



VITAMINS / SUPPLEMENTS

Low Melatonin Linked to Risk of Advanced Prostate Cancer

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Epidemiological and experimental studies suggest the hormone melatonin, which plays a role in regulating the sleep-wake cycle, may play a role in the development of prostate cancer, as lower melatonin levels have been associated with an increased risk of prostate (and breast) cancer. This evidence includes [a recent study](#) presented at the American Association for Cancer Research – Prostate Cancer Foundation Conference on Advances in Prostate Cancer Research in January 2014.

In this study, a strong association was shown between urine levels of the main breakdown product of melatonin, 6-sulfatoxymelatonin, and risk of prostate cancer.¹

Melatonin and Prostate Cancer: Compelling Recent Evidence

Researchers 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 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 (ng/ml) 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 who did not report sleep problems.



During the study, 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 (17.14 ng/ml) had a 75 percent decreased risk for advanced prostate cancer. Additionally, a 31 percent decreased risk for prostate cancer overall was observed in men with higher 6-sulfatoxymelatonin levels.

Melatonin-Sleep Cycles and Prostate Cancer Risk

The body's circadian pacemaker is located in the suprachiasmatic nuclei (SCN) of the hypothalamus, and is a major determinant of the timing, duration and structure of sleep. Upon darkness, melatonin is released from the pineal gland, but this function requires an intact projection from the circadian pacemaker in the SCN to the pineal gland via the superior cervical ganglion. Severance of the superior cervical ganglion, as occurs in tetraplegia, has been shown to abolish melatonin production.

In support of the melatonin-prostate cancer link, individuals who sleep in rooms with less darkness, and/or shift workers who experience disrupted circadian pacemaker function and less darkness during sleep, have been shown to have lower melatonin levels and a greater risk of prostate cancer (and breast cancer) in some studies.

Moreover, totally blind individuals, who theoretically may have a less disturbed melatonin secretion profile because of light exposure, have been shown to have [lower risks](#) of prostate and breast cancer.²

Anti-Cancer Effects of Melatonin

Many experimental studies have shown that melatonin inhibits or slows down tumor growth (including prostate cancer), both *in vitro* and *in vivo*, whereas suppression of melatonin via constant light exposure or pinealectomy increases tumor growth in a dose-dependent manner in experimental models.

The anti-cancer effects of melatonin can be explained via its modulation of cell-cycle length through control of the p53/p21 pathway, and its anti-mitotic and antioxidant activity. The p53 tumor suppressor gene is an important surveillance system within the cell that identifies the emergence of cancerous mutations and initiates either apoptosis (programmed cell death) or induces the action of DNA repair enzymes to reverse DNA damage that is repairable before cancerous changes occur within the cell.

The p21 tumor suppressor gene works in close coordination with the p53 tumor suppressor gene, especially during the process of cell division (mitosis). Melatonin also exerts profound immunomodulation effects, which have been shown to be important in cancer prevention and adjunctive treatment of various types of solid tumors.

Melatonin is a potent antioxidant that may facilitate reduction of oxidative stress implicated in prostate cancer progression. Some studies also show that melatonin secretion may be reduced in prostate cancer patients, as compared with men diagnosed with prostate cancer *in situ* or benign prostatic hyperplasia.

A single case report, published in 2003, showed that melatonin supplementation inhibited prostate cancer progression temporarily in a patient with advanced prostate disease (bone metastasis). The dosage used in this case was 5 mg per day, administered at 10:00 p.m. each evening for six weeks.²

According to David Blask, MD, PhD, Laboratory of Experimental Neuroendocrinology / Oncology Bassett Research Institute, Cooperstown, N.Y., "At physiological concentrations, melatonin suppresses cell growth and multiplication and inhibits cancer cell proliferation *in vitro* through specific cell-cycle effects. At pharmacological concentrations, melatonin suppresses cancer cell growth and multiplication. At physiological and pharmacological concentrations, melatonin acts as a differentiating agent in some cancer cells, and lowers their invasive and metastatic status by altering adhesion molecules and maintaining gap junction intercellular communication. In other cancer cell types, melatonin, alone or with other agents, induces programmed cell death."⁴

Key Points and Clinical Relevance

Melatonin levels begin to decline after the onset of puberty. By age 40, our melatonin levels are markedly lower than they were at age 13. The age-related decline in melatonin secretion has been shown to be correlated with many [sleep disturbance](#) problems reported in adult life, decreased immune function, more rapid accumulation of oxidative damage in the brain linked to Alzheimer's disease, and an increased risk of breast and prostate cancer.

Many anti-aging experts suggest that taking 0.5-3.0 mg of melatonin approximately one hour prior to bedtime after age 40 may be an important way to improve sleep quality and duration, improve immune function, slow oxidative damage to the brain, and reduce risk of breast and prostate cancer. The 2014 study highlighted in this paper lends further credence to the link between low melatonin levels and increased risk of prostate cancer.

References

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