Topical Therapies for Cutaneous Malignancy

Dr J von Nida
MBBS FACD
How are solar keratoses treated by general practitioners in Australia?

International Journal of Dermatology 2006, 45, 272-276

- Cryotherapy (63%)
- Excision (18%)
- Combination of Cryotherapy and Excision (5%)

- Topical treatments were infrequently used.
Topical Therapies

- 5FU
- Imiquimod
- PDT
- Cryotherapy
- Retinoids
- Salicylic Acid
- ?Diphenycyclopropenone
Lesions Typically Treated with Topical Therapy

- Solar Keratoses
- Bowen’s Disease (SCC in situ)
- Superficial BCC
Solar Keratoses

- Appear on chronically sun-exposed sites.
- Present as erythematous macules with superimposed hyperkeratosis.
- Generally multiple and may be confluent.
- If tenderness or thickening is evident on lateral palpation this can indicate possible malignant transformation.
- DDx:- Bowen’s Disease, SCC, Solar Lentigo or Lentigo Maligna if pigmented.
Bowen’s Disease (intraepidermal SCC)

- Present’s as well-defined, round/oval, erythematous, hyperkeratotic plaques.
- Often found on lower legs.
- Generally asymptomatic.
- May eventually develop into invasive SCC.

- DDx:- Superficial BCC, Psoriasis, SCC, SSMM
Superficial BCC

- Generally occur on the trunk and limbs.
- Bright pink, shiny, well-defined macular lesions.
- Pearly appearance is enhanced by stretching the skin.
- Enlarge slowly but rarely bleed or ulcerate.

- DDx:- Bowen’s disease, Solar keratosis, Psoriasis, Eczema.
Liquid Nitrogen Cryotherapy

- ~-200°C.
- Simple, fast.
- Mild discomfort.
- Lesions may blister and then leave a brownish scab which clears to leave a hypopigmented scar.
- Useful for solar keratoses.
- Has been reported for small BCC’s on trunk and extremities.
5-Fluorouracil

- Indicated for the treatment of solar keratoses and Bowen’s disease.
- Efficacy has been reported as 84.8%.
- Treatment is applied twice daily for 3-4 weeks (depending on site treated).
- Considerable erythema, discomfort and swelling can occur.
- Cost ~$32 - $45.
5FU - Adverse Effects

- Local reaction - redness, pain, pruritus.
- Hyperpigmentation.
- Scarring.
Imiquimod

- Thought to work by modification of the immune response and stimulation of apoptosis in the BCC cells.
- Superficial BCC - 5x/week application for 6 weeks - 90% clinical response at 12 weeks and 84% clinical response at 1 year. Geisse J. et al JAAD;50:722-33.
- Severity of erythema, erosion and scabbing/crusting correlated positively with the histologic response.
Imiquimod - Adverse Effects

- Skin Reaction - redness, swelling, pain, weeping.
- Flu like symptoms - fever, headache, muscle and joint pain.
- Hyper- or Hypopigmentation.
- Cutaneous reaction at distant site.
Superficial BCC - Aldara
5 Times/Week for 6 Weeks

Initiation visit

Week 3

Individual patient responses may vary and rest periods from therapy may be required
Superficial BCC - Aldara
5 Times/Week for 6 Weeks

Week 6 - end of treatment

12 weeks posttreatment

Individual patient responses may vary and rest periods from therapy may be required
Picato Gel (Ingenol Mebutate)

- 0.015% - Face and Scalp – daily for 3/7

- 0.05% - Trunk + Extremities – daily for 2/7

- Unknown mechanism of action.

- Efficacy of ~50% at 12 months post Rx.
Euphorbia peplus
Picato Reaction
Picato

Apply to the affected area once daily for 3 consecutive days.¹

Tubes not actual size.
Picato
Solaraze

- 3% Diclofenac Sodium Gel.
- Twice daily application for 60-90 days.
- ~50% clearance (30 days after Rx).
- ? Better tolerated.
Salicylic Acid

- Reduces hyperkeratosis.
- Probably not curative.
- 2% - 8% in sorbelene or aqueous cream applied daily.
- Can be used with other keratolytics eg. 10% urea.
Photodynamic Therapy

• Useful for the treatment of superficial neoplastic skin lesions (actinic keratoses, Bowen’s disease, superficial BCC’s).
• ALA application selectively induces the production of intracellular porphyrins. Epithelial tumours synthesize much higher amounts of protoporphyrin IX than the surrounding tissue.
• Stinging pain during the treatment.
• Protocols are still being developed.
Vitamin D

Dr J von Nida
FACD
What is Vitamin D?

- Fat Soluble Sterosteroids responsible for enhancing intestinal absorption of Ca + PO4.
- Vitamin D2 (ergocalciferol)
- Vitamin D3 (cholecalciferol)
- Body can synthesize (cholecalciferol) in the skin (Cholesterol + UV).
- Negative Feedback Loop that prevents toxicity.
Vitamin D Deficiency

• Controversial

• Adequate > 50nmol/l
• Mild Defn 25 – 50 nmol/l
• Defn < 25nmol/l

• In Tasmania ~50% of the population is mildly deficient.
Vit D Supplementation

Ish-Shalom et al JCEM 93:3430 2008

• 1000iu/ day - variable response but ~12nmol/l increase.

• Metabolism, age, storage (Vit D is stored in fat – obese).

• Vit D toxicity (usually if > 500nmol/l)

• Vit D3 4000iu/day 5/12 – no problems (Vieth, AJCN 2001)

• Takes 3/12 to reach plateau.
Sun Exposure + Vit D

• 1000iu/day
• Perth – 9mins exposure to face and dorsum hands at 9am in Spring. (AMJ)
• Expose 15% BSA to 1/3 MED most days – 6-8mins Dec-Jan just before 11am or just after 3pm - ~13nmol/l increase.
• BJD paper
Vit D + Bones

• Vit D deficiency has become a worldwide issue in the elderly and remains common in children and adults.

• Low blood 25-hydroxy-vitamin D can result in impaired bone mineralization and bone damage which leads to bone-softening.
Osteomalacia (Rickets)

• Childhood disease.
• Impeded bone growth, soft weak bones + deformity of the long bones.
• Caused by – Ca or Ph deficiency as well as a lack of Vit D.
• Dietary risk factor – abstaining from animal foods.
• Nigeria, Denver
Osteoporosis

• Decrease in bone mineral density.
• Higher risk of fractures.
• Vitamin D inadequacy is common among patients with osteoporosis. (<20ng/mL).
• Supplementing with Vit D – increase bone density + slow bone turnover in seniors.
• Supplementing pt’s with low Vit D can reduce the risk of osteoporotic fractures esp. hip.
Vit D + Autoimmunity
Nature Medicine 18(2) Feb 2012

• Evidence is lacking.

• Higher levels of Vit D were associated with lower risk of MS.

• The critical window for Vit D intake or level needed to affect risk of Autoimmune diseases is not known.
Vit D + Pregnancy
Aghajafari et al 2013 BMJ 346

• Low Vit D – Gestational Diabetes, Pre-Eclampsia and Small Infants.

• The benefit of supplementation is unclear.

• 4000iu Vit D daily is required to achieve required blood levels.
Vit D + Cancer

Buttigliero et al The Oncologist 16 (9):1215-27

- Low Levels of Vit D may be associated with a higher death rate in some cancers BUT...

- Vit D supplementation produces contradictory and inconclusive results.

- Both hypo- and hyper- vitaminosis D may negatively affect prognosis in cancer
Vit D Receptor Polymorphisms

- VDR is a member of the nuclear receptor family of transcription factors.
- Downstream targets of this receptor are involved principally in mineral metabolism though the receptor regulates a variety of other pathways such as those involved in the immune response and cancer.
- Polymorphisms of the receptors exist.
Evidence

• Beyond its use to prevent osteomalacia the evidence for other health effects of Vit D supplementation in the general population is inconsistent.

• The best evidence of benefit is for bone health and a decrease in mortality in elderly women.
Guidelines for our patients

Summary of the risks and benefits of sun exposure position statement
Australian and New Zealand Bone and Mineral Society, Osteoporosis Australia, Australasian College of Dermatologists and The Cancer Council Australia.

Sun protection is usually required if the ultraviolet (UV) index is 3 and above (and people are advised to check the forecast UV index in their local area).

Most people achieve adequate vitamin D levels through incidental sun exposure, but people living in the southern Australian states in winter may need 2–3 hours of sun exposure on the hands, arms and face each week.

Some people are at high risk of developing skin cancer and need more rigorous sun protection than the general population.

Some subgroups of the population, such as the frail and elderly, and people who cover most of their body with clothing for cultural or religious reasons, may need to consult their doctor to have their vitamin D status investigated and supplemented if necessary.