Local and general hypoxia in restless legs syndrome/Willis-Ekbom disease (RLS/WED).

A review of what we know today

Jan Ulfberg, MD PhD, Umeå University Hospital, Sweden

Oxygen has an important function in the biosynthesis of dopamine (1).

It was claimed by Ekbom in 1945 that the symptoms of restless legs syndrome/Willis-Ekbom disease (RLS/WED) were due to impaired circulation in the small vessels of the lower extremities leading to local hypoxia (2). Anderson and collaborators demonstrated impaired microvascular circulation indicating local hypoxa in the legs in patients with RLS/WED in comparison to matched controls by using bilateral great toe laser doppler flowmetry together with whole-body thermography (3). A proliferation of endothelial cells was found in biopsies taken from tibialis anterior muscles in patients suffering from RLS/WED, indicating that lower extremities are affected by hypoxia (4). Recently Salminen et al., by measuring oxygen partial pressure on the skin in the legs, reported that peripheral hypoxia is associated with RLS/WED (5). Moreover, RLS/WED has been associated with activation of the hypoxia-inducable factor (HIF-1) in the substantia nigra (6).

A high prevalence of RLS/WED symptoms in disorders associated with hypoxia, such as chronic pulmonary obstructive disease (COPD) and obstructive sleep apnea (OSA) has been reported (7, 8). According to altitude, a 4-fold prevalence of RLS/WED is reported among people living in Ecuador at 2816 meters, compared with those living at 4 meters above sea level (9).

Future studies, addressing this issue are warranted.

References

1. Meiser J et al. Complexity of dopamine metabolism. Cell Commun Signal 2013 May 17; 11 (1):34. doi: 10.1186/1478-811X-11-34.
2. Ekbom KA. Acta Med. Suppl 1945;158: 5-123. Thesis.
3. Anderson KN et al. J Sleep Res. 2013; 22: 315-21.
4. Wahlin- Larsson B et al. Muscle Nerve 2009; 40: 556-61.
5. Salminen AV et al. Neurology 2014;**82**:1856-61.
6. Patton SM et al. Eur J Neurol. 2011;**18**:1329-35.
7. Kaplan Y et al. Can J Neurol Sci. 2008;**35**:352-7.
8. Lakshminarayanan S et al. Mov Disord. 2005;**20**:501-3.
9. Castillo PR et al. Mayo Clin Proc. 2006;**81**:1345-47.