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Research Article

**HIGH-ALTITUDE PULMONARY OEDEMA: NEWER
TREATMENT MODALITIES FOR AN AGE-OLD PROBLEM**¹Dr Fouzia Iqbal, ²Dr Sana Abbas, ³Dr Salman Tahir¹King Edward Medical College²Xi'an jiaotong University China.³Foundation University Islamabad**Article Received:** August 2020**Accepted:** September 2020**Published:** October 2020**Abstract:**

Background & objectives: High-altitude pulmonary oedema (HAPE) poses a challenge to the healthcare providers in remote mountainous areas, low resource settings. Mountain terrain with high-altitudes has low convenience of resources. We conducted the study to evaluate the rise in peripheral capillary saturation of oxygen (SpO₂) by using a partial rebreathing mask (PRM) in comparison to Hudson's mask among patients with HAPE.

Methods: This was a randomized single centered, crossover study which was conducted to determine the efficiency of PRM in comparison to Hudson's mask. 88 total patients with HAPE were included in the study, referred to a secondary healthcare facility at an altitude of 11,500 feet from January to October 2013 were studied. A crossover after adequate wash-out on both modalities was conducted for first two days of hospital admission. All patients with HAPE were managed with bed rest and stand-alone oxygen supplementation with no adjuvant pharmacotherapy.

Results: The mean SpO₂ on ambient air on arrival was 66.92±10.8 per cent for all patients with HAPE. Higher SpO₂ values were achieved with PRM in comparison to Hudson's mask on day one (86.08±5.15 vs. 77.23±9.09%) and day two (89.94±2.96 vs. 83.39±5.93%). The difference was more pronounced on day one as compared to day two.

Interpretation & conclusions: Mean SpO₂ values were found to be significantly higher among HAPE patients using PRM compared to those on Hudson's mask. Further studies to understand the translation of this incremental response in SpO₂ to clinical benefits (recovery times, mortality rates and hospital stay) need to be undertaken.

Key words Environmental illness - high-altitude pulmonary oedema - occupational health - oxygen delivery systems - oxygen therapy

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INTRODUCTION:

With increasing tourism and military deployment worldwide in high-altitude areas (HAAs), the incidence of high-altitude illnesses (HAIs) is increasing. Also contributing to this increased rate is the faster transportation by air to HAA, decreasing the period of acclimatization. Hypobaric hypoxia is the underlying pathophysiological crux for all HAIs¹. The management of these diseases revolves around descent from altitude and/or effective oxygen supplementation therapy². While numerous oxygen delivery systems are used in clinical practice, the efficacy of each system is dictated by the delivered fraction of oxygen in inspired air (FiO₂). Devices which provide high FiO₂ achieve higher blood oxygenation.

A literature search showed several reviews on various oxygen delivery systems in both physiological and pathological conditions³⁻⁶. Two groups of investigators also studied the effect of oxygen demand systems in patients with chronic obstructive pulmonary diseases^{7,8}. No similar study has been found specifically for the treatment of HAI. Therefore, this study was undertaken to determine the rise in peripheral capillary saturation of oxygen (SpO₂) by using a partial rebreathing mask (PRM) in comparison to Hudson's mask among patients of high-altitude pulmonary oedema (HAPE).

MATERIAL & METHODS:

A single-center, interventional randomized crossover study design was formulated to determine the efficiency of PRM in comparison to Hudson's mask in patients with HAPE. This study was conducted at a tertiary care Mayo hospital Lahore.

A total of 104 patients were screened during a period of 10 months between January and October 2018. The Lake Louise criteria⁹ for HAPE, *i.e.* the presence of at least two pulmonary signs among wheezing or rales in at least one lung field, tachycardia, central cyanosis, tachypnoea, and any two pulmonary symptoms among cough, weakness or decreased exercise performance, chest tightness or congestion, dyspnea at rest, were used to screen patients. All consecutive patients with positive chest X-ray (CXR) for HAPE during the study period were included. Uniformity for clinical severity was maintained in all patients using scoring criteria of Vock *et al*¹⁰. Other inclusion criteria followed were previously healthy subjects aged >18 yr. with no known co-morbidities and willingness to participate. Exclusion criteria were highlanders with HAPE, fresh diagnosis of other co-morbidities (hypertension, diabetes mellitus), simultaneous presence of high-altitude cerebral oedema (HACE) and withdrawal of informed consent.

Of the total number of patients screened, 88 patients with HAPE were included in the study (Fig. 1).

Study protocol: The patients were allocated to two interventional groups based on the first used oxygen delivery system (group 1 Hudson's mask first and group 2 PRM first). Patients in each interventional group were crossed over after an adequate wash-out period. Patients were selected by alphabetic randomization, in which all individuals with given first names starting from A to M were randomized to group 1 and N to Z were randomized to group 2. Four hourly clinical monitoring by vital parameters (pulse, blood pressure, SpO₂) was done in intensive care centre settings. Any patient with clinical deterioration in either interventional group was treated as per clinical status.

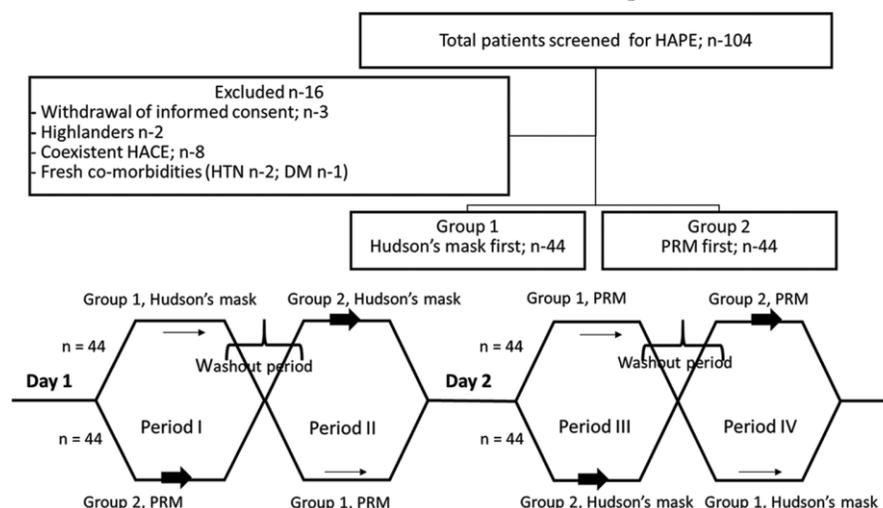


Fig. 1. Consort diagram and crossover design of the study. HAPE, high-altitude pulmonary oedema; HACE, high-altitude cerebral oedema; PRM, partial rebreathing mask; HTN, hypertension; DM, diabetes mellitus.

Day one: First, peripheral capillary saturation of oxygen (SpO₂) on ambient air at admission was recorded for all patients. Group 1 patients were treated with oxygen delivered via Hudson's mask and group 2 patients with PRM. After four hours of initial therapy, the patients were switched to the other modality of oxygen delivery for the next four hours, after either a wash-out interval of 30 min or a decline in SpO₂ levels, whichever was earlier. Finally, patients from group 1 were continued on Hudson's mask till the next day and group 2 patients with PRM.

Day two: On the next day of treatment, baseline SpO₂ levels were taken after either a wash-out period of 30 min in which no oxygen supplementation was given or a decline in SpO₂ levels, whichever was earlier. The sequence of delivery modalities was then switched. Group 1 patients were now started with PRM and group 2 with Hudson's mask. Each system was followed by the other with intervening wash-out period as described earlier. For every treatment modality, SpO₂ recorded at the end of four hours of continuous use of either Hudson's mask or PRM was used for statistical analysis (Fig. 1).

Statistical analysis: Statistical analysis was carried out using R Core Team (2017). R: A Language and Environment for Statistical Computing¹¹. Bland-Altman plot was drawn to compare oxygen delivery through the PRM and Hudson's mask. For analysis, a $P \leq 0.05$ was set to be statistically significant.

RESULTS & DISCUSSION:

The mean SpO₂ on ambient air, on arrival, was 66.92 ± 10.8 per cent for all patients with HAPE. Mean SpO₂ values were found to be higher in patients using PRM on both days one and two, as shown in the Table. Boxer plots for mean SpO₂ levels are as shown in Fig. 2. Bland-Altman analysis (Fig. 3) showed that PRM had greater SpO₂ across all ranges of SpO₂ values. The difference between PRM and Hudson's mask at average SpO₂ of 80 per cent was 10.27 per cent [95% confidence interval (CI): 9.62-10.92]. With each one per cent increase in average SpO₂, the difference decreases by 0.62 per cent (95% CI: -0.71 to -0.53%). The difference decreased at higher SpO₂ concentrations.

Table. Mean SpO₂ on days one and two using different oxygen delivery systems

Oxygen delivery system	SpO ₂ (%), mean \pm SD	
	Day one	Day two
Ambient air	66.92 \pm 10.8	75.41 \pm 8.45
Hudson's mask	77.23 \pm 9.09	83.39 \pm 5.93
PRM	86.08 \pm 5.15	89.94 \pm 2.96

SD, standard deviation; PRM, partial rebreathing mask; SpO₂, peripheral capillary saturation of oxygen

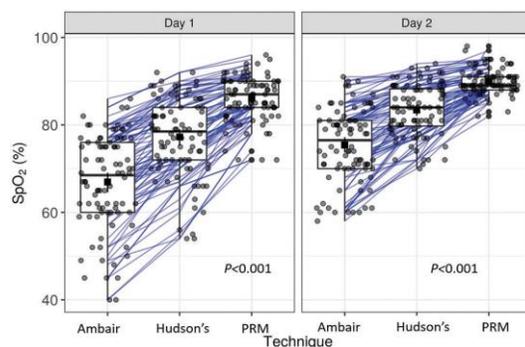


Fig. 2. Boxer plot with different oxygen delivery systems on days one and two. Square dots with bars, Mean with 95% confidence interval. SpO₂, Peripheral capillary oxygen saturation; Ambient air, ambient air; Hudson's, Hudson's mask; PRM, partial rebreathing mask.

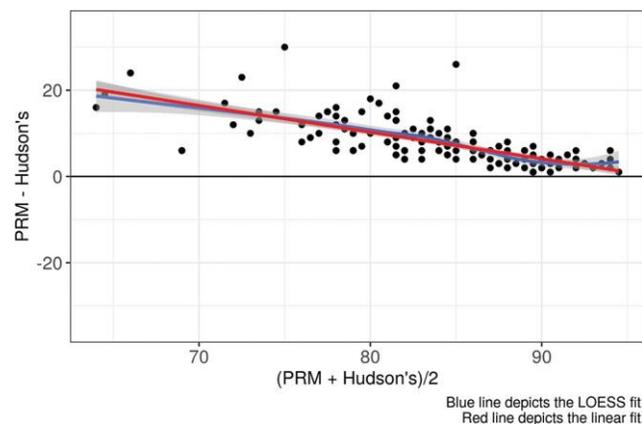


Fig. 3. Bland-Altman analysis for Hudson's mask versus partial rebreathing mask (PRM).

The partial pressure of oxygen (PO_2) is the driving force for the diffusion of oxygen molecules from inspired air to alveolar air, then into the blood and ultimately into the cells and mitochondria. This is known as the oxygen cascade¹². The PO_2 in inspired air (PIO) is given by the equation¹³:

$PIO = FiO \times (Pb - 47 \text{ mmHg})$, where Pb is barometric pressure, and 47 mmHg is vapour pressure of H_2O at 37°C.

The proportion of air comprised of oxygen (FiO_2 , 20.94%) remains constant at the highest altitude up to upper troposphere. The alveolar vapour pressure of water is also constant at 47 mmHg. Hence, the PIO_2 and thus the oxygen cascade is directly affected by barometric pressure (Pb)¹².

Pb diminishes exponentially with increasing altitude. Other variables which decrease Pb include lower temperature, inclement weather during winter and high latitude. Although the effect of these variables upon Pb is not nearly as significant as altitude, it becomes physiologically substantial at elevations over approximately 2800 m¹⁴. Therefore, diminished PIO_2 at high altitude is the direct result of low Pb . As PIO_2 decreases, so does the partial pressure of alveolar oxygen (PAO_2), arterial PO_2 (PaO_2) and SpO_2 resulting in tissue hypoxia. This form of hypoxia is hypobaric hypoxia, and represents the initial cause of HAI.

Treatment modalities for HAI in general and HAPE in particular, have seen a sea change in the last decade. While drugs such as calcium channel blockers and diuretics were the chief weapon of the treatment arsenal, more and more research are now pointing to oxygen therapy as being the superior alternative. A

randomized controlled trial suggested that HAPE could be adequately treated by oxygen therapy and bed-rest alone, in situations where descent was not possible and pharmacological agents showed no added advantage¹⁵.

The Hudson's mask is a simple facemask that has been described as a variable performance oxygen delivery system¹⁶. Concentration of up to 60 per cent can be achieved with moderate oxygen flow rates (6-10 l/min). These are most commonly used due to wide availability and ease of use. The use of non-rebreather masks to achieve greater FiO_2 has also been studied^{17,18}. A low-flow device, the partial rebreather mask, can deliver 40-70 per cent oxygen at flow rates of 6-10 l/min¹⁹. The oxygen flow should keep the reservoir bag at least one-third to one-half full on inspiration²⁰. Our study showed superior results with a PRM which could be explained by the delivery of higher FiO_2 due to the use of a reservoir.

Our study was limited by the inclusion of only male patients, and therefore, the data cannot be generalized to females. Clinical outcomes (recovery times, days of hospitalization and mortality) were also not correlated with the improved SpO_2 levels.

In conclusion, our study showed the PRM to be consistently superior to conventional devices such as the Hudson's mask, in the delivery of higher flow rates and maintenance of higher SpO_2 for quicker clinical recovery. The SpO_2 for patients on PRM was consistently higher on day one and two as compared to those on Hudson's mask.

Conflicts of Interest: None.

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