International Conference 'Advances in Pneumology'
Bonn, 17-18 June 2011

INTERMITTENT HYPOXIA AS TWO-FACED JANUS: BENEFICIAL AND ADVERSE EFFECTS ON PATIENTS

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Intermittent hypoxia (IH) is defined as repeated hypoxia episodes interspersed with episodes of normoxia. Oxygen, this two-faced Janus, is necessary for life, but this very aggressive molecule has to get into an organism in strictly dosed quantity. IH is the most frequent form of hypoxia, occurring in the developing mammals. It has been widely accepted that for the majority of a population recurrent episodes of hypoxia are more often encountered during lifetime than sustained hypoxia. During the last decades the IH was gradually progressing as a procedure revealing its notable preventative, curative and rehabilitative potential. It has been referred as an effective stimulus evoking various respiratory, cardiovascular, metabolic, and cellular responses. Numerous modern studies collectively show that IH (1) increases exercise tolerance, hypoxic ventilatory response, hematocrit and blood hemoglobin content; (2) stimulates endothelial NO production provoking vasodilatation, opening of reserve capillaries and preventing Ca2+ overload; (3) stimulates angiogenic growth factor synthesis by endotheliocytes and monocytes; (4) augments the activity of parasympathetic nerve system; (5) enhances antioxidant defense system and increases the resistance of Na+-K+ ATPase to oxidative stress; (6) induces changes within mitochondria increasing the O2 utilization efficiency of ATP production; (7) mobilizes hematopoietic progenitors and augments cellular and humoral elements of innate immunity. Another distinct source of information about the effects of IH provides observation over patients with chronic recurrent apneas, especially obstructive sleep apnea syndrome (OSAS). Different patterns of IH are also registered during Cheyne-Stokes or Kussmaul breathing where periods of hyperventilation succeeds apneas lasting several seconds to minutes. Irregular breathing patterns accompany acute mountain sickness after rapid ascent to high altitude. So, from clinical point of view short-term reduction in oxygen delivery may be a major risk factor for heart and lung diseases, stroke and even sudden death. Pathophysiological effects induced by IH consist in (1) chemoreflex-mediated increase in sympathetic nerve activity, respiratory motor output and the modulation of peripheral chemoreflex sensitivity; (2) systemic arterial blood pressure elevation; (3) stroke and myocardial ischemia; (4) neuromechanical reflex bronchoconstriction; (5) fatigue, headaches, cognitive impairments, irritability and mood disturbances; (5) increased oxidative stress; (6) activation of inflammatory pathways, increased levels of TNFalpha, IL-6, IL-8 and C-reactive protein. The central question is why the intermittent hypoxia imposed by OSAS and other pathological events vs. that administered therapeutically can produce such divergent effects on an organism. Underlying reason is the dose of hypoxic impact and the mode of application. It should be noted that low doses of hypoxia might not be sufficient stimuli to mobilize adaptive mechanisms, whilst severe or prolonged hypoxia may provoke dangerous pathological processes. Extensive evidence in animals and humans has shown controlled

intermittent hypoxia conditioning programs to be safe, efficacious modalities for prevention and treatment of many diseases. However, substantial variations in the intensity of hypoxia, duration and number of hypoxic exposures per session, and number and frequency of sessions complicate comparisons of results of different studies. For example, due to still scarce number of data, that analyze the effectiveness of IH exposure of patients with COPD and bronchial asthma, it is difficult to recommend IH as a routine therapy for these diseases. But the preliminary results of current research are very promising. Specific prognostic criteria are being developed to assess each patient's adaptability to IH. Intensive studies on approaches to dosage selection are being performed. Moreover, safe, portable, inexpensive IH devices - hypoxicators - are being developed and tested. However, taking into account the increasing prevalence of respiratory and cardio-vascular disease, every effort to reduce morbidity and mortality, associated with these diseases is justified. We believe that one day, maybe in next future Intermittent Hypoxia will be useful in the prevention and treatment of different diseases and as in the adaptation to physical exercise and stay on high altitudes.