Abstract

Epidemiological and experimental studies have shown that insufficient or disturbed sleep can have a strong effect on glucose metabolism. In addition, sleep plays an important modulatory role in the hypothalamic-pituitary adrenal axis. The impact of disturbed or short sleep in chronic sleep disorders, such as insomnia, obstructive sleep apnoea (OSA), restless legs syndrome (RLS) and narcolepsy that alone results in poor quality of sleep and sleepiness, has not been sufficiently explored. Similarly, there is a lack of adequate research that examines the effect of narcolepsy on pregnancy.

In prospective study, we compared 11 patients with narcolepsy and cataplexy with 11 matched controls, and next we investigated three other patients groups (25 patients with OSA, 18 with RLS and 21 with primary insomnia) compared with 33 healthy controls. To examine the glucose metabolism and the function of the hypothalamic-pituitary-adrenal axis, the patients underwent an oral glucose tolerance test and a dexamethasone suppression- CRH stimulation test. In addition, we measured the level of TNF-alpha and its soluble receptors and the level of IL-6 in patients with narcolepsy. In a retrospective cohort study conducted in 12 European countries, we collected 216 patients with narcolepsy and cataplexy and 33 patients with narcolepsy without cataplexy. The patients filled out structured questionnaires about narcolepsy, delivery and newborns.

In comparison to controls, we did not find a higher prevalence of impaired glucose metabolism in patients with narcolepsy and cataplexy. The response of hypothalamic-pituitary-adrenal axis in stimulation on CRH was not changed, and we found mildly enhanced negative feedback activity. The level of cytokines was slightly increased. In patients with OSA and RLS, but not with primary insomnia we found significantly higher prevalence of impaired glucose tolerance when compared to healthy controls. Further, there was a statistically significant positive correlation between 2 hours plasma glucose values and the apnea-arousal index in OSA and the periodic leg movement index in RLS. Furthermore, we did not find significant differences between patient groups and healthy controls in dexamethasone suppression- CRH stimulation test.

Patients with symptomatic narcolepsy during the first pregnancy were older and had higher body mass index before pregnancy than patients who were asymptomatic before pregnancy. Weight gain during pregnancy was higher in patients with narcolepsy and cataplexy than in patients with narcolepsy without cataplexy. More patients with narcolepsy and cataplexy had impaired glucose tolerance or anaemia during pregnancy compared to patients with narcolepsy without cataplexy.

Three patients had cataplexy episode during delivery. Caesarean section was performed more frequently in patients with narcolepsy and cataplexy. The main weight and height of newborn did not differ between groups. The care of newborn was more difficult because of narcolepsy symptoms.

Our study confirms that narcolepsy with cataplexy by itself is not associated with disturbance of glucose metabolism, but goes along with a subtle dysregulation of inflammatory cytokine production. We also found that dynamic hypothalamic-pituitary-adrenalin system response is not altered, whereas negative feedback to dexamethasone might be slightly enhanced. In patients with RLS and OSA we found higher prevalence of impaired glucose metabolism in comparison to healthy controls, which we consider as the effect of sleep fragmentation after repeated arousals. The function of hypothalamo-pituitary-adrenal axis tested by dexamethasone suppression-CRH stimulation test in patients with RLS, OSA or insomnia is normal. It suggests that the frequently observed abnormalities of the hypothalamic-pituitary-adrenal system in psychiatric disorders are unlikely to be a consequence of altered sleep. Our international retrospective study suggests that women with narcolepsy have pregnancy outcomes comparable to women in the general population, but may require more psychological and practical childcare support from families during the postpartum period.

Key words:
Narcolepsy – Metabolism - Hypothalamo-pituitary - adrenal axis – Pregnancy