KOCAELİ ÜNİVERSİTESİ
Tıp Fakültesi

NON-MELANOM DERİ KANSERLERİNDE GÜNCEL KORUNMA YÖNTEMLERİ

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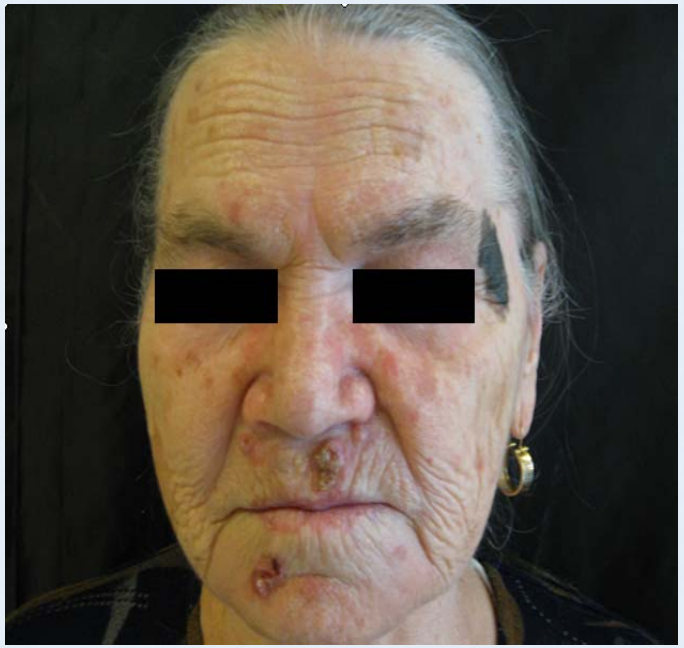
Deri ve Zührevi Hastalıkları AD

Non-melanom deri kanserleri (NMDK)

- Bazal hücreli karsinom (BHK) (%80)
- Skuamöz hücreli karsinom (SHK) (%15)
- Son 20 yılda en çok artış gösteren ve dünyada en sık görülen kanser tipi
- USA'de her yıl 2 milyon yeni olgu



Etyolojik faktörler

BHK

- **Ultraviyole*** ve iyonize radyasyon
- **İmmünsüpresyon**
- Genetik faktörler - Tümör süpresör PTCH gen mutasyonu

SHK

- **Ultraviyole *** ve iyonize radyasyon
- **İmmünsüpresyon**
- Çevresel karsinojenler (Zift, katran, nitrozüre vb)
- Prekürsör lezyonlar (AK, yanık skarı,..)
- HPV enfeksiyonları
- Genodermatozlar (albinizm, kseroderma pigmentozum….)

Korunma yöntemleri

Kanser Oluşumunun Engellenmesi (Primer korunma)

1. Güneşten korunma
2. Prekanseröz lezyonların tedavisi
3. Kemoprevensiyon (Yüksek riskli hastalarda!)
4. Diğer: nutrisyonel faktörler, eğitim….

Erken tanı ve tedavi (sekonder - tersiyer korunma)

1. Tarama, eğitim
2. Muayene (Kendi kendini muayene etme…)
3. Takip

1. Güneşten korunma

ULTRAVİOLE (UV) IŞINLARI

D vitamini sentezi

Melanin yapımının uyarılması-derinin korunması

İnsan psikolojisine yararlı etkisi

Psoriasis gibi hastalıklarda tedavi edici etkisi

Güneş yanığı

DNA foto hasarı-mutasyon ve **deri kanseri oluşumu**

Fototoksik- fotoallerjik reaksiyonlar

Deri yaşlanması

İmmünsüpresyon

(Enfeksiyon ve **deri kanserleri)**

Güneşten korunma

- **A (Avoid- kaçınmak):** Saat 10.00-16.00 saatleri arasında güneşe çıkılmaması
- **B (Block-engellemek):** Sık dokumalı, açık renkli, kuru giysiler giyinilmesi, şapka, şemsiye, gözlük kullanılması
- **C (Cover-up- kaplamak):** Güneş koruyucu krem kullanılması
- **D (Do not- yapmayacaksın):** Fazla güneş banyosu yapılmaması, solaryum gibi yapay bronzlaşma yöntemlerinin kullanılmaması
- **E (Education-eğitim):** Özellikle çocukların ve gençlerin UV nin zararlı etkileri konusunda eğitilmesi, bilgilendirilmesi.

Güneşten koruyucu krem kullanırken;

- Hem UVA ya hem de UVB ye karşı koruyan geniş spektrumlu, suya dayanıklı güneş koruyucular tercih edilmesi
- Güneşe çıkmadan 30-60 dk önce uygulanması
- Tüm güneş gören bölgelere ve uygun miktarda (cm2 ye 1.5-2 mgr) sürülmesi
- Uzun süre güneşte kalanlarda, deniz ve havuza girenlerde 2 saatte bir tekrar uygulanması
- SPF 15 üzerindeki koruyucuların tercih edilmesi
- Son kullanma tarihine dikkat edilmesi gerekmektedir. (Ort 2-3 yıl)

Güneşten koruyucu kremlerin;

Avantajları ☺

- Güneş yanığını önlerler.
- Deri yaşlanmasını azaltırlar
- NMDK artmasına neden olan immünsüpresyonu azaltırlar.

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Dezavantajları ☹

- Kozmetik açıdan kötü görünüm
- Isınınca etkileri azalır
- Diğer: fotoalerjik-alerjik,sistemik emilim?
- **D vit sentezinde yetersizlik!!!**

Br J Dermatol. 2012 Aug;167(2):391-5. doi: 10.1111/j.1365-2133.2012.11004.x.

The relation between sunscreen layer thickness and vitamin D production after ultraviolet B exposure: a randomized clinical trial.

Faurschou A[1], Beyer DM, Schmedes A, Bogh MK, Philipsen PA, Wulf HC.

Author information

Abstract

BACKGROUND: Sunscreens absorb ultraviolet B (UVB) and it is a major concern that sunscreen use may lead to vitamin D deficiency.

OBJECTIVES: To investigate the relation between the amount of sunscreen applied and the vitamin D serum level in humans after UVB exposure under controlled conditions.

METHODS: Thirty-seven healthy volunteers with fair skin types were randomized to receive an inorganic sunscreen with sun protection factor (SPF) 8 of 0 mg cm(-2) , 0.5 mg cm(-2) , 1 mg cm(-2) , 1.5 mg cm(-2) , or 2 mg cm(-2) thickness on the upper body, approximately 25% of the body area. Participants were irradiated with a fixed UVB dose of 3 standard erythema doses 20 min after sunscreen application. This procedure was repeated four times with a 2- to 3-day interval. Blood samples were drawn before the first irradiation and 3 days after the last to determine the serum vitamin D level expressed as 25-hydroxyvitamin D(3) [25(OH)D].

RESULTS: The vitamin D serum level increased in an exponential manner with decreasing thickness of sunscreen layer in response to UVB exposure. For all thicknesses of sunscreen, the level of 25(OH)D increased significantly after irradiation ($P<0.05$), except for the group treated with 2 mg cm(-2) , in which the increase in 25(OH)D was not statistically significant ($P=0.16$).

CONCLUSIONS: Vitamin D production increases exponentially when thinner sunscreen layers than recommended are applied (<2 mg cm(-2)). When the amount of sunscreen and SPF advised by the World Health Organization are used, vitamin D production may be abolished. Re-evaluation of sun-protection strategies could be warranted.

Güneşten korunma ve D Vitamini

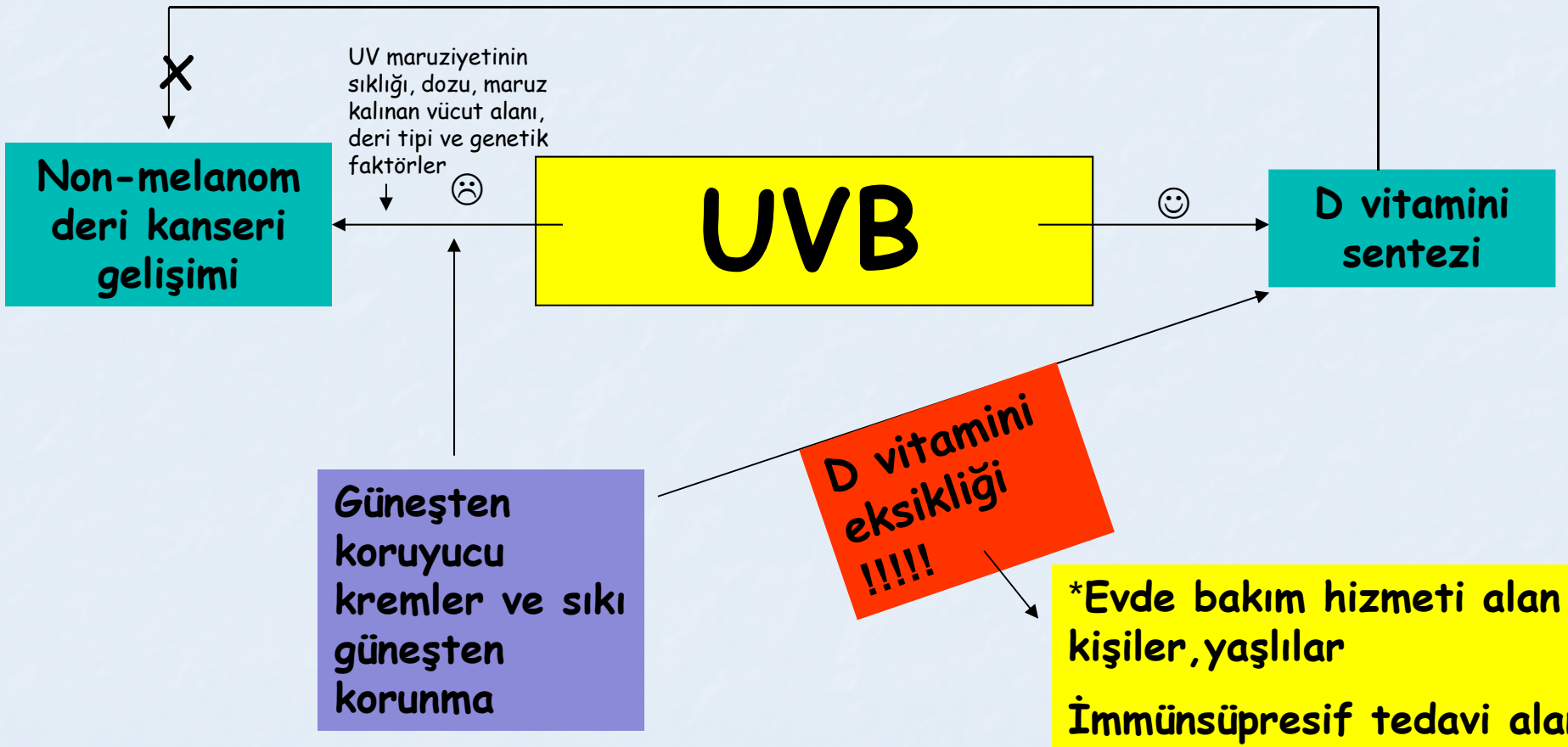
- OTH da SPF-8 güneş koruyucu kremlerin deride D vitamini sentezini %95 azalttığı, kıyafetlerin ise tam blok sağlayarak D vitamini sentezini tamamen engellediği gösterilmiştir

- Yeterli D vitamini sentezi için güneşten korunmanın iyi ayarlanması

- Riskli grupta D vitamini düzeyinin aralıklı bakılması, eksiklik tespit edilen kişilere oral D vitamini verilmesi önerilmektedir

Reichrath J, et al. Adv Exp Med Biol. 2008;624:203-14.

NMDK, UV-B, D Vitamini



D Vitamini ve NMDK

- Aktif D vitamininin; BHK oluşumundan sorumlu tutulan Hedgehog sinyal yolunun inhibisyonunu
- SHK gelişiminden sorumlu olan p53 gen aracılı DNA hasarına yanıtın modulasyonunu
- NMDK oluşma riskini azalttığı bildirilmiştir.
- VDR polimorfizmi (FokI ve BsmI) öz. FokI ff taşıyıcılarında deri kanserlerinde anlamlı artış !!!!
- D vitamini eksikliği; visseral maligniteler, hipertansiyon, kardiyovasküler hastalıklar vb hastalıkların oluşumundan sorumlu

J Clin Oncol. 2011 Aug 1;29(22):3078-84. doi: 10.1200/JCO.2011.34.5967. Epub 2011 Jun 27.

Calcium plus vitamin D supplementation and the risk of nonmelanoma and melanoma skin cancer: post hoc analyses of the women's health initiative randomized controlled trial.

Tang JY[1], Fu T, Leblanc E, Manson JE, Feldman D, Linos E, Vitolins MZ, Zeitouni NC, Larson J, Stefanick ML.

Author information

Abstract

PURPOSE: In light of inverse relationships reported in observational studies of vitamin D intake and serum 25-hydroxyvitamin D levels with risk of nonmelanoma skin cancer (NMSC) and melanoma, we evaluated the effects of vitamin D combined with calcium supplementation on skin cancer in a randomized placebo-controlled trial.

METHODS: Postmenopausal women age 50 to 79 years (N = 36,282) enrolled onto the Women's Health Initiative (WHI) calcium/vitamin D clinical trial were randomly assigned to receive 1,000 mg of elemental calcium plus 400 IU of vitamin D3 (CaD) daily or placebo for a mean follow-up period of 7.0 years. NMSC and melanoma skin cancers were ascertained by annual self-report; melanoma skin cancers underwent physician adjudication.

RESULTS: Neither incident NMSC nor melanoma rates differed between treatment (hazard ratio [HR], 1.02; 95% CI, 0.95 to 1.07) and placebo groups (HR, 0.86; 95% CI, 0.64 to 1.16). In subgroup analyses, women with history of NMSC assigned to CaD had a reduced risk of melanoma versus those receiving placebo (HR, 0.43; 95% CI, 0.21 to 0.90; P(interaction) = .038), which was not observed in women without history of NMSC.

CONCLUSION: Vitamin D supplementation at a relatively low dose plus calcium did not reduce the overall incidence of NMSC or melanoma. However, in women with history of NMSC, CaD supplementation reduced melanoma risk, suggesting a potential role for calcium and vitamin D supplements in this high-risk group. Results from this post hoc subgroup analysis should be interpreted with caution but warrant additional investigation.

Güneş koruyucu kremler ve DNA onarım enzimleri

J Drugs Dermatol. 2013 Sep;12(9):1017-21.

Topical application of preparations containing DNA repair enzymes prevents ultraviolet-induced telomere shortening and c-FOS proto-oncogene hyperexpression in human skin: an experimental pilot study.

Emanuele E, Altabas V, Altabas K, Berardesca E.

Abstract

The exposure to ultraviolet radiation (UVR) is one of the most important risk factors for skin aging and increases the risk of malignant transformation. Telomere shortening and an altered expression of the proto-oncogene c-FOS are among the key molecular mechanisms associated with photoaging and tumorigenesis. Photolyase from A. nidulans and endonuclease from M. luteus are xenogenic DNA repair enzymes which can reverse the molecular events associated with skin aging and carcinogenosis caused by UVR exposure. Therefore, the purpose of this study was to investigate whether the topical application of preparations containing DNA repair enzymes may prevent UVR-induced acute telomere shortening and FOS gene hyperexpression in human skin biopsies. Twelve volunteers (Fitzpatrick skin types I and II) were enrolled for this experimental study, and six circular areas (10 mm diameter) were marked out on the nonexposed lower back of each participant. One site was left untreated (site 1: negative control), whereas the remaining five sites (designated sites 2-6) were exposed to solar-simulated UVR at 3 times the MED on four consecutive days. Site 2 received UVR only (site 2: positive control), whereas the following products were applied to sites 3-6, respectively: vehicle (moisturizer base cream; applied both 30 minutes before and immediately after each irradiation; site 3); a traditional sunscreen (SS, SPF 50) 30 minutes before irradiation and a vehicle immediately after irradiation (site 4); a SS 30 minutes before irradiation and an endonuclease preparation immediately after irradiation (site 5); a SS plus photolyase 30 minutes before irradiation and an endonuclease preparation immediately after irradiation (site 6). Skin biopsies were taken 24 h after the last irradiation. The degree of telomere shortening and c-FOS gene expression were measured in all specimens. Strikingly, the combined use of a SS plus photolyase 30 minutes before irradiation and an endonuclease preparation immediately after irradiation completely abrogated telomere shortening and c-FOS gene hyperexpression induced by the experimental irradiations. We conclude that the topical application of preparations containing both photolyase from A. nidulans and endonuclease from M. luteus may be clinically useful to prevent skin aging and carcinogenesis by abrogating UVR-induced telomere shortening and c-FOS gene hyperexpression.

2. Prekanseröz lezyonların (Aktinik keratoz!!) tedavisi

- Kriyoterapi
- 5-fluorourasil
- İmiquimod, resiquimod
- Topikal diklofenak sodyum
- Fotodinamik tedavi
- Cerrahi eksizyon
- Dermabrazyon
- Kimyasal peeling
- Lazer
- İngenol mebutate
- Retinoidler, T4 endonükleaz V gibi kemopreventif ajanlar

3. Kemoprevensiyon

* Karsinojenik ilerlemeyi tersine çevirmesi, baskılaması ve önlemesi amacıyla farklı kimyasal ajanların kullanılması

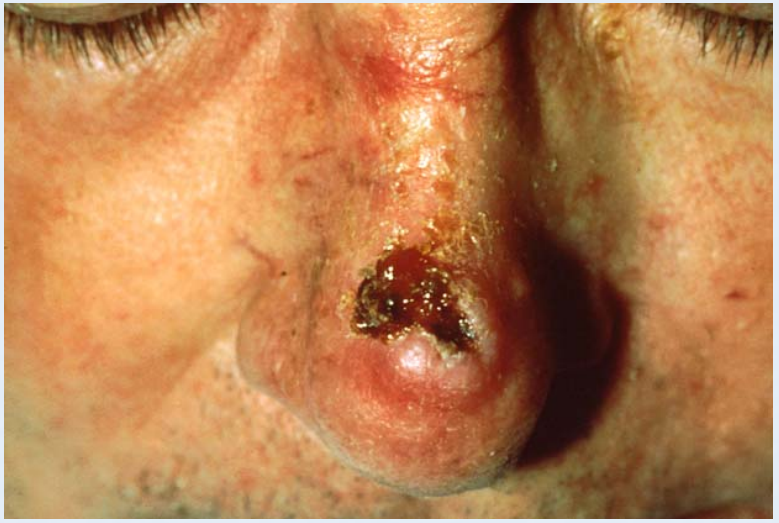
* Güvenli olmalı, toksik olmamalı, etkili olmalı

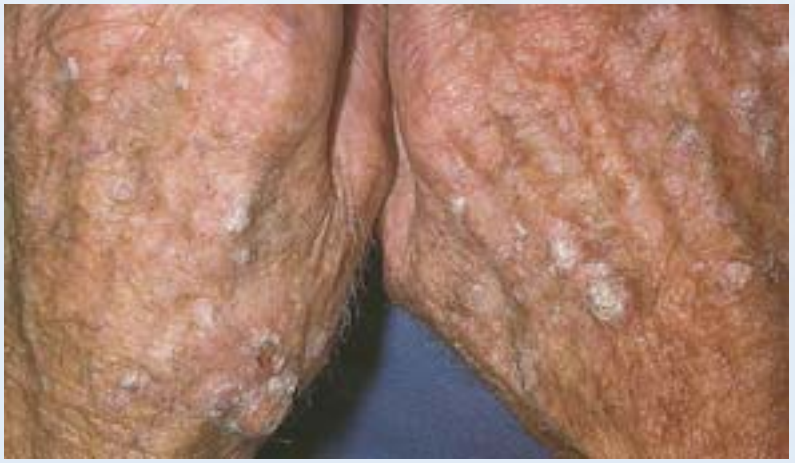
Soltani-Arabshahi R, Tristani-Firouzi P. Facial Plast Surg 2013; 29: 373-383.

Endikasyonları

- Çok sayıda NMDK gelişme riski yüksek olan

- Sayılamayacak kadar çok sayıda aktinik keratozu olan





Çok sayıda NMDK gelişme riski yüksek olanlar;

1. İmmünsüpresyon:

. Organ transplantasyonu yapılan hastalar (OTH)
. KLL veya non-Hodgkin lenfoma gibi hematolojik malignitesi olanlar
. Kronik immünsüpresif tedavi alanlar
. HIV pozitif hastalar

2. Kronik radyasyon ve yoğun UV maruziyeti

. Şiddetli fotohasar
. Puva tedavisi almış psoriasis hastaları
. Kronik radyasyon dermatiti

3. Genetik sendromlar

. Nevoid BHK sendromu
. Kseroderma pigmentosum
. Epidermodisplazia verrüsiformis
. Bazex sendromu
. Rombo sendromu

4. Diğer

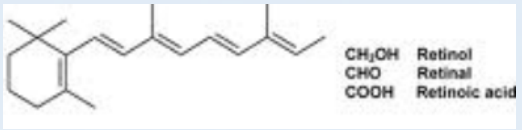
. Kronik arsenik maruziyeti

Soltani-Arabshahi R, Tristani-Firouzi P. Facial Plast Surg 2013; 29: 373-383.

Kemoprevensiyonda kullanılan ajanlar

- **Oral ve topikal retinoidler**
- Fotodinamik tedavi
- **Non-steroid antiinflamatuvarlar (COX-2 inhibitörleri,** Topikal diklofenak sodyum)
- **T4 endonükleaz V**
- **Difluoromethilornitin (DFMO)**
- **Capesitabine**
- **Lunasin**
- **Antioksidanlar**

Retinoidler



- Kemoprevensiyonda en çok kullanılan ajanlar
- Keratinositlerin diferansiyasyonunu ve apopitozunu düzenlerler
- Antiproliferatif ve kanser önleyici etkileri de gösterilmiştir

Endikasyonları

- Asitretin: OTH, ciddi güneş hasarı olan kişiler
- İsotretinoin: Kseroderma pigmentozum, nevoid basal hücreli karsinom sendromu

Retinoidlerin NMDK önlenmesinde önerilen kullanım şekilleri;

- **Asitretin;** 10 mg/gün başlanılması, 2-4 hafta sonra dozun artırılarak 15-25 mg/gün hedef doza çıkılması,
- **İsotretinoin;** 0.25 mg/kg/gün ile tedaviye başlanması, dozun her ay 0.125-0.25 mg/kg artırılarak 0.5 mg/kg'a çıkılması
- Kullanılan süre; 6 ay- 15 yıl
- En düşük etkili dozda uzun süre kullanımı, laboratuar incelemelerinin her ay tekrarlanması,yan etkilerinin izlenmesi gerekmektedir.

Soltani-Arabshahi R, Tristani-Firouzi P. Facial Plast Surg 2013; 29: 373-383.

Retinoidler ve kemoprevensiyon

- Çalışmaların çoğu yüksek riskli hastalarda retinoidlerin SHK için kemopreventif etkili olduğunu, ancak BHK oluşma riski üzerine etkileri olmadığını göstermektedir

Soltani-Arabshahi R, Tristani-Firouzi P. Facial Plast Surg 2013; 29: 373-383.

Topikal retinoidler

J Invest Dermatol. 2012 Jun;132(6):1583-90. doi: 10.1038/jid.2011.483. Epub 2012 Feb 9.

Tretinoin and the prevention of keratinocyte carcinoma (Basal and squamous cell carcinoma of the skin): a veterans affairs randomized chemoprevention trial.

Weinstock MA[1], Bingham SF, Digiovanna JJ, Rizzo AE, Marcolivio K, Hall R, Eilers D, Naylor M, Kirsner R, Kalivas J, Cole G, Vertrees JE; Veterans Affairs Topical Tretinoin Chemoprevention Trial Group.

Collaborators (61)

Author information

Abstract

Keratinocyte carcinoma (KC) is the most common cancer in the United States, with no proven means for prevention other than systemic retinoids, which have significant toxicity, and sunscreen. Topical tretinoin has been used for KC chemoprevention, although this use is unproven. Hence, we conducted the randomized Veterans Affairs Topical Tretinoin Chemoprevention Trial of high-dose topical tretinoin for KC prevention. We randomized 1,131 patients to topical 0.1% tretinoin or a matching vehicle control for 1.5-5.5 years. The primary outcomes were time to development of new basal cell carcinoma (BCC) and new invasive squamous cell carcinoma (SCC) on the face or ears. The effects were not significant (P=0.3 for BCC and P=0.4 for SCC). The proportions of the tretinoin and control groups who developed a BCC at 5 years were 53 and 54% and an invasive SCC at 5 years were 28 and 31%. These differences (95% confidence intervals) were: for BCC, 1.0% (-6.5, 8.6%); for SCC, 3.6% (-3.1, 10.3%). No differences were observed in any cancer-related end points or in actinic keratosis counts. The only quality of life difference was worse symptoms in the tretinoin group at 12 months after randomization. This trial in high-risk patients demonstrates that high-dose topical tretinoin is ineffective at reducing risk of KCs.

Non-steroid antiinflamatuvarlar (NSAİD)

- UVB maruziyeti:
  Siklooksijenaz-2 (COX-2) düzeyinin ve
  Prostaglandin sentezinin (PGE2, PGF2alfa) artışına
  Keratinositlerin proliferasyonuna
  NMDK oluşumuna katkı

- Özellikle SHK olmak üzere NMDK de COX-2 aşırı üretildiği

- Hayvan çalışmalarında COX-2 enziminin genetik olarak eksik üretildiği ve COX-2 inh. kullanıldığı farelerde daha az sayıda NMDK geliştiği

- NSAİD ⟶ COX-2 inhibisyonu ⟶ NMDK kemopreventif etki, çelişkili sonuçlar

Elmets CA, et al. J İnvest Dermatol 2014.

Prev Med. 2014 Aug 20. pii: S0091-7435(14)00315-6. doi: 10.1016/j.ypmed.2014.08.024. [Epub ahead of print]

Non-melanoma skin cancer and NSAID use in women with a history of skin cancer in the Women's Health Initiative.

Wysong A[1], Ally MS[2], Gamba CS[3], Desai M[3], Swetter SM[4], Seiffert-Sinha K[5], Sinha AA[5], Stefanick ML[3], Tang JY[6].

Author information

Abstract

OBJECTIVE: Evidence for the effect of non-steroidal anti-inflammatory drugs (NSAIDs) on non-melanoma skin cancer (NMSC) risk is inconsistent. We prospectively examined whether regular, inconsistent, or no/low-use of NSAIDs is associated with lower NMSC risk among 54,728 postmenopausal Caucasian women in the Women's Health Initiative Observational Study enrolled between 1993 and 1998.

METHODS: Logistic regression models were used to assess odds of NMSC after adjusting for skin type, sun exposure history and indication for NSAID use.

RESULTS: There were 7652 incident cases of NMSC (median follow-up: 6.9years). There was no association between regular NSAID-use and NMSC risk relative to no/low-users. However, in a subgroup analysis of 5325 women with a history of skin cancer (incident NMSC: 1897), odds of NMSC were lower among regular NSAID users whether <5years (OR 0.82, 95% CI: 0.70-0.95) or ≥5years (OR 0.82, 95% CI: 0.69-0.98) of use compared to no/low-users. Inconsistent NSAID use and acetaminophen use were not associated with NMSC risk.

CONCLUSION: Overall, NSAID use was not associated with NMSC risk. However, in women with a history of skin cancer, regular NSAID use was associated with 18% lower odds of NMSC. Future studies on potential chemopreventative effects of NSAIDs should focus on subjects with prior history of NMSC.

Cancer. 2012 Oct 1;118(19):4768-76. doi: 10.1002/cncr.27406. Epub 2012 May 29.

Nonsteroidal anti-inflammatory drugs and the risk of skin cancer: a population-based case-control study.

Johannesdottir SA[1], Chang ET, Mehnert F, Schmidt M, Olesen AB, Sørensen HT.

Author information

Abstract

BACKGROUND: Nonsteroidal anti-inflammatory drugs (NSAIDs) may prevent the development of cancer by inhibiting cyclooxygenase (COX) enzymes, which are involved in carcinogenesis. Therefore, the authors of this report examined the association between NSAID use and the risk of squamous cell carcinoma (SCC), basal cell carcinoma (BCC), and malignant melanoma (MM).

METHODS: From 1991 through 2009, all incident cases of SCC (n = 1974), BCC (n = 13,316), and MM (n = 3242) in northern Denmark were identified. Approximately 10 population controls (n = 178,655) were matched to each case by age, gender, and county of residence. The use of aspirin, other nonselective NSAIDs, or selective COX-2 inhibitors was ascertained through a prescription database. Conditional logistic regression analyses adjusted for potential confounders were used to compute odds ratios as estimates of incidence rate ratios (IRRs).

RESULTS: For NSAIDs overall, ever use (>2 prescriptions) compared with nonuse (≤2 prescriptions) was associated with a decreased risk of SCC (IRR, 0.85; 95% confidence interval [CI], 0.76-0.94) and MM (IRR, 0.87; 95% CI, 0.80-0.95), especially for long-term use (≥7 years) and high-intensity use (>25% prescription coverage during the total duration of use). NSAID use was not associated with a reduced risk of BCC overall (IRR, 0.97; 95% CI, 0.93-1.01), but the risk of BCC at sites other than the head and neck was reduced in association with long-term use (IRR, 0.85; 95% CI, 0.76-0.95) and high-intensity use (IRR, 0.79; 95% CI, 0.69-0.91). All estimates of reduced risk were driven primarily by the use of nonselective NSAIDs and older COX-2 inhibitors (diclofenac, etodolac, and meloxicam).

CONCLUSIONS: The current results indicated that NSAID use may decrease the risk of SCC and MM.

J Natl Cancer Inst. 2010 Dec 15;102(24):1835-44. doi: 10.1093/jnci/djq442. Epub 2010 Nov 29.

Chemoprevention of nonmelanoma skin cancer with celecoxib: a randomized, double-blind, placebo-controlled trial.

Elmets CA[1], Viner JL, Pentland AP, Cantrell W, Lin HY, Bailey H, Kang S, Linden KG, Heffernan M, Duvic M, Richmond E, Elewski BE, Umar A, Bell W, Gordon GB.

Author information

Abstract

BACKGROUND: Preclinical studies indicate that the enzyme cyclooxygenase 2 plays an important role in ultraviolet-induced skin cancers. We evaluated the efficacy and safety of celecoxib, a cyclooxygenase 2 inhibitor, as a chemopreventive agent for actinic keratoses, the premalignant precursor of nonmelanoma skin cancers, and for nonmelanoma skin cancers, including cutaneous squamous cell carcinomas (SCCs) and basal cell carcinomas (BCCs).

METHODS: A double-blind placebo-controlled randomized trial involving 240 subjects aged 37-87 years with 10-40 actinic keratoses was conducted at eight US academic medical centers. Patients were randomly assigned to receive 200 mg of celecoxib or placebo administered orally twice daily for 9 months. Subjects were evaluated at 3, 6, 9 (ie, completion of treatment), and 11 months after randomization. The primary endpoint was the number of new actinic keratoses at the 9-month visit as a percentage of the number at the time of randomization. In an intent-to-treat analysis, the incidence of actinic keratoses was compared between the two groups using t tests. In exploratory analyses, we evaluated the number of nonmelanoma skin cancers combined and SCCs and BCCs separately per patient at 11 months after randomization using Poisson regression, after adjustment for patient characteristics and time on study. The numbers of adverse events in the two treatment arms were compared using $\chi(2)$ or Fisher exact tests. All statistical tests were two-sided.

RESULTS: There was no difference in the incidence of actinic keratoses between the two groups at 9 months after randomization. However, at 11 months after randomization, there were fewer nonmelanoma skin cancers in the celecoxib arm than in the placebo arm (mean cumulative tumor number per patient 0.14 vs 0.35; rate ratio [RR] = .43, 95% confidence interval [CI] = 0.24 to 0.75; P = .003). After adjusting for age, sex, Fitzpatrick skin type, history of actinic keratosis at randomization, nonmelanoma skin cancer history, and patient time on study, the number of nonmelanoma skin cancers was lower in the celecoxib arm than in the placebo arm (RR = 0.41, 95% CI = 0.23 to 0.72, P = .002) as were the numbers of BCCs (RR = 0.40, 95% CI = 0.18 to 0.93, P = .032) and SCCs (RR = 0.42, 95% CI = 0.19 to 0.93, P = .032). Serious and cardiovascular adverse events were similar in the two groups.

CONCLUSIONS: Celecoxib may be effective for prevention of SCCs and BCCs in individuals who have extensive actinic damage and are at high risk for development of nonmelanoma skin cancers.

T4 endonükleaz V

- E.coli kaynaklı polipeptit
- UV ye bağlı gelişen DNA da oluşan siklobütan primidin dimerlerinin tamirini sağlar
- XP lu 30 hastada T4E5 in topikal olarak 1 yıl kullanımının yeni AK ve BHK gelişimini engellediği gösterilmiş.

Lancet. 2001 Mar 24;357(9260):926-9.

Difloromethilornitin (DFMO)

- UV kaynaklı deri kanserlerinin oluşumunda önemli basamaklardan biri olan Ornitin dekarboksilazın inhibisyonu
- Dokularda poliamin düzeylerini azaltarak antikanserojen etki
- Oral 500 mg/m2/gün
- Yan etki: ototoksik

Cancer Prev Res (Phila). 2010 Jan;3(1):35-47. doi: 10.1158/1940-6207.CAPR-09-0096.

A randomized, double-blind, placebo-controlled phase 3 skin cancer prevention study of {alpha} -difluoromethylornithine in subjects with previous history of skin cancer.

Bailey HH[1], Kim K, Verma AK, Sielaff K, Larson PO, Snow S, Lenaghan T, Viner JL, Douglas J, Dreckschmidt NE, Hamielec M, Pomplun M, Sharata HH, Puchalsky D, Berg ER, Havighurst TC, Carbone PP.

Author information

Abstract

Preclinical studies have shown that the inhibition of ornithine decarboxylase (ODC) by alpha-difluoromethylornithine (DFMO) and resultant decreases in tissue concentrations of polyamines (putrescine and spermidine) prevents neoplastic developments in many tissue types. Clinical studies of oral DFMO at 500 mg/m(2)/day revealed it to be safe and tolerable and resulted in significant inhibition of phorbol ester-induced skin ODC activity. Two hundred and ninety-one participants (mean age, 61 years; 60% male) with a history of prior nonmelanoma skin cancer (NMSC; mean, 4.5 skin cancers) were randomized to oral DFMO (500 mg/m(2)/day) or placebo for 4 to 5 years. There was a trend toward a history of more prior skin cancers in subjects randomized to placebo, but all other characteristics including sunscreen and nonsteroidal anti-inflammatory drug use were evenly distributed. Evaluation of 1,200 person-years of follow-up revealed a new NMSC rate of 0.5 events/person/year. The primary end point, new NMSCs, was not significantly different between subjects taking DFMO and placebo (260 versus 363 cancers, P = 0.069, two-sample t test). Evaluation of basal cell (BCC) and squamous cell cancers separately revealed very little difference in squamous cell cancer between treatment groups but a significant difference in new BCC (DFMO, 163 cancers; placebo, 243 cancers; expressed as event rate of 0.28 BCC/person/year versus 0.40 BCC/person/year, P = 0.03). Compliance with DFMO was >90% and it seemed to be well tolerated with evidence of mild ototoxicity as measured by serial audiometric examination when compared with placebo subjects. The analysis of normal skin biopsies revealed a significant (P < 0.05) decrease in 12-0-tetradecanoylphorbol-13-acetate-induced ODC activity (month 24, 36, and 48) and putrescine concentration (month 24 and 36 only) in DFMO subjects. Subjects with a history of skin cancer taking daily DFMO had an insignificant reduction (P = 0.069) in new NMSC that was predominantly due to a marked reduction in new BCC. Based on these data, the potential of DFMO, alone or in combination, to prevent skin cancers should be explored further.

Xeloda® (capecitabine)

Dermatol Surg. 2013 Apr;39(4):634-45. doi: 10.1111/dsu.12049. Epub 2013 Feb 4.

Capecitabine to reduce nonmelanoma skin carcinoma burden in solid organ transplant recipients.

Endrizzi B[1], Ahmed RL, Ray T, Dudek A, Lee P.

⊕ Author information

Abstract

BACKGROUND: Solidorgan transplant recipients (SOTRs) are at greater risk of nonmelanoma skin cancer (NMSC) than the general population, in large part because of their immunosuppression. Select individual SOTRs demonstrate a rate of tumor development at the upper end of their cohort. Capecitabine, a prodrug converted in the body to 5-fluorouracil (5-FU), may alter the risk for development of NMSC in an individual SOTR with a high rate of tumor development.

OBJECTIVE: To report observations of a series of 10 SOTRs treated with capecitabine as adjuvant prevention for high-incidence NMSC.

METHODS: Ten SOTRs were administered cycles of low-dose oral capecitabine (0.5-1.5 g/m(2) per day) for days 1 to 14 of a 21-day treatment cycle. Measurements (skin screenings, laboratory and toxicity monitoring) were performed every 1 to 3 months. Incidence rates of squamous cell carcinoma (SCC) before and during treatment were determined and compared using the Wilcoxon signed-rank test.

RESULTS: The average incidence rate (mean ± SD) of SCC before treatment (0.56 ± 0.28 SCCs/month, range 0.17-1.17 SCCs/month) declined to 0.16 ± 0.11 SCCs/month (range 0-0.33 SCCs/month) during the first 12 months of treatment (mean reduction 68 ± 30.0%, range 0-100%, $p < .005$). Reduction in actinic keratosis was observed. Common side effects included fatigue, nausea, hand-and-foot syndrome, gout, and poor renal function. Seven of 10 participants required dose adjustment, and two of these were discontinued from the study drug because of side effects.

LIMITATIONS: Case series design, small observational population.

CONCLUSIONS: SOTRs experienced a clinically and statistically significant decline in incident SCCs during treatment with low-dose oral capecitabine, with varying degrees of side effects. Larger randomized trials will determine the dose and efficacy of capecitabine for adjuvant treatment of NMSC in SOTRs.

Postepy Biochem. 2014;60(1):84-9.

[Lunasin--a novel chemopreventive peptide].

[Article in Polish]

Wołosik K, Markowska A, Kuźmicz I.

Abstract

Lunasin is a bioactive peptide originally isolated from soybean and has demonstrated chemopreventive and anticancer properties against: skin, colon, prostate and breast cancers. Lunasin by binding to the receptors of colon cancer cells prevents its adhesion to the liver tissue. When the receptor is blocked, new blood vessels cannot differentiate which prevent the spread of cancer. In the model estrogen-independent breast cancer, lunasin and aspirin administration inhibits cell proliferation, arrest cell cycle in S-phase as well as a decreases expression of cancer genes. Lunasin has also been found to exert potent antioxidant properties, reducing lipopolysaccharide induced production of ROS by macrophage cells, and acting as a potent free radical scavenger. Using the modifying the of DNA method it has been demonstrated that CpG islands were hypomethylated in RWPE-1 cell lines and hypermethylated RWPE-2 in cell line.Despite of numerous and promising evidence of antitumor activity of lunasin, there are still not explained all the mechanisms of its action in the processes of carcinogenesis.

Protein Pept Lett. 2013 Apr;20(4):424-32.

Chemopreventive properties of Peptide Lunasin: a review.

Hernández-Ledesma B[1], Hsieh CC, de Lumen BO.

Author information

Abstract

Cancer has become one the most common causes of death in developed countries and has been defined as the medical challenge of our times. Accumulating evidence support the notion that prevention can be a major component of cancer control. Chemoprevention, a relatively new and promising strategy to prevent cancer, is defined as the use of natural and/or synthetic substances to block, reverse, or retard the process of carcinogenesis. Plant-based foods, containing significant amounts of bioactive phytochemicals, may provide desiderable health benefits beyond basic nutrition to reduce the process of cancer. In the last few years, proteins and peptides have become one group of nutraceuticals that show potential results in preventing the different stages of cancer including initiation, promotion, and progression. Lunasin is a 43- amino acid peptide identified in soybean and other plants whose anti-carcinogenic activity has been demonstrated both in in vitro and in vivo assays. Moreover, this peptide has been found to exert anti-inflammatory and antioxidant properties that could contribute to its chemopreventive effects. Lunasin's bioactivity and its molecular mechanism(s) of actions are summarized in this review.

Antioksidanlar

- UV'e bağlı gelişen fotohasara ve reaktif oksijen radikalleri tarafından oluşturulan hücre hasarına karşı koruyucu etkileri var

- Genellikle sebze ve meyvelerde doğal olarak bulunan maddeler

- Karotenoidler, A, C, E vitaminleri, polifenoller, ubiquinon, selenyum, koenzim Q10, yeşil çay, curcumin (Hint Safranı), silimarin, genistein, apigenin, diallil sülfit,

Kaynakları

- Beta karoten: Ispanak, marul, brokoli, lahana, havuç, kavun, şeftali, kaysı,kırmızı-yeşil biber

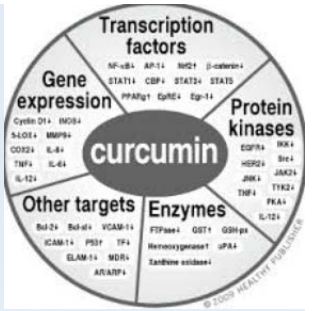
  *likopen:karoten ailesine ait pigment, domates, karpuz, kırmızı greyfurt, kayısı

- Polifenoller: yeşil çay, üzüm çekirdeği

  *Resveratrol: üzüm, sert kabuksuz meyveler, yer fıstığı ve kırmızı şarapta doğal olarak bulunan polifenolik bir antioksidan

- Selenyum:et, yumurta sarısı, tahıllar, baklagiller ve fındık, fıstık gibi kabuklu yemişlerdir

Curcumin (Hint Safranı):



antimutojenik ve antikarsinojenik, antioksidan ve antiinflamatuar etkileri var

Otolaryngol Head Neck Surg. 2013 May;148(5):797-803. doi: 10.1177/0194599813476845. Epub 2013 Feb 5.

Curcumin inhibits UV radiation-induced skin cancer in SKH-1 mice.

Phillips J[1], Moore-Medlin T, Sonavane K, Ekshyyan O, McLarty J, Nathan CA.

Author information

Abstract

OBJECTIVE: As skin cancer incidence increases, research has focused on novel chemopreventive agents that inhibit tumor formation. In prior experimentation, curcumin, a naturally occurring food substance and anticarcinogenic agent, inhibited cutaneous squamous cell carcinoma xenograft growth. We hypothesize curcumin will inhibit UVB radiation-induced skin cancer growth in mice, approximating a human chemopreventive model.

STUDY DESIGN: Randomized experimental animal and laboratory study.

SETTING: Louisiana State University Health Sciences Center-Shreveport, Louisiana.

SUBJECTS AND METHODS: SKH-1 mice were pretreated with oral or topical curcumin or oral or topical control (n = 11/group) for 14 days. Mice received UVB radiation 3 times weekly for 24 weeks or were not radiated. Number of tumors formed and time to tumor onset for each mouse were recorded through tumor harvest after week 24. Tumor multiplicity and time to tumor onset were compared.

RESULTS: Time to tumor onset was significantly shorter in control mice compared to mice receiving either oral (P = .025) or topical (P = .015) curcumin. A significant difference in the average number of tumors formed per mouse was seen, as fewer tumors were formed in the oral curcumin (P = .01) and topical curcumin (P = .01) groups, compared with respective controls. No significant difference in average number of tumors per mouse was seen between oral and topical curcumin (P = .56), suggesting that both routes were equally effective.

CONCLUSION: Curcumin appears to inhibit skin cancer formation and prolong time to tumor onset when administered by either an oral or topical route. These data suggest that curcumin may have chemopreventive potential against skin cancer, necessitating future experimentation with human subjects.

- **Silimarin (Meryemana Dikeni):** Silimarin deri kanseri önleyici özellikleri olan antioksidan bir bileşik olarak bilinir.

- **Genistein:** Soyada bulunan bir isoflavon olan genisteinin deride antioksidan ve antikarsinojenik etkileri gösterilmiş.

- **Diallil Sülfid:** Sarımsak ve soğanda bulunan güçlü bir antioksidan maddedir.

Nutr Cancer. 2012;64(5):770-80. doi: 10.1080/01635581.2012.676142. Epub 2012 Apr 20.

Diallyl trisulfide induces apoptosis of human basal cell carcinoma cells via endoplasmic reticulum stress and the mitochondrial pathway.

Wang HC[1], Hsieh SC, Yang JH, Lin SY, Sheen LY.

Author information

Abstract

Diallyl trisulfide (DATS), an active component of garlic oil, has attracted much attention because of its anticancer effect on several types of cancers. However, the mechanism of DATS-induced apoptosis of basal cell carcinoma (BCC) is not fully understood. In the present study, we revealed that DATS-mediated dose-dependent induction of apoptosis in BCC cells was associated with intracellular reactive oxygen species accumulation and disrupted mitochondrial membrane potential. Western analysis demonstrated concordant expression of molecules involved in mitochondrial apoptosis, including DATS-associated increases in phospho-p53, proapoptotic Bax, and decreases in antiapoptotic Bcl-2 and Bcl-xl in BCC cells. Moreover, DATS induced the release of cytochrome c, apoptosis-inducing factor, and HtrA2/Omi into the cytoplasm, and activated factors downstream of caspase-dependent and caspase-independent apoptosis, including nuclear translocation of apoptotic-inducing factor and endonuclease G and the caspase cascade. These results were confirmed by pretreatment with the antioxidant N-acetyl-L-cysteine and the caspase inhibitor (z-VAD-fmk), the latter of which did not completely enhance the viability of DATS-treated BBC cells. Exposure to DATS additionally induced endogenous endoplasmic reticulum stress markers and intracellular $Ca2^{-}$ mobilization, upregulation of Bip/GRP78 and CHOP/GADD153, and activation of caspase-4. Our findings suggest that DATS exerts chemopreventive potential via ER stress and the mitochondrial pathway in BCC cells.

- Ancak bu ajanların insanlarda deri kanserini önleyici etkilerinin netleşmesi için daha fazla çalışmalara gereksinim vardır.

4. Nutrisyonel faktörler

- Düşük yağ oranına sahip,
- Sebze ve narenciye ağırlıklı beslenme
- Antioksidanların tüketilmesi
- D vit eksikliği açısından riskli hastalarda D vitamininden zengin beslenme

Cancer Res. 2012 Jul 1;72(13):3282-9. doi: 10.1158/0008-5472.CAN-11-3511.

Increased caffeine intake is associated with reduced risk of basal cell carcinoma of the skin.

Song F[1], Qureshi AA, Han J.

Author information

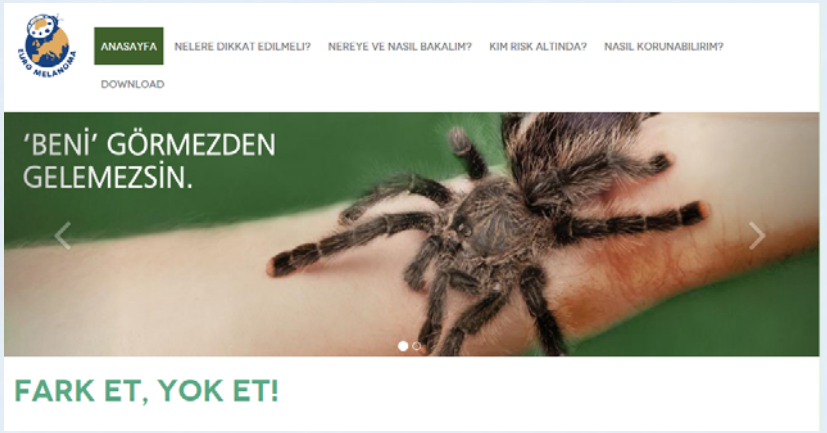
Abstract

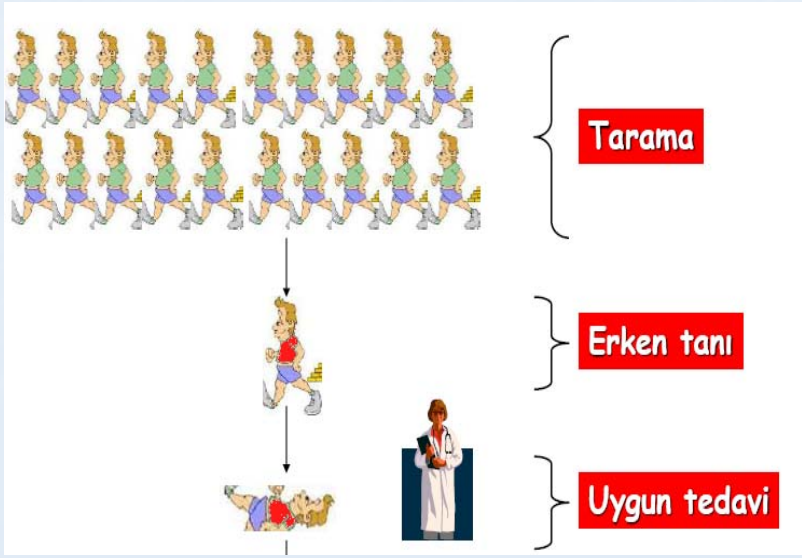
Studies in animals suggest that caffeine administration helps prevent squamous cell skin cancer development, but there have been limited epidemiologic studies on the association between caffeine consumption and skin cancer risk. Using data from the Nurses' Health Study and the Health Professionals Follow-up Study, we prospectively examined risks of basal cell carcinoma (BCC, 22,786 cases), squamous cell carcinoma (SCC, 1,953 cases), and melanoma (741 cases) in relation to caffeine intake. Cox proportional hazard models were used to calculate relative risks (RR) and 95% confidence intervals (CI). The amount of caffeine intake from all dietary sources was inversely associated with BCC risk. Compared with the lowest quintile, the highest quintile had the lowest risk (RR, 0.82 in women; 95% CI:,0.77-0.86 and RR, 0.87 in men; 95% CI, 0.81-0.94; Ptrend<0.0001 in both). A significant inverse association was also found between caffeinated coffee consumption and BCC risk. Compared with individuals who consumed caffeinated coffee less than 1 cup per month, women who consumed more than 3 cups/d had the lowest risk (RR, 0.79; 95% CI, 0.74-0.85; Ptrend<0.0001) and the RR for men was 0.90 (95% CI, 0.80-1.01; Ptrend=0.003). Caffeine from other dietary sources (tea, cola, and chocolate) was also inversely associated with BCC risk. Decaffeinated coffee consumption was not associated with a similar decrease in BCC risk. In contrast, caffeine intake was not found to be inversely associated with risks of SCC or melanoma. Our findings argue that caffeine intake in men and women is inversely associated with risk of BCC.

Sekonder ve tersiyer korunma

Tarama

- Deri kanserlerinin erken tanısı için **toplum taramaları**





Eğitim ve kendi kendini muayene etme

- Güneşten korunma ve NMDK nin belirtileri konusunda bilgi verilmesi, eğitim kampanyaları
- Ayda bir kere kendi kendini muayene etmesi
  (öz. Ailesinde ve kendisinde nonmelanom deri kanseri öyküsü olanların ve predispozan bir faktöre sahip kişilerin)
- Yılda bir kez doktora muayene olması , şüpheli lezyon varsa hemen doktora başvurması

Araştırmalar

- Risk katkısı olan genlerin tanımlanması ve hedef tedavilerin geliştirilmesi : Östrojen reseptör beta agonisti (Erb-041) vb
- Erken tanı için yeni, daha duyarlı ve özel biyomarkırların geliştirilmesi

Sonuç olarak;

- Güneşten korunma önemli
- Çok sayıda NMDK gelişme riski olanlara kemoprevensiyon!!!
- OTH da immünsüpresif tedavilerin modifiye edilmesi-
- Beslenmeye dikkat edilmesi…..,
- Eğitim!!!!!!!!

Skin cancer prevention: a link between primary prevention and early detection?

The aim of this paper was to determine if there is any link between primary prevention and early detection for skin cancer. Results from a study of a large random sample of Gold Coast residents (N = 995) identified an association (P < 0.01) between individual primary prevention and early detection activities. People were also more likely to use both prevention methods if they had personal experience with skin cancer (P = 0.01) or if they were male (P = 0.05). **Future primary prevention and early detection skin cancer programs might be most effective if they are combined.**

Aust J Public Health. 1994 Dec;18(4):417-20.

Çocuklar gibi deri kanserleri de her zaman kurallara uymazlar

teşekkürler.....