21. Circulation in neonatal llamas and sheep: a tale of two species

Aníbal J. Llanos[1], Felipe A. Beñaldo[1], Claudio E. Araya-Quijada[1], María Serón-Ferré[1], Emilio A. Herrera[1], Víctor R. Reyes[1], Germán Ebensperger[1]

Mammalian neonates are born at high and lowlands, with high and low environmental PO2, respectively. However, regardless of the place of birth, is mandatory to all newborns to establish a pulmonary function once they enter into this breathing world. To that, the neonate mounts a high blood flow-low vascular resistance pulmonary circulation instead of the low blood flow-high vascular resistance that the fetus had in utero. Most of these dramatic changes occur smoothly after birth at sea level, although some newborns are unable to successfully change the pulmonary circulation resulting in pulmonary hypertension of the neonate (PHTN). At high altitude, fetal-to-neonatal transition is more difficult in lowland species due to the low PO2, and the respiratory distress syndrome of the neonate, that includes the PHTN, is 9 times more frequent at high than low altitudes. In contrast to neonates from lowland species, the neonatal llama can launch efficiently a pulmonary function at altitudes over 3000 up to 4500 m of altitude, without pulmonary arterial hypertension. To understand some mechanisms producing this remarkable adaptation, we studied the nitric oxide (NO) and carbon monoxide (CO) roles in the regulation of the pulmonary circulation in lowland and highland newborn sheep and llamas. We used neonatal sheep (Ovis aries) and llamas (Lama glama) whose gestation and delivery took place at low (580 m; Santiago) or high altitude (3600 m; Putre Research Station, INCAS). In vivo, we measured the cardiopulmonary function basally and with a NO synthase (NOS) blockade and calculated the production of carbon monoxide by the lung. In vitro, we determined eNOS and soluble guanylate cyclase (sGC) expression, NOS activity, and hemoxygenase-1 (HO-1) expression in the lung. Pulmonary arterial pressure was elevated at high altitude in sheep but not in llamas. Sheep at high altitude relative to sea level had significantly greater total lung NOS activity and eNOS protein, but reduced sGC, HO-1 expression and carbon monoxide production. In contrast, llamas showed no difference in NO function between altitudes, but a pronounced increase in pulmonary carbon monoxide production and HO expression at high altitude. In the llama, enhanced pulmonary CO, rather than NO, protects against pulmonary hypertension in the newborn period at high altitude. This shift in pulmonary dilator strategy from NO to CO may give insight into new treatments for excessive pulmonary vasoconstriction. FONDECYT 1140647, 1050479, Chile and The Wellcome Trust, CRIG 072256, UK.

1 Programa de Fisiopatología, Instituto de Ciencias Biomédicas (ICBM), Facultad de Medicina e International Center for Andean Studies (INCAS), Universidad de Chile, Chile
Correspondencia: Aníbal J. Llanos; anibal.llanos@gmail.com