Oral Nicotinamide and the Prevention of Skin Cancers: A Guide for Patients and Caregivers

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What is Nicotinamide?

Skin cancer is the most common form of cancer globally, affecting millions of people each year[1]. Current guidelines from the American Academy of Dermatology (AAD) recommend typical sun protection measures, such as using broad-spectrum sunscreen with SPF 30 or higher, wearing protective clothing, seeking shade, and avoiding tanning beds[2]. However, recent studies have shown that oral nicotinamide, a form of vitamin B3, could play a significant role in preventing skin cancers, particularly non-melanoma skin cancers (NMSC) like basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)[3, 4, 5].

Nicotinamide, or niacinamide, is found in foods like meat, fish, nuts, and grains. It is different from niacin, another form of vitamin B3, and has unique properties beneficial for skin health. Over the years, nicotinamide has been studied for its potential to repair DNA damage caused by ultraviolet radiation from the sun which is a major risk factor for developing skin cancers[3, 4].

How Does It Help With Skin Cancer Prevention?

The protective effect of nicotinamide works by enhancing DNA repair and reducing UV-induced immunosuppression. Nicotinamide helps prevent mutations that can lead to malignant growth by enhancing the skin's natural repair processes. Additionally, nicotinamide supports cellular energy production by replenishing stores of NAD^+ and $NADP^+$ which are coenzymes essential for metabolic processes and DNA repair. This increased energy availability allows cells to more effectively repair DNA damage caused by UV exposure[3, 4].

The Role of Nicotinamide in Skin Cancer Prevention

A phase 3 clinical trial published in the NEJM investigated the effects of nicotinamide on skin cancer prevention among individuals at high risk due to previous NMSC. In this double-blind, placebo-controlled trial, 386 participants received 500 mg of oral nicotinamide twice daily. The results were encouraging: the nicotinamide group saw a 23% reduction in new NMSC cases compared to the placebo group over a 12-month period. Notably, participants also experienced fewer actinic keratoses, which are precursors to squamous cell carcinoma[5].

In contrast, a separate phase 3, double-blind, randomized controlled trial published in the NEJM assessed the efficacy of nicotinamide in preventing skin cancer among transplant recipients, who are highly susceptible due to immunosuppression. The study concluded that nicotinamide did not

significantly reduce the occurrence of NMSC or actinic keratoses over 12 months, indicating that its beneficial effects observed in the general population might not extend to immunosuppressed individuals[6].

While the primary focus of research has been on NMSC, there is also interest in nicotinamide's potential to prevent other forms of skin cancer, including melanoma. In laboratory experiments, researchers found that nicotinamide significantly reduced melanoma cell numbers by up to 90%, enhanced DNA repair, and a 10-fold increase in cell death. These findings indicate that nicotinamide may help repair oxidative DNA damage and reduce UV-induced damage for melanoma treatment and prevention[7].

Safety and Accessibility

One of the advantages of nicotinamide is its safety profile. Unlike many other chemopreventive agents, nicotinamide is well-tolerated, with minimal side effects including gastrointestinal symptoms and skin flushing. This makes it a viable option for long-term use in individuals at high risk of skin cancers. Additionally, as an over-the-counter supplement, it is easily accessible and relatively affordable, further enhancing its potential as a widespread preventive measure[8].

Recommended Dosage and Use

The recommended dosage used in the first NEJM study was 500 mg taken twice daily. Nicotinamide’s effects are dose-dependent, meaning the therapeutic benefits were specifically observed with this dosage. The study reported minimal side effects, most commonly gastrointestinal symptoms, which were generally mild and transient. It is essential to consult with a physician before starting any new supplement regimen, especially for individuals with underlying health conditions or those taking other medications[5].

Oral Nicotinamide and the Prevention of Skin Cancers

Oral nicotinamide presents a promising and practical approach to reducing the risk of skin cancers, especially non-melanoma types like BCC and SCC. Its ability to enhance DNA repair and reduce UV-induced damage makes it an interesting tool in the fight against skin cancer. With its excellent safety profile and accessibility, nicotinamide could become a keystone of skin cancer prevention, complementing traditional methods and helping expand skin cancer protection. As research continues, the potential benefits of nicotinamide may expand, offering greater protection for those at risk of other skin conditions.

1. Gordon R. Skin cancer: an overview of epidemiology and risk factors. *Semin Oncol Nurs*. 2013;29(3):160-169. doi:10.1016/j.soncn.2013.06.002

2. American Academy of Dermatology. Sunscreen FAQs. AAD. https://www.aad.org/media/stats-sunscreen. Accessed May 15, 2024.
3. Rolfe HM. A review of nicotinamide: treatment of skin diseases and potential side effects. *J Cosmet Dermatol*. 2014;13(4):324-328. doi:10.1111/jocd.12119
4. Hunt SV, Jamison A, Malhotra R. Oral nicotinamide for non-melanoma skin cancers: A review. *Eye (Lond)*. 2023;37(5):823-829. doi:10.1038/s41433-022-02036-z
5. Chen AC, Martin AJ, Choy B, et al. A Phase 3 Randomized Trial of Nicotinamide for Skin-Cancer Chemoprevention. *N Engl J Med*. 2015;373(17):1618-1626. doi:10.1056/NEJMoa1506197
6. Allen NC, Martin AJ, Snaidr VA, et al. Nicotinamide for Skin-Cancer Chemoprevention in Transplant Recipients. *N Engl J Med*. 2023;388(9):804-812. doi:10.1056/NEJMoa2203086
7. Scatozza F, Moschella F, D'Arcangelo D, et al. Nicotinamide inhibits melanoma in vitro and in vivo. *J Exp Clin Cancer Res*. 2020;39(1):211. Published 2020 Oct 7. doi:10.1186/s13046-020-01719-3
8. Huber R, Wong A. Nicotinamide: An Update and Review of Safety & Differences from Niacin. *Skin Therapy Lett*. 2020;25(5):7-11.