

Decreased melatonin secretion associated with higher risk of developing type 2 diabetes

April 2 2013

With previous evidence suggesting that melatonin may have a role in glucose metabolism, researchers have found an independent association between decreased secretion of melatonin and an increased risk for the development of type 2 diabetes, according to a study in the April 3 issue of *JAMA*.

"Melatonin receptors have been found throughout the body in many tissues including pancreatic [islet cells](#), reflecting the widespread effects of melatonin on [physiological functions](#) such as [energy metabolism](#) and the regulation of body weight," according to background information in the article. "Loss-of-function mutations in the melatonin receptor are associated with [insulin resistance](#) and [type 2 diabetes](#). Additionally, in a cross-sectional analysis of persons without diabetes, lower nocturnal melatonin secretion was associated with increased insulin resistance." A prospective association between melatonin secretion and type 2 diabetes has not been previously reported.

Ciaran J. McMullan, M.D., of Brigham and Women's Hospital, Boston, and colleagues conducted a study to investigate the association of melatonin secretion and the incidence of type 2 diabetes. The analysis consisted of a case-control study nested within the Nurses' Health Study cohort. Among participants without diabetes who provided urine and blood samples at baseline in 2000, the researchers identified 370 women who developed type 2 diabetes from 2000-2012 and matched 370 controls. Statistical analyses for determining associations between melatonin secretion at baseline and incidence of type 2 diabetes included

controlling for demographic characteristics, [lifestyle habits](#), measures of sleep quality, and biomarkers of inflammation and endothelial dysfunction.

Secretion of melatonin varied widely among participants in the study; the median (midpoint) urinary ratio of 6-sulfatoxymelatonin to creatinine was 67.0 ng/mg in the highest category compared with 14.4 ng/mg in the lowest category. The median ratio was significantly higher among controls (36.3 ng/mg) than among cases (28.2 ng/mg). Insulin sensitivity was higher among women with higher urinary ratios of 6-sulfatoxymelatonin to creatinine.

The researchers found that after controlling for body mass index and other lifestyle factors, menopausal status, family history of diabetes, history of hypertension, use of beta-blockers or non-steroidal anti-inflammatory drugs, region of the United States, and plasma biomarkers of diabetes risk, participants in the lowest category of urinary ratio of 6-sulfatoxymelatonin to creatinine had a 2.2 times higher odds of developing type 2 diabetes compared to participants in the highest category.

Women in the lowest category of melatonin secretion had an estimated diabetes incidence rate that was more than double that of women in the highest category (as measured by cases per 1,000 person-years).

"It is interesting to postulate from these data, in combination with prior literature, whether there is a causal role for reduced melatonin secretion in diabetes risk. Further studies are needed to determine whether increasing [melatonin](#) levels (endogenously via prolonged nighttime dark exposure or exogenously via supplementation) can increase insulin sensitivity and decrease the incidence of type 2 diabetes," the authors conclude.

More information: *JAMA*. 2013;309(13):1388-1396

Provided by The JAMA Network Journals

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