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Adrenomedullin: A Player at High Altitude?

To the Editor:

Adrenomedullin is a potent vasodilating peptide first isolated from pheochromocytoma.1 Adrenomedullin induces vasorelaxation by activating adenylate cyclase and by stimulating the release of nitric oxide via specific receptors.2-3 The messenger RNA is strongly expressed in the human lungs but also in various tissues including heart, aorta, kidneys, thyroid, and adrenal medulla.2 Adrenomedullin plasma levels are raised in experimental pulmonary hypertension.4 Hypoxemia at high altitude induces increased pulmonary arterial resistance with subsequent increase in pulmonary arterial pressure and can result in life-threatening pulmonary edema.5

To examine the pathophysiological significance of adrenomedullin in hypoxic conditions, we measured plasma adrenomedullin concentrations in 10 healthy mountaineers (three women and seven men; mean ± SD age, 32 ± 5 years) at Capanna Regina Margherita high-altitude research laboratory at Monte Rosa, Italy (altitude, 4,559 m above sea level). Three days after baseline examination at 540 m (barometric pressure, 740 mm Hg), the subjects ascended to 4,560 m (barometric pressure, 410 mm Hg) within a period of 72 h. The ascent consisted of transport by cable car to an altitude of 3,200 m and a 2-h climb to an altitude of 3,600 m, where the subjects stayed for 2 nights. Then another 5-h climb brought the subjects to the high-altitude research laboratory at 4,560 m. The subjects were examined after a 4-h rest on the day of arrival (day 1) and the next morning (day 2). Blood samples were taken with tubes that contained 1 mg/mL disodium EDTA and 500 U/mL aprotinin, centrifuged immediately and stored at −20°C. Plasma ADM levels were measured by specific radioimmunoassay (Phoenix Pharmaceuticals; Mountain View, Calif; intra-assay CV, <5.0%; detection limit, 3.01 pg/mL).

All subjects had severe hypoxia at high altitude (arterial oxygen saturation, 78±5%; partial pressure of oxygen, 45±4 mm Hg; partial pressure of carbon dioxide, 32±3 mm Hg). All subjects developed symptoms of acute mountain sickness (Lake Louise acute mountain sickness score, range, 4 to 9; mean±SD, 6.0±1.1), but none of the subjects developed high-altitude pulmonary edema or high-altitude cerebral edema. Plasma adrenomedullin concentrations were significantly higher at high altitude (day 1, mean±SD, 32.4±8.3 pg/mL; day 2, 34.1±9.1 pg/mL) as compared with baseline measurements (18.4±3.5 pg/mL; p<0.001) (Figure 1).

The results suggest that adrenomedullin is involved in pathophysiological changes at high altitude. Exposure to an altitude of 4,560 m leads to a twofold increase in pulmonary arterial pressure.5 The role of adrenomedullin in the regulation of pulmonary circulation at high altitude is not clear at present, but high levels of adrenomedullin may be a response to counter hypoxic vasoconstriction in the pulmonary arterial circulation.

The pathophysiological significance of adrenomedullin in the development of high-altitude pulmonary edema needs to be elucidated in further studies.

Marcell Toeyger, MD
Gunter Hartmann, MD
Maximilian Schlosshauer, MD
Hubert Haartann, MD
Matthias Tschep, MD
Rainald Fischer, MD
Rudolf M. Huber, MD
Department of Medicine
Klinikum Innenstadt
Ludwig-Maximilians-University
Munich, Germany

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Solitary Pulmonary Lesion Evaluations

To the Editor:

The article by Goldberg-Kahn et al (April 1997) in which the authors compared the cost-effectiveness of four different strate-