Actinic keratosis

“Doc, can you do anything about these crusty bits on my scalp – they won’t go away!”

This clinical review in the DTB reviews the management of actinic keratosis – a common primary care skin problem, becoming more prevalent as our population ages (DTB 2013;51:81). They are caused by chronic sun exposure and are usually found on sun-exposed skin areas, e.g. scalp, hands, forearms, face.

Actinic keratosis statistics:
- Prevalence increases with age, affecting 34% of men and 18% of women aged over 70y.
- Reports of the risk of malignant transformation vary widely from 0.025 to 16% per year.
- An increased number of lesions increases the risk of malignant transformation.

Clinical appearance and differential diagnosis

Actinic keratoses (AKs) are usually pink, brown or red scaly patches on the skin. They may be graded:

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Slightly palpable (by touch rather than sight – there may be slight colour change or they may just feel crusty!)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 2</td>
<td>Moderately thick and visible</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Very thick and hyperkeratotic</td>
</tr>
</tbody>
</table>

Individual lesions are often associated with a ‘field change’ in the surrounding skin, and subclinical palpable, but not visible, lesions may be present.

The differential diagnosis includes Bowen’s disease, squamous cell carcinoma (SCC), keratoacanthoma, basal cell carcinoma, seborrhoeic keratosis and lentigo maligna.

Prevention

This is by reducing sun exposure, and using physical (e.g. hats, long-sleeved clothes) and chemical (sun screen) barriers. Avoidance of tanning beds is also important.

Patients with AKs should be shown how to check the skin for new lesions, and features of suspicious lesions should be discussed.

Which lesions are at highest risk of malignancy?

The natural history of AKs is that 10–15% regress, the majority remain unchanged or proliferate benignly, and a small proportion (between 0.025 and 16%!) progress to SCC. Most lesions can be managed in primary care but a small number will need referring. Risky lesions include:
- Those >1cm in diameter.
- Confluent lesions.
- Rapid enlargement.
- Bleeding, induration, inflammation.
- Patients on immunosuppression, e.g. transplant patients.

Refer to a dermatologist if:
- There is diagnostic uncertainty.
- Features of malignancy.
- Progression despite treatment.
- Concerns about management, e.g. lesions in areas of poor healing such as shins.
- High-risk patient, e.g. immunosuppressed.

Treatment options

Conservative management
- Many AKs regress spontaneously, and safety netting alone may be sufficient for grade 1 lesions.
- Emollients or sun blocks are also an option, the latter having the combined benefits of smoothing existing lesions and preventing new ones.

Topical treatments
Local inflammation is pretty universal with topical treatments, and can make adherence difficult.

- Warn patients about inflammation, and recommend treating one body area at a time, not to use around the eyes, wash hands carefully after use and avoid UV exposure while treating.
- Show patients pictures of expected inflammation.
- Options include:
  - Diclofenac 3% for mild (grade 1) lesions.
  - Fluorouracil for thin lesions.
  - Fluorouracil and salicylic acid for moderately-thick lesions.
  - Imiquimod for confluent lesions (also licensed for BCCs – see prescribing info later in article).

**Ingenol mebutate gel (Picato)**

**Suspension of marketing authorisation, January 2020**

The MHRA and the European Medicines Agency have suspended the licence for this product due to concerns about increased risk of skin cancer.

- We should no longer prescribe this treatment.
- Advise patients to be vigilant for the development of any new skin lesions within the treatment area, and to seek medical advice promptly should any occur.
- Yellow card any suspected adverse reactions.

In many areas, ingenol is recommended second line after fluorouracil – check your local formulary/prescribing guidelines and ensure they are updated following this guidance.

**So which option works best?**

A Dutch study has attempted to answer this question. Researchers randomised just over 600 patients to one of the 4 most common treatments, looking for a >75% reduction in actinic keratoses after treatment. They found that at 12 months that fluorouracil had performed best: 75% success for fluorouracil compared with 54% for imiquimod, 38% for photodynamic therapy and only 29% for ingenol mebutate gel. Time to onset ranged from weeks to months.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Regimen</th>
<th>Cost for 1 course</th>
</tr>
</thead>
<tbody>
<tr>
<td>3% diclofenac gel with hyaluronic acid</td>
<td>Twice daily for 60–90d</td>
<td>£76.60 (2 x 50g tubes)</td>
</tr>
<tr>
<td>5% fluorouracil cream</td>
<td>Once or twice daily for 3–4w</td>
<td>£32.83 (1 x 40g tube)</td>
</tr>
<tr>
<td>0.5% fluorouracil cream</td>
<td>Once daily for 6–12w</td>
<td>£76.60 (2 x 25ml)</td>
</tr>
<tr>
<td>5% imiquimod</td>
<td>3 nights per week for 4w – after a 4w break, if lesions persist, repeat for a further 4w</td>
<td>£48.50 (1 x 4w treatment pack) £97.00 (2 x 4w treatment packs)</td>
</tr>
<tr>
<td>3.75% imiquimod</td>
<td>Up to 2 sachets, once daily before bedtime for 2w, have a 2w break and then repeat for a further 2w</td>
<td>£113–£226 depending on whether treatment area requires 1 or 2 sachets</td>
</tr>
</tbody>
</table>

**Physical treatments**

**Cryotherapy**

- Most commonly-used physical treatment in primary care.
- Remember, it does not allow histological diagnosis so, if diagnosis is uncertain, it should not be used.
- It works best for thin lesions and is only suitable to treat a few lesions at a time.
- It does not address the ‘field change’ of the skin, and follow-up treatments may be required.
- Side-effects of treatment are redness, blistering, pain, swelling and hypo- or hyperpigmentation.
- A Cochrane review comparing cryotherapy with fluorouracil showed that more people had complete clearance with fluorouracil. However, it did not report dropout rates. Imiquimod and cryotherapy seemed to be equally effective.
- May be most effective when used in combination with a ‘field clearing treatment’ such as imiquimod or diclofenac, but this increases side-effects.

**Photodynamic therapy**

- Secondary care-based treatment where photosensitising cream is applied to lesions, and then a light source is applied.
- One treatment is usually adequate for most lesions (thick lesions or immunosuppressed individuals may require two).
- It is still finding its niche but is likely to be offered where lesions have failed to respond to other treatments.
Surgery

- Reserved for lesions in sensitive areas, e.g. eyelids, or where malignancy is suspected and histology required.
- This is because of the large areas of skin affected!

Actinic keratosis

- Mild lesions may be observed or treated with emollients or sun block – there is inadequate evidence to support treatment of all lesions to prevent malignant transformation.
- Treatment has two parts: treating individual lesions and the damaged skin field.
- In primary care, cryotherapy is useful to treat a small number of individual lesions.
- Consider diclofenac 3% to treat field change with mild lesions (palpable but not visible), fluorouracil for thin lesions, imiquimod for confluent lesions.
- Ingenol carries increased risks of skin cancer, and should not be used.
- Counsel patients carefully about inflammatory side-effects of topical treatments.
- Refer patients with features suspicious of malignancy, e.g. induration, rapid expansion, large size, ulceration or immunosuppression, or if lesions fail to respond to treatment.
- Educate all patients about sun protection and self-examination of skin.

Check your recent prescribing – do you have any patients currently using ingenol who should be advised to stop?

We make every effort to ensure the information in these articles is accurate and correct at the date of publication, but it is of necessity of a brief and general nature, and this should not replace your own good clinical judgement, or be regarded as a substitute for taking professional advice in appropriate circumstances. In particular check drug doses, side-effects and interactions with the British National Formulary. Save insofar as any such liability cannot be excluded at law, we do not accept any liability for loss of any type caused by reliance on the information in these articles.
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