

## Melatonin may lower prostate cancer risk

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Higher levels of melatonin, a hormone involved in the sleep-wake cycle, may suggest decreased risk for developing advanced prostate cancer, according to results presented here at the AACR-Prostate Cancer Foundation Conference on Advances in Prostate Cancer Research, held Jan. 18-21.

Melatonin is a hormone that is produced exclusively at night in the dark and is an important output of the circadian rhythm, or the body's inherent 24-hour clock. Many biological processes are regulated by the circadian rhythm, including the sleep-wake cycle. Melatonin may play a role in regulating a range of other hormones that influence certain cancers, including breast and prostate cancers.

"Sleep loss and other factors can influence the amount of melatonin secretion or block it altogether, and health problems associated with low melatonin, disrupted sleep, and/or disruption of the circadian rhythm are broad, including a potential risk factor for cancer," said Sarah C. Markt, M.P.H., doctoral candidate in the Department of Epidemiology at Harvard School of Public Health in Boston. "We found that men who had higher levels of melatonin had a 75 percent reduced risk for developing advanced prostate cancer compared with men who had lower levels of melatonin.

"Our results require replication, but support the <u>public health</u> implication of the importance of maintaining a stable light-dark and sleep-wake cycle," added Markt. "Because melatonin levels are potentially modifiable, further studies of melatonin and <u>prostate cancer risk</u> and



progression are warranted."

To investigate the association between urine levels of the main breakdown product of melatonin, 6-sulfatoxymelatonin, and risk of prostate cancer, Markt and colleagues conducted a case-cohort study of 928 Icelandic men from the AGES-Reykjavik cohort between 2002 and 2009. They collected first morning void urine samples at recruitment, and asked the participants to answer a questionnaire about sleep patterns.

The researchers found that one in seven men reported problems falling asleep, one in five men reported problems staying asleep, and almost one in three reported taking sleeping medications.

The median value of 6-sulfatoxymelatonin in the study participants was 17.14 nanograms per milliliter of urine. Men who reported taking medications for sleep, problems falling asleep, and problems staying asleep had significantly lower 6-sulfatoxymelatonin levels compared with men without sleep problems, according to Markt.

Of the study participants, 111 men were diagnosed with prostate cancer, including 24 with advanced disease. The researchers found that men whose 6-sulfatoxymelatonin levels were higher than the median value had a 75 percent decreased risk for advanced prostate cancer. A 31 percent decreased risk for prostate cancer overall was observed as well, but this finding was not statistically significant.

"Further prospective studies to investigate the interplay between sleep duration, sleep disturbance, and <u>melatonin</u> levels on risk for <u>prostate</u> <u>cancer</u> are needed," said Markt.

More information: Abstract: 270322\_1

Title: Urinary melatonin levels, sleep disruption and risk of prostate



cancer; Presenter: Sarah C. Markt, M.P.H.

Introduction: The pineal hormone melatonin is a key output of the circadian rhythm and has anti-carcinogenic properties in experimental models. No study has investigated the prospective association between melatonin levels and prostate cancer risk.

Methods: We conducted a case-cohort study of 928 Icelandic men nested within the AGES-Reykjavik cohort. 6-sulfatoxymelatonin concentrations were measured on first morning void urine samples collected pre-diagnostically at the baseline visit in 2002-2006. Baseline questionnaire data included information on sleep patterns and covariates. Ascertainment of prostate cancer diagnoses and mortality among men was obtained by linking the cohort to the nationwide Icelandic Cancer Registry and the Causes of Death Registry through 2009. We used weighted Cox proportional hazards models to assess the association between first morning void 6-sulfatoxymelatonin and prostate cancer risk, adjusting for potential confounders.

Results: A total of 111 men were diagnosed with incident prostate cancer, including 24 with advanced disease. Men who reported sleep problems at baseline had lower 6-sulfatoxymelatonin levels compared to those who reported no sleep problems. Men with 6-sulfatoxymelatonin levels higher than the median had a borderline statistically significant decreased risk of prostate cancer overall (HR = 0.69, 95% CI: 0.44-1.08). Moreover, men with higher 6-sulfatoxymelatonin levels had a 75% significantly reduced risk of advanced disease compared to men with lower levels (HR = 0.25, 95% CI: 0.08-0.80).

Conclusion: Higher urinary 6-sulfatoxymelatonin levels were associated with a decreased risk of prostate cancer, particularly advanced disease. These data provide support for the influence of the circadian rhythm in prostate carcinogenesis.



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