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Title: Low circulating levels of invariant natural killer T (iNKT) cells in patients with obstructive sleep apnoea syndrome and impaired functional response to hypoxia: Implications for cancer co-morbidity

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Body: Background Recent epidemiological studies link obstructive sleep apnoea syndrome (OSAS) with increased cancer incidence and mortality. Invariant natural killer T (iNKT) cells are innate immune cells that play a key role in cancer immunity, with low circulating level of iNKT cells predicting worse prognosis in some forms of cancer. The relationship of OSAS severity with iNKT cell levels has not been examined. Methods We measured circulating iNKT cells by flow cytometry in 29 otherwise healthy male snorers being assessed by inpatient polysomnography for OSAS, and examined the relationship of OSAS severity and nocturnal hypoxaemia with iNKT levels, along with the impact of subsequent nCPAP. Using iNKT cell lines, we evaluated the effect of exposure to hypoxia for 24 hours on apoptosis and cytotoxicity. Results Patients with severe OSAS had markedly less iNKT cells (0.15%) compared to matched patients with moderate (0.22%) or no sleep apnoea (0.38%) (p<0.005). The level of iNKT cells correlated inversely with apnoea-hypopnoea index (r=-0.6369; p<0.001) and oxygen desaturation index (r=-0.6846; p<0.005). No such relationship was seen with body mass index or age. Following 6 months nCPAP therapy, iNKT cell frequency increased (p<0.05). Exposure of iNKT cells to hypoxia resulted in increased apoptosis (p<0.05), and impaired cytotoxicity (p<0.05). Conclusion Patients with OSAS have significantly reduced levels of circulating iNKT cells, which increase with nCPAP. Furthermore, hypoxia leads to impaired iNKT cell function. These observations may partly contribute to increased cancer risk in OSAS.