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Title: Serum levels of insulin-like growth factor binding protein-3 and vascular endothelial growth factor in obstructive sleep apnea patients. Effect of CPAP treatment

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Body: Background: Intermittent hypoxia in obstructive sleep apnea (OSA) is associated with increased cardiovascular risk, via activation of inflammatory pathways. Hypoxia modifies Vascular Endothelial Growth Factor (VEGF) and Insulin-like Growth Factor Binding Protein-3 (IGFBP-3) levels, which could contribute to atherogenesis and predict future cardiovascular events. Aim of the study was to compare serum levels of VEGF and IGFBP-3 in OSA patients vs. controls, to explore associations with anthropometric and sleep parameters and to study the effect of CPAP treatment on these levels. Materials and methods: In 65 patients with OSA (AHI 59.9±26.8/h) and in 31 age and BMI matched controls (AHI<15/h) (AHI 6.5±4.4/h), serum levels of VEGF and IGFBP-3 were measured. The measurement was repeated after 6 months to OSA patients under CPAP therapy. All participants were non-smokers, without any cardiovascular comorbidities. Results: At baseline, serum VEGF levels in OSA patients were significantly higher compared to controls (398.4±229 vs. 229.9±149.8 pg/ml, p<0.001), while IGFBP-3 levels were lower (1.41±0.56 vs. 1.61±0.38 µg/ml, p=0.039). VEGF levels were correlated with AHI (r=0.336, p=0.001) and ODI (r=0.282, p=0.007). At the 6-month follow-up, VEGF levels decreased in patients under CPAP treatment (341±206, p<0.001), while IGFBP-3 levels increased (1.94±0.6, p<0.001). Conclusion: In OSA patients, serum levels of VEGF are elevated, while IGFBP-3 levels are low. Six months of CPAP treatment modify these levels, indicating an augmented cardiovascular risk in untreated OSA patients, which is ameliorated after CPAP therapy.