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Original Research Paper

Clinical Research

EFFECT OF MAGNESIUM SULPHATE VIA INHALATIONAL AND INTRAVENOUS ROUTE IN COPD PATIENTS ON VENTILATOR

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ABSTRACT

Magnesium as a bronchodilator has a well established role in exacerbation of asthma however it is generally not used in exacerbation of Chronic Obstructive Pulmonary Disease (COPD). Aim of this research was to study the effect of magnesium sulphate given via inhalational and intravenous (IV) route in COPD patients on mechanical ventilation COPD patients admitted to ICU on ventilator support were divided in three groups: (IV Group)- 20 min Intravenous infusion of magnesium sulphate 1gm dissolved in 100ml of 0.9% saline solution along with nebulisation with salbutamol (2.5 mg in 5ml). (Neb Group) Nebulised salbutamol (2.5mg in 2.5ml normal saline) + 2.5ml magnesium sulphate (1gm in 2.5ml normal saline) + 20min intravenous infusion of isotonic saline. (Control Group) Nebulised salbutamol (2.5mg in 2.5ml normal saline) + 2.5ml normal saline + 20min intravenous infusion of isotonic saline. The patients were monitored for peak inspiratory pressure, mean airway pressure every 5 min for half an hour after drug administration everyday. Patients were followed for weaning and total duration of mechanical ventilation requirement was noted.

Fall in peak inspiratory pressure was remarkably higher in IV group (19.79 %) as compared to NEB group (12.21%) and control (10%). Similarly, mean airway pressure fall in IV group , NEB group and control group was (19.86%, 16.1% ,15%) respectively . Initiation of ventilation and weaning was also early in IV group followed by NEB and control group respectively. So to conclude MgSO4 given by I/V route was more effective than nebulisation route and supplement Mg either by I/V or nebulization route had a beneficial effect over isolated salbutamol in COPD patients on ventilator.

KEYWORDS : COPD, magnesium sulphate, critically ill patient

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is one of the most common conditions worldwide with significant mortality, morbidity and economic costs. COPD is caused by mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), relative contribution of these vary from patient to patient [1]. COPD affects more than 400 million people worldwide [2] , and accounts for over 500000 deaths annually in India alone [3]. Magnesium as a bronchodilator has a well established role in exacerbation of asthma [4]. However it is generally not used in exacerbation of COPD. Aim of this research was to study the effect of magnesium sulphate given via inhalational and IV route in COPD patients on mechanical ventilation in intensive care unit on Peak inspiratory pressure, mean airway pressure, weaning and duration of mechanical ventilation.

MATERIAL & METHODS

After approval from the institute ethical committee and informed written consent, this double blind randomized control trial was conducted in known or suspected COPD patients aged 18 years and above admitted to ICU with Partial pressure of arterial carbon dioxide (PaC02) >45mmHg with Respiratory rate >24/min , pH < 7.35 and Partial pressure of arterial oxygen (Pa02) <50mm. Patients with hypersensitivity to magnesium sulphate and pre existing cardiovascular disease and renal disease and pregnant patients were excluded from the study. Patients admitted to ICU who fulfilled the inclusion criteria and gave informed consent were divided in three groups and randomised to following treatment regimens by tossing dice: 1.(I/V Group)- 20 min Intravenous infusion of magnesium sulphate 1gm dissolved in 100ml of 0.9% saline solution along with nebulization with salbutamol (2.5 mg in 5 ml normal saline) 2.(Nebulization Group) Nebulised salbutamol (2.5mg in 2.5ml normal saline) + 2.5ml magnesium sulphate (1gm in 2.5ml normal saline) + 20min intravenous infusion of 100ml isotonic saline. 3. (Control Group) Nebulised salbutamol (2.5mg in 2.5ml normal saline) + 2.5ml isotonic saline + 20 min intravenous infusion of 100 ml isotonic saline.

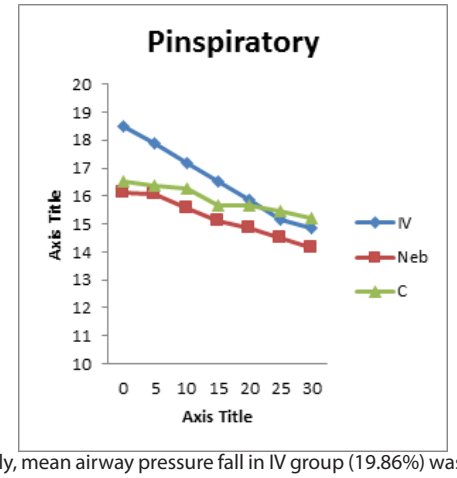
The patients were monitored for peak inspiratory pressure, mean airway pressure every 5 min for half an hour after drug administration everyday. Patients were followed for weaning and total duration of mechanical ventilation requirement was noted.

The results were analysed using one of the following statistical tests ANOVA , chi square, or Kaplan meir using SPSS, SAS. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

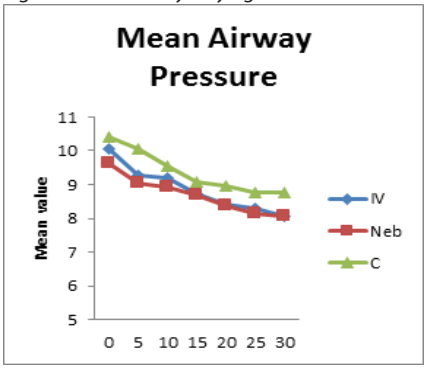
RESULTS

A total of 68 COPD patients were assessed for eligibility, among them 50 patients were included in the study with 17 patients in IV group, 19 in NEB group and 14 in control group. All 3 groups were comparable to each other in terms of demographic variables like age and sex. In terms of confounding factors like duration of pack years, duration of steroid intake, baseline PH values and serum magnesium concentration the three groups were similar and statistically not significant.

Changes in peak inspiratory pressure over a period of 30 mins was remarkably higher in IV group (19.79 %) as compared to NEB group (12.21%) and control group (10%), these changes were statistically significant.



Similarly, mean airway pressure fall in IV group (19.86%) was higher than NEB group (16.1%) and control group (15%). Fall in plateau pressure was more marked in both the study groups with 17.79% in IV group and 12.941 in NEB group and just 8% in control groups, these findings were statistically very significant.



Initiation of weaning from ventilation was also early in IV group followed by NEB and control groups respectively. With more than 50% patients were taken up for weaning by day 3 in IV group, while by day 4 and 5 in NEB and control group.

Table: INITIATION OF WEANING

Weaning	IV		Neb		C	
	No.	%	No.	%	No.	%
Day 1	0	0.00	0	0.00	0	0.00
Day 2	7	41.18	1	5.26	1	7.14
Day 3	4	23.53	6	31.58	3	21.43
Day 4	2	11.76	8	42.11	3	21.43
Day 5	3	17.65	3	15.79	3	21.43
Day 6	1	5.88	1	5.26	4	28.57
	17	100.00	19	100.00	14	100.00

Total duration of mechanical ventilation was significantly less in IV group. 65% patients in IV group were taken off ventilator on day 3 while the number was just 21% each in NEB and control group, with majority of patients taken off ventilator in NEB group by day 5 and control by day 6.

TABLE : DURATION ON VENTILATION

Days	IV		Neb		C	
	No.	%	No.	%	No.	%
2	0	0.00	0	0.00	0	0
3	11	64.71	4	21.05	3	21.43
4	0	0.00	5	26.32	3	21.43
5	3	17.65	8	42.11	2	14.28
6	3	17.65	2	10.53	6	42.86
	17	100.00	19	100.00	14	100.00

DISCUSSION

Magnesium has been referred to as "Nature's physiologic calcium blocker"[5]. This notion was further verified by lindeman et al [6], they studied the effect of magnesium sulphate on broncho-constriction and concluded that magnesium acts in the airway as a voltage-sensitive calcium channel blocker like nifedipine. The vast majority of work done on the bronchodilatory properties of magnesium and its subsequent application to patient care has been done on asthma. The evidence base for Mg use in COPD is sparse with researchers summarizing that due to the similarity between COPD and asthma and their usual treatment what appears to work in one may well be useful for other.

The aim of our study was to study the effect of magnesium sulphate given via inhalational and IV route in patients on mechanical ventilation in intensive care unit in terms of Changes in peak inspiratory pressure, mean airway pressure, weaning from mechanical ventilation & Duration of patient on mechanical ventilation.

The three groups (IV/ NEB/ Control) were comparable on the basis of demographic data and potential confounding factors. Therapeutic intervention was done and no significant difference in physiological parameters such as heart rate, blood pressure, respiratory rate or any serious adverse effect was noted at the end of intervention.

Although experimental data from as far back as 1912 suggested that magnesium relaxed bronchial smooth muscles of animals [7], however first successful use of magnesium in treatment of asthma in human was documented in 1940 [8].

In our study we found that administration of magnesium with iv route resulted in relieve of bronchospasm as demonstrated by marked reduction in P-inspiratory pressure and mean airway pressure, this was in line with previous studies [9,10], which concluded that intravenous magnesium sulphate use was safe and efficacious in COPD patient with improved PEFR in study group. Our result also corresponds to that of Juan Abreu Gonzale et al [11], which concluded that IV MgSO4 enhances the effect of inhaled β 2-agonists.

In our study we found that IV Magnesium sulfate was remarkably better than nebulized magnesium sufate, however the latter was also effective and superior to beta agonist alone in therapeutic effect. The result is inline with finding of Rodney Hughes et al [12], in asthma patients which showed improved FEV1 in magnesium group as compared to placebo.

Based on the observation we found that MgSO4 given by I/V route was more effective than nebulisation route and supplement Mg either by I/V or nebulization route had a beneficial effect over isolated salbutamol. It caused more reduction in airway pressure probably by increased bronchodilatory response of beta 2 agonist by increased receptor affinity for the agonist or by facilitating the externalization of the receptors on the surface of the cellular membranes of the target organ. COPD is defined as disease in which airway obstruction is irreversible and bronchodilatory response is limited. We believe the enhancing effect on salbutamol induced bronchodilation that we observed with administration of IV MgSO4 to be noteworthy in view of the limited bronchodilatory effect of beta 2 agonist in COPD. The result of this enhanced bronchodilatory effect was evident in our study. We found that majority of patients in IV group could be taken up for weaning by 2nd or 3rd day while for nebulization and control group it was 4th to 5th day. And finally patients in I/V group required lesser duration of ventilator support with 11 out of 17 patients requiring only 3 days of ventilator support while in nebulization group only 4 out of 19 patients could be taken off from ventilatory support while in control group only 3 out of 14 patients could be taken off from ventilator support at the end of day 3. Time taken to remove 50% patient from ventilator support was 3 days in IV group, while 5 days in nebulization and control group.

CONCLUSION

In conclusion, we found that MgSO4 given by I/V route was more

effective than nebulisation route and supplement Mg either by I/V or nebulisation route had a beneficial effect over isolated salbutamol it caused more reduction in airway pressure probably by increased bronchodilatory response of beta2 agonist. Administration of MgSO4 especially by I/V and also nebulization route reduces the duration of ICU stay, duration of assisted ventilator requirement and duration of weaning. Thus, MgSO4 is a potential additive drug to the current treatment protocol of management of acute exacerbation of COPD.

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