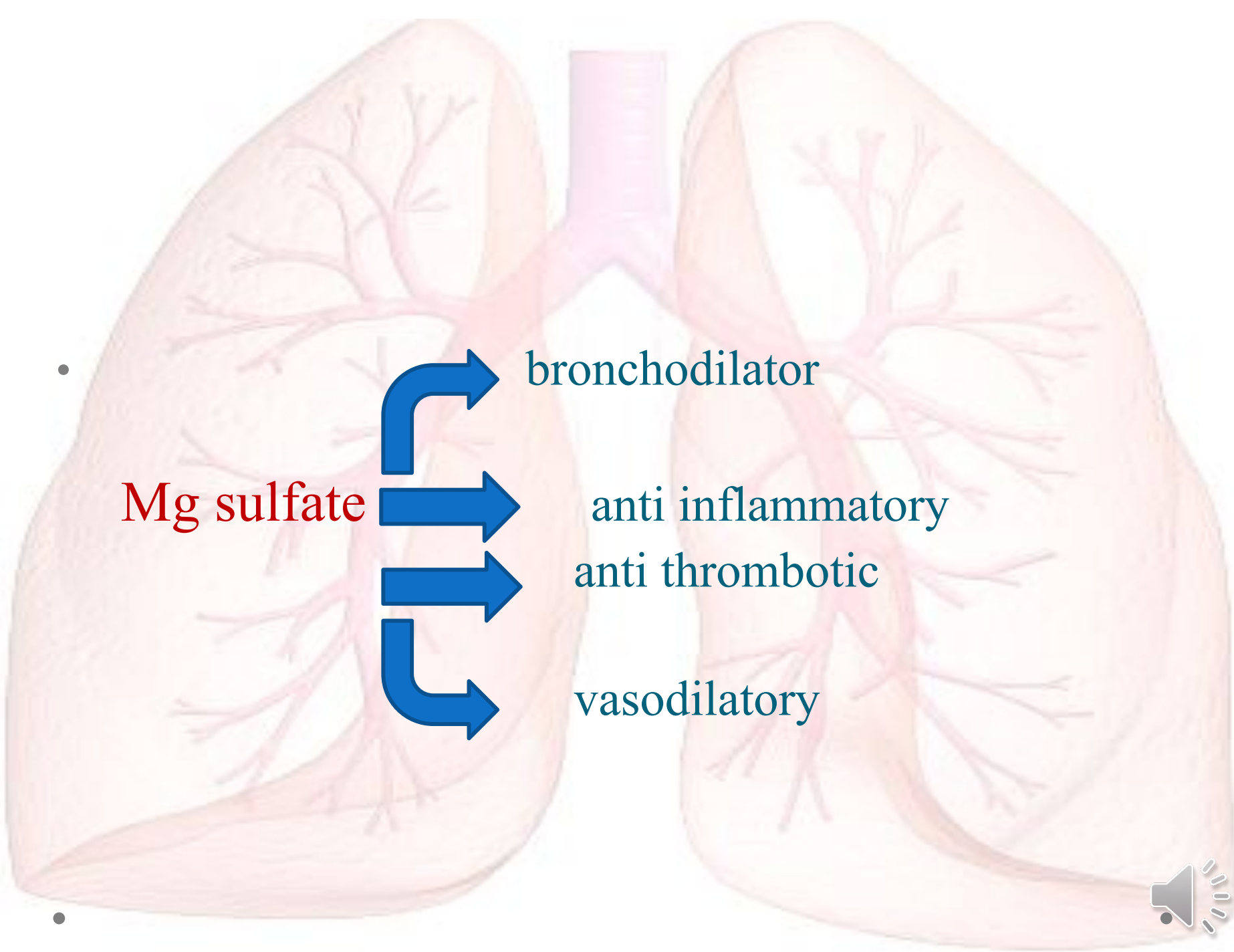
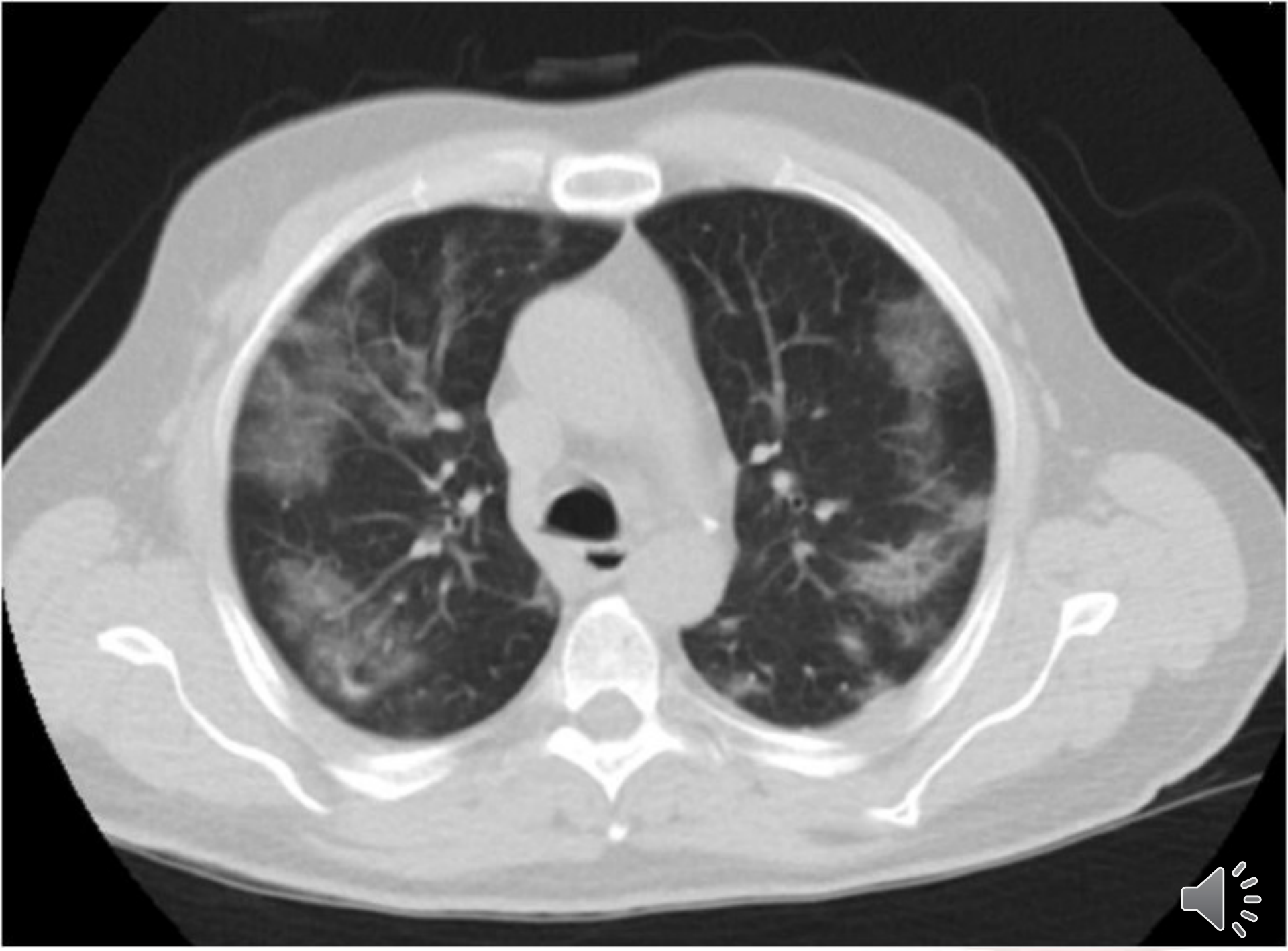
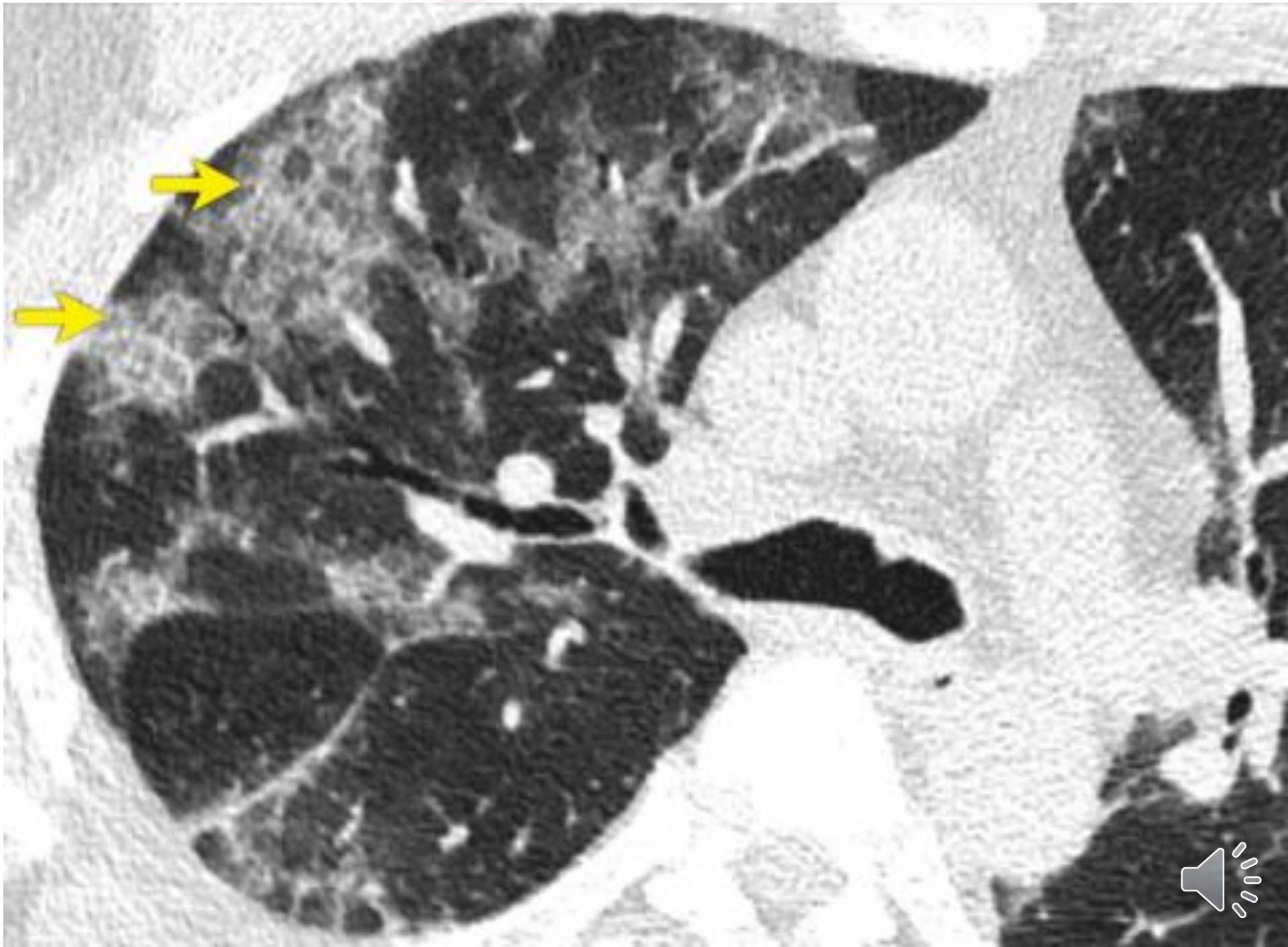

Mg sulfate
bronchodilator
anti inflammatory
anti thrombotic
vasodilatory





COVID-19: a hypothesis regarding the ventilation-perfusion mismatch

Mario G. Santamarina1,2, Dominique Boisier3 , Roberto Contreras4 , Martiniano Baque5 , Mariano Volpacchio6 and Ignacio Beddings

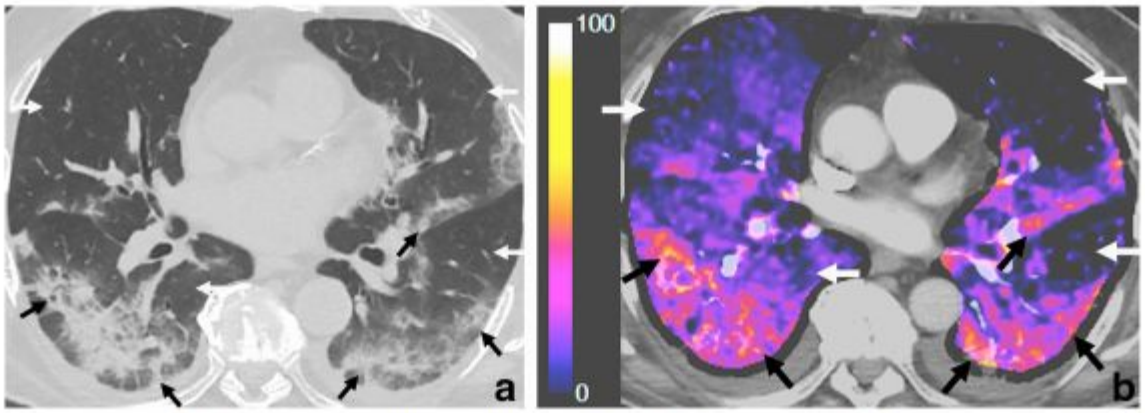
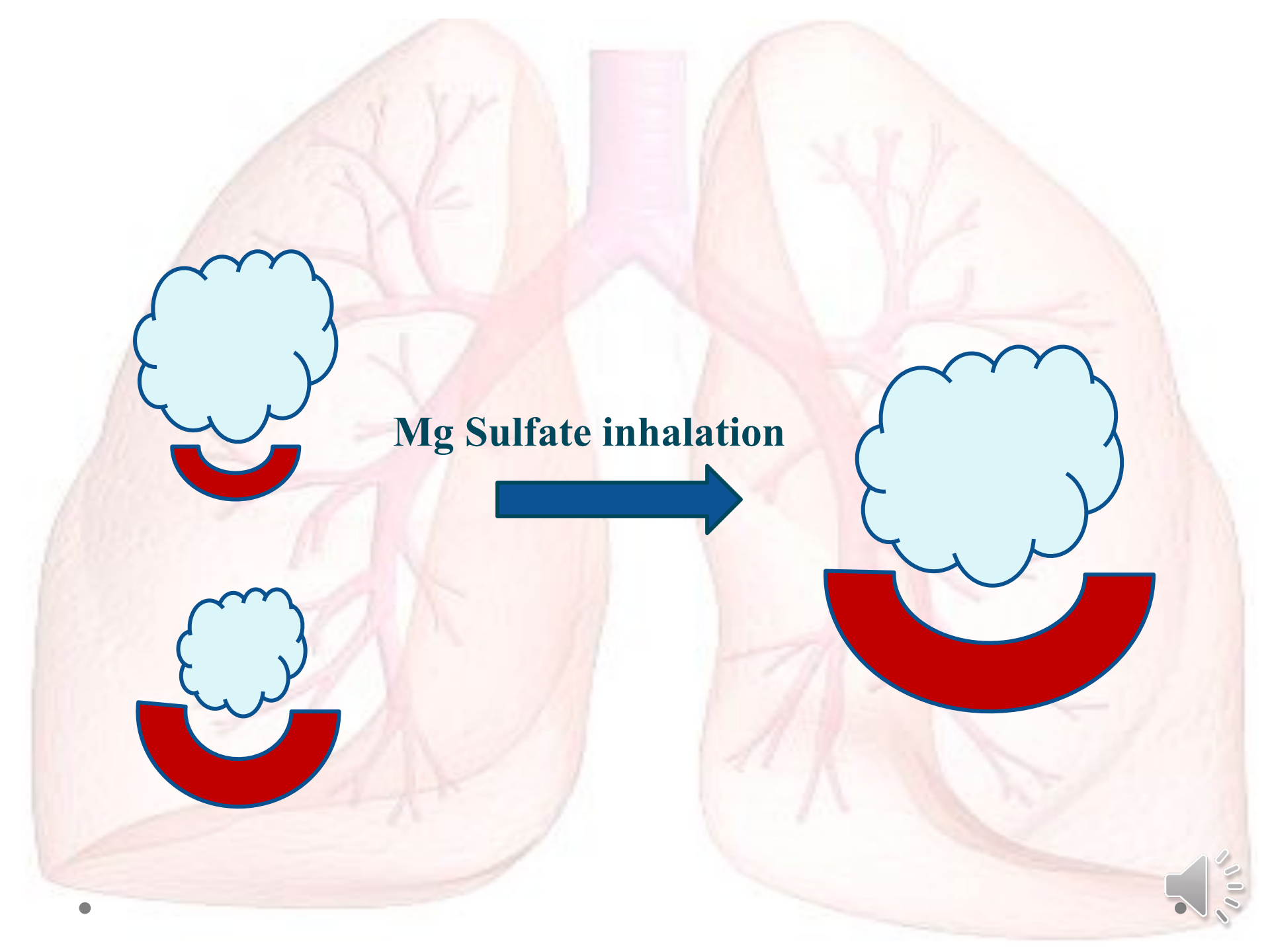


Fig. 2 a, **b** Prominent hypoperfusion in the well-aerated lung and hyperperfusion in areas of injured lung. Seventy-eight-year-old male patient, RT-PCR-confirmed COVID-19, 10 days since symptom onset, with hypoxemia, (PaO_2/FiO_2) 206, D-dimer 1600 ng/mL progressively increasing. There are extensive foci of consolidation and ground-glass opacities, associated with septal thickening, with a predominantly posterior and subpleural bilateral distribution, which correlate with the areas of hyperemia and iodine pooling in subtraction CT iodine maps (black arrows). There are areas of markedly decreased perfusion in both lungs, which correlate with the apparently healthy lung parenchyma in conventional chest CT images (white arrows). Bilateral pleural effusion. This could be explained by an increased blockage of ACE2 receptors in the lung endothelium, leading to increased local levels of angiotensin II, which leads to vasoconstriction and ventilation/perfusion mismatch. This patient was managed with invasive mechanical ventilation, with highly compliant lung parenchyma, in accordance with the type 1 or L phenotype described by Gattinoni et al.


Mg Sulfate inhalation


USE
NO OIL
UNDER
1·4700 kpa
150 Kg/cm²
UPPER LEVEL
DISTILLED WATER
PREFERED
LOWER LEVEL

- When Mg sulfate is used in an oxygen manometer chamber , FIO2 will be almost constant before, after and during inhalation of magnesium sulfate, because we do not change the type of oxygen masks.
- And we can evaluate variation of spO2 with steady oxygen .

Pilot Study

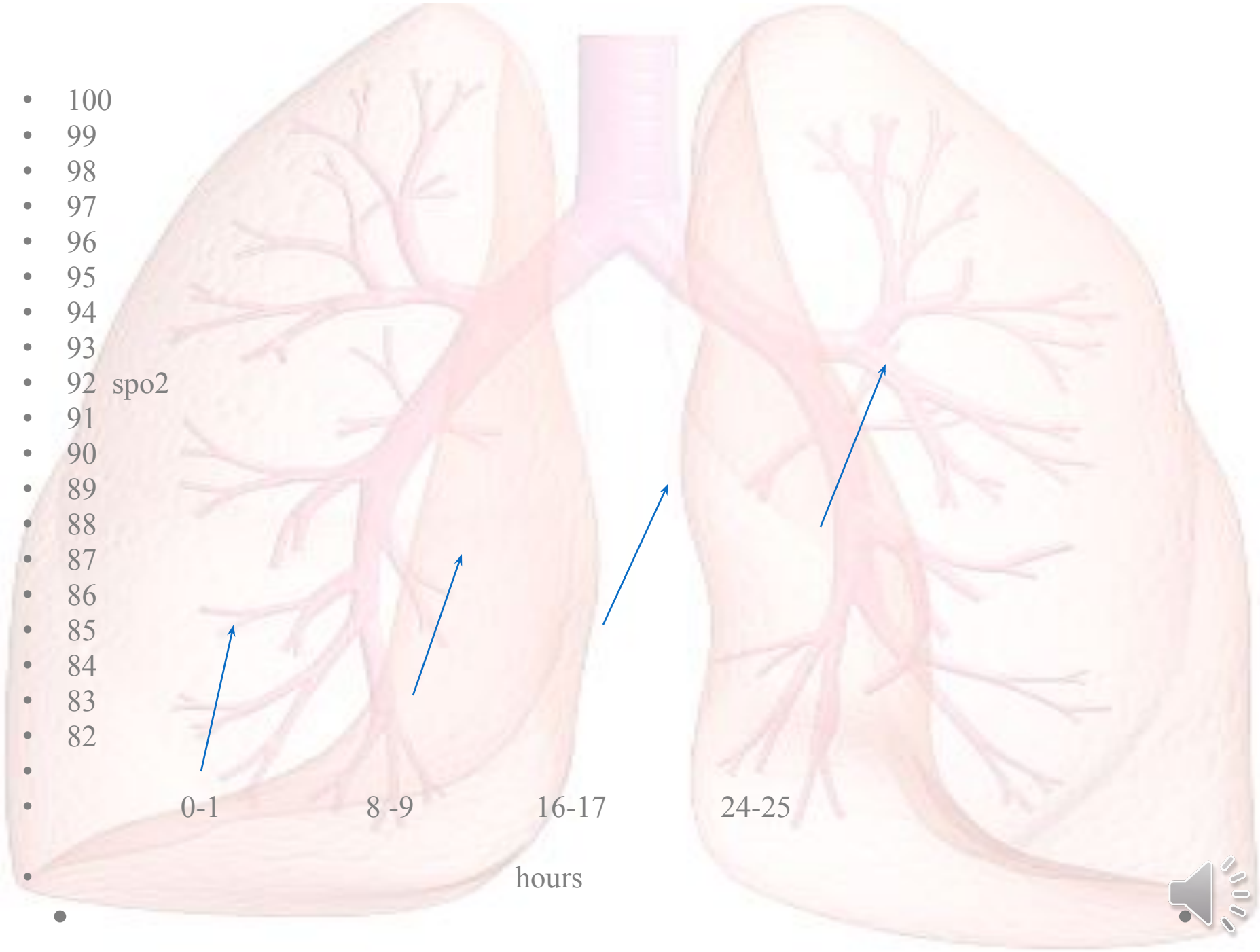
- About 20 patients
- Some different doses of Mg sulfate with different concentrations

- In 1gr Mg sulfate in 50 cc distilled water we achieved best results

- In lower concentration, there was low efficacy
- In higher concentration there was airway irritation in some patients

Pilot Study

- None of them had systemic adverse effect
- In our pilot study we measured serum Mg level every day
- we do not know exactly, how much this nebulizer route can increase serum magnesium level
- It seems that the inhalation of Mg sulfate doesn't enhance Mg serum level significantly.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0-1
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16-17
24-25
hours

Good for sever patients but not critically ill

- our preliminary findings showed that inhalation of Mg sulfate could not improve oxygenation in critically ill conditions and in patients whose hypoxemia has another reason such as intra pulmonary shunt.

Our current study

Evaluation of the efficacy and safety of inhaled magnesium sulphate in combination with standard treatment in patients with moderate or severe COVID-19: A structured summary of a study protocol for a randomized controlled trial

Current study

- A multi-center , open-label, randomized controlled trial (RCT) with two parallel arms design (1:1 ratio)
- Hospitalized Patients aged 18-80 years
- Location of trial is in 3 hospitals (2 in Tehran 1 in Yazd)
- Confirmed diagnosis of SARS-CoV-2 infection based on poly (PCR) of nasopharyngeal secretions

  or clinical manifestations along with chest computed tomography (chest CT) scan Presenting with moderate or severe COVID-19 lung involvement confirmed with chest CT scan and arterial oxygen saturation below 93% .
- Initiation of drug : before ≤48 hours hospitalization
-

Intervention and control group

1- Patients in the intervention arm will be given both standard treatment for COVID-19 (according to the national guideline) and magnesium sulphate (5 cc of a 20% injectable vial or 2 cc of a 50% injectable vial will be diluted by 50 cc distilled water and nebulized via a mask) every eight hours for five days.

2- Patients in the control (comparator) arm will only receive standard treatment for COVID-19.

Main outcomes

- Improvement of respiratory function and symptoms including

  1- arterial blood oxygen saturation,

  2- dyspnoea (according to NYHA functional classification),

  3- and cough

- within the first five days of randomization.

Trial Status

- **Recruitment of the participants started on July 30, 2020, and it is anticipated to be completed by February 28, 2021.**

Thank you for your attention