Medicina Intensiva 48 (2024) 546–554

medicina intensiva

http://www.medintensiva.org/en/

SCIENTIFIC LETTER

Acute respiratory distress syndrome at high altitude: Considerations for diagnosis and treatment

Síndrome de distrés respiratorio agudo en la altitud: consideraciones sobre el diagnóstico y tratamiento

To the Editor,

Acute respiratory distress syndrome (ARDS) is an acute respiratory failure due to inflammation triggered by pulmonary and non-pulmonary injuries that lead to altered permeability of the alveolar-capillary barrier and profound hypoxemia. ARDS was redefined by a panel of experts in Berlin in 2012.[1] Although the Berlin criteria improved the validity and reliability of the definition, they did not make it possible to diagnose ARDS in specific settings.[2] The Kigali modification proposed a mechanism to identify ARDS in resource-limited settings because the Berlin definition requires positive pressure ventilation, arterial blood gas measurements, and chest X-rays. These requirements mean that many ARDS patients cannot be diagnosed in many parts of the world, which is important because a lack of recognition leads to treatment failure.[3]

Since all estimates of the incidence of ARDS come from developed countries, which have significant differences vs developing countries on the availability of intensive care unit (ICU) beds, human and material resources (mechanical ventilation, gas determination, etc.), and decision-making criteria such as end-of-life decisions, Kigali proved important. The Kigali modification proposed replacing the ratio of partial pressure of oxygen (PaO_2) to the fraction of inspired oxygen (FiO_2) with the oxygen saturation (SpO_2) to FiO_2 ratio when blood gas determination is not possible, forgoing the requirement of mechanical ventilation with PEEP 5 cmH_2O in places where ventilation capacity is low, allowing the use of lung ultrasound in addition to chest X-ray to define bilateral opacities, validating alternative diagnostic modalities in resource-rich settings, and preventing ARDS by screening patients in all hospital areas, not just ICUs.[2,3]

Another specific setting is altitude. Critical care medicine at altitude (CCA) is the medicine that manages critically ill patients residing at an altitude of 1500 m above sea level (masl) or higher; this affects 2% of the world's population. The consideration of 1500 masl is because adaptations derived from the progressive decrease in barometric pressure, following the ascent to altitude, and changes to arterial blood gas tests are observed from that altitude upwards. The highest altitude ICUs in the world are located in Cerro de Pasco, Peru at 4380 masl and El Alto, Bolivia at 4150 masl.[4] From a practical standpoint, it has been proposed to categorize altitude related to CCA into 3 levels: medium altitude (1500 masl up to 2500 masl), high altitude (2500 masl up to 3500 masl), and very high altitude (3500 masl up to 5800 masl).[4]

The CCA framework is very similar to that outlined in the Kigali modification: low economic resources, lack of ICU beds, specialized personnel, limited material resources, etc., with the addition of altitude.[5] At altitudes above 1500 masl, variables such as barometric pressure, inspired O_2 pressure (PIO_2), and PaO_2 are decreased, and the higher the altitude, the greater the decrease (Table 1).[4,6] Another important factor differentiating it from sea level is the mean pulmonary arterial pressure, which at altitudes above 1600 masl is $\geq$ 18 mmHg, and in the presence of high-altitude ARDS, can far exceed 20 mmHg, variables that must be considered in treatment and use of PEEP.[7]

If ARDS were diagnosed at high altitude (HA-ARDS) using the Berlin criteria, the clinical application of strategies such as high-flow nasal cannula oxygenation would delay its diagnosis. The Berlin Consensus stratified the severity levels of ARDS but was aware of the difficulty in applying it at altitude and proposed a correction formula to diagnose in populations located above 1000 masl (($PaO_2/FiO_2 \times$ barometric pressure)/760).[1] However, the PaO_2/FiO_2 ratio measured in various studies and calculated using the Berlin Consensus formula does not seem to be consistent with reality,[4] and in acclimatized patients on invasive mechanical ventilation, this adjustment equation appears to be inaccurate.[8]

Therefore, the diagnostic criteria for HA-ARDS remain controversial: severity stratification must be discussed and reconsidered, especially in poorly adapted patients, as well as the replacement of the SpO_2/FiO_2 ratio with the PaO_2/FiO_2 ratio, as has been proposed in low-income countries.[2,3] In a study conducted at 2600 masl, the SpO_2/FiO_2 and PaO_2/FiO_2 ratios were correlated, and it was concluded that both have similar diagnostic performance to treat severely hypoxemic ventilated patients.[9]

In a consensus conference on HA-ARDS diagnostic criteria in Western China, Zhang et al. noted that, although it has the same etiology, disease, and physiology as low-altitude ARDS, HA-ARDS is influenced, from >1500 masl, by the progressive increase in altitude, the drop in PIO_2, and the environmental factors of high altitudes, which result

DOI of original article: https://doi.org/10.1016/j.medin.2024.04.006

Table 1 Relationship among altitude, barometric pressure, and gasometric values.[4]

Altitude (masl)	PB/PIO_2 (mmHg)	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	SaO_2 (%)	PaO_2/FiO_2[a]
Sea level	760/160	100	45	95	476
1818[b]	699/147	78.19	34.6	96.24	372
2640[c]	560/118	68.6	31.2	93.6	327
3600[d]	495/104	55.9	28.4	86	266
4380[e]	457/96	54.18	27.7	87	258

Masl, meters above sea level; PaO_2/FiO_2, partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ratio.
[a] Values measured in various studies with ambient air (FiO_2 at 21%).
[b] Huánuco, Peru.
[c] Bogotá, Colombia.
[d] La Paz, Bolivia.
[e] Cerro de Pasco, Peru.

Table 2 Proposed bases for managing HA-ARDS by the High-Altitude Critical Care Medicine Expert Committee of the Pan American and Iberian Federation of Critical Care and Intensive Therapy.

- Early recognition and diagnosis of HA-ARDS. Prevent HA-ARDS by screening patients in all hospital areas, not just at the ICUs setting.
- Use the Kigali modification in income-limited settings: replace PaO_2/FiO_2 with SpO_2/FiO_2 when blood gas determination is not possible, forgo the requirement of mechanical ventilation with PEEP 5 cmH_2O in places with low ventilation capacity, allow the use of lung ultrasound in addition to chest X-ray to define bilateral opacities.
- Improve oxygenation to reverse hypoxic pulmonary vasoconstriction:
  - ◯ At altitudes between 1000 a masl nd 3000 masl, it is recommended to start oxygenation when SpO_2 is <90%-to-88%, always considering the clinical context.
  - ◯ At altitudes above 3000 masl, when SpO_2 is <8 5%.
- Oxygenation targets at altitude: Gasometric values can serve as a guide to achieve oxygenation close to the different altitudes where patients reside.
  - ◯ At altitudes > 2500 masl up to 3500 masl, maintain SpO_2 between 91% and 96% (93%) and PaO_2 between 61.1 and 68.6 mmHg (64.5 mmHg).
  - ◯ At altitudes > 3500 to up 4380 masl, maintain SpO_2 between 86.2% and 87% (86.61%) and PaO_2 between 54.18 and 55.9 mmHg (55.04 mmHg).
  - ◯ Avoid hyperoxia: > 2500 masl up to 3500 masl > 96% and 3500 up to 4380 > 87%.
- Control hypercapnia, maintaining $PaCO_2$ according to its gasometric value at each altitude level.
- Monitor pulmonary arterial pressure using advanced echocardiography to avoid right ventricular dysfunction or its surrogates, such as tricuspid annular plane systolic excursion (TAPSE), basal and mid diameters, RV/LV ratio, RV area, paradoxical septal movement, free RV wall thickness, etc., using basic or point-of-care echocardiography.
- In adults on mechanical ventilation with HA-ARDS, it is recommended to reduce pulmonary stress, stretch/strain, atelectrauma, and barotrauma:
  - ◯ Use tidal volumes from 4 mL/kg up to 8 mL/kg of weight.
  - ◯ Avoid excessive alveolar distending pressure by keeping it < 15 cmH_2O.
  - ◯ When lung compliance is decreased (<40 mL/cmH_2O), a gradual increase in PEEP up to a maximum of 14—15 cmH_2O with control of PEEP effects is proposed (in individualized cases, more may be required).
  - ◯ If PEEP > 10 cmH_2O is used, right heart dysfunction should be monitored.
  - ◯ Keep plateau pressure < 30 cmH_2O.
- For adults on invasive mechanical ventilation with moderate-to-severe ARDS, prone position ventilation (PPV) from 12 through 16 h is proposed. Pulmonary hypertension is present in patients with HA-ARDS, and PPV should be implemented early, with prolonged duration to reduce lung injury and protect cardiac function.
- For adults on mechanical ventilation with HA-ARDS, a conservative fluid strategy is proposed. Due to the complex pathophysiological mechanism of HA-ARDS, often due to acute pulmonary edema at altitude, inadequate fluid therapy would increase pulmonary blood flow, induce or worsen pulmonary edema, lead to more severe hypoxemia, and harm right heart function.
- Usual critical patient support care: nutritional support, glucose control, deep vein thrombosis and stress ulcer prophylaxis, etc.

in significant pathophysiological changes, clinical signs and symptoms, and arterial blood gas parameters.[10]

In conclusion, people living at high altitudes exhibit physiological and anatomical differences derived from physiological adaptation mechanisms. Therefore, HA-ARDS also has its own pathophysiological features. The diagnostic and management strategies for HA-ARDS are different from those for ARDS in lower altitude areas and remain unclear. The clinical definition of ARDS complicates the management of this syndrome regarding quantification in resource-limited settings or at altitude. It is necessary to develop methods to identify and treat ARDS in the overall context, even if it may require adapting the current Berlin definition and validate potential changes to avoid missing out on the opportunity to effectively diagnose and treat these patients and improve their outcomes in the mentioned settings.

Table 2 shows the bases for managing HA-ARDS by the High-Altitude Critical Care Medicine Expert Committee of the Pan American and Iberian Federation of Critical Care and Intensive Therapy.

Funding

None declared.

Conflicts of interest

None declared.

References

1. ARDS Definition Task ForceRanieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307:2526–33, http://dx.doi.org/10.1001/jama.2012.5669.
2. Buregeya E, Fowler RA, Talmor DS, Twagirumugabe T, Kiviri W, Riviello ED. Acute respiratory distress syndrome in the global context. Glob Heart. 2014;9:289–95, http://dx.doi.org/10.1016/j.gheart.2014.08.003.
3. Riviello ED, Buregeya E, Twagirumugabe T. Diagnosing acute respiratory distress syndrome in resource limited settings: the Kigali modification of the Berlin definition. Curr Opin Crit Care. 2017;23:18–23, http://dx.doi.org/10.1097/MCC.0000000000000372.
4. Tinoco-Solórzano SA, Nieto VH, Vélez-Páez JL, Molano D, Viruez-Soto A, Villacorta-Córdoba F, et al. Medicina intensiva en la altitud. Revisión de alcance. Rev Med Intensiva Cuid Crít. 2020;13:218–25.
5. Bolivia tiene 190 intensivistas y 430 UTI, 38% de lomínimo requerido. Sociedad Boliviana de Medicina Crí-tica y Terapia Intensiva. EJU.tv; 2020 [Accessed 6 April 2024]. Available from: https://eju.tv/2020/04/bolivia-tiene-190-intensivistas-y-430-uti-38-de-lo-minimo-requerido/2020
6. Avellanas Chavala ML. A journey between high altitude hypoxia and critical patient hypoxia: what can it teach us about compression and the management of critical disease? Med Intensiva (Engl Ed). 2018;42:380–90, http://dx.doi.org/10.1016/j.medin.2017.08.006.
7. Guo L, Sun J, He Z, Shi Q, Ma S. Understanding acute respiratory distress syndrome in high-altitude environments: a comprehensive review of diagnosis and treatment. Med Sci Monit. 2023;29:e939935, http://dx.doi.org/10.12659/MSM.939935.
8. Jibaja M, Ortiz-Ruiz G, García F, Garay-Fernández M, de Jesús Montelongo F, Martinez J, et al. Hospital mortality and effect of adjusting PaO_2/FiO_2 according to altitude above the sea level in acclimatized patients undergoing invasive mechanical ventilation. A multicenter study. Arch Bronconeumol (Engl Ed). 2020;56:218–24, http://dx.doi.org/10.1016/j.arbres.2019.06.024.
9. Ortiz G, Bastidas A, Garay-Fernández M, Lara A, Benavides M, Rocha E, et al. Correlation and validity of imputed PaO_2/FiO_2 and SpO_2/FiO_2 in patients with invasive mechanical ventilation at 2600 m above sea level. Med Intensiva (Engl Ed). 2022;46:501–7, http://dx.doi.org/10.1016/j.medine.2021.05.010.
10. Zhang SF, Lin SX, Gao W, Liu HP, Liu Y, Zhang DH, et al. Report of the consensus conference on diagnostic criteria of ALI/ARDS at high altitudes in Western China. Intensive Care Med. 2001;27:1539–46, http://dx.doi.org/10.1007/s001340101052.

Adrián Avila-Hilari[a,g], Amilcar Tinoco-Solórzano[b,g], Jorge Vélez-Páez[c,g], Daniel Molano Franco[d,g], Felipe de Jesús Montelongo[e,g], Manuel Luis Avellanas-Chavala[f,g,*]

[a] *Unidad de Terapia Intensiva, Hospital Municipal Boliviano Holandés, El Alto, Bolivia*
[b] *Centro de Investigación de Medicina en la Altura, Facultad de Medicina Humana, Universidad de San Martín de Porres, Huanyaco, Peru*
[c] *Unidad de Terapia Intensiva, Hospital Pablo Arturo Suárez, Quito, Ecuador*
[d] *Unidad de Cuidados Intensivos, Hospital San José, Bogotá, Colombia*
[e] *Áreas Críticas, Hospital General Las Americas, Instituto de Salud del Estado de México, Ecatepec de Morelos, Mexico*
[f] *Médico Especialista en Medicina Intensiva, Huesca, Spain*
[g] *Comité de Expertos de Medicina Crítica en la Altitud, Federación Panamericana e Ibérica de Medicina Crítica y Terapia Intensiva (FEPIMCTI), Panama City, Panama*

* Corresponding author.
E-mail address: mlavellanas@gmail.com
(M.L. Avellanas-Chavala).