Topical imiquimod or fluorouracil therapy for basal and squamous cell carcinoma: a systematic review

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CRD summary
This review concluded that evidence supported use of topical imiquimod for superficial basal cell carcinoma (BCC) and topical fluorouracil for superficial BCC and squamous cell carcinoma in situ. These conclusions should be interpreted with caution as the evidence base seemed to be generally poor quality and there was a possibility of publication, language and reviewer biases.

Authors' objectives
To investigate clearance rates and adverse effects of topical imiquimod or fluorouracil therapy in the treatment of non-melanoma skin cancers, such as basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

Searching
MEDLINE, CANCERLIT and The Cochrane Library were searched for English-language studies (dates not reported). Search terms were reported. References of retrieved studies were examined.

Study selection
Prospective, retrospective and case studies of topical imiquimod or fluorouracil with at least four participants with non-melanoma skin cancer and a follow-up of at least six months or post-treatment histological examination were eligible for inclusion. Studies were excluded if the tumour subtype was not differentiated, if tumours with mixed histologic findings were treated, if topical and/or surgical combination therapy was used and if the study included immunocompromised patients or used preparations that were not commercially available.

Imiquimod studies were of treatment of superficial, nodular and infiltrative BCC and invasive SCC and SCC in situ. Fluorouracil studies were of treatment of superficial BCC and SCC in situ. Treatment regimens varied.

It was unclear how many reviewers selected studies for inclusion.

Assessment of study quality
Methodological quality of the studies was not assessed. The studies were graded according strength of recommendation according to study design by two reviewers. The SORT criteria were used: class A (recommendation based on consistent and good-quality patient-oriented evidence), class B (recommendation based on inconsistent or limited quality patient-oriented evidence); and class C (recommendation based on consensus, usual practice, opinion, disease-oriented evidence or case series for studies of diagnosis, prevention, treatment or screening).

Data extraction
Clearance rates and adverse event rates were extracted as percentages of patients who achieved clinical clearance or experienced an adverse event.

The number of reviewers who performed data extraction was not reported.

Methods of synthesis
The percentages were presented as ranges within a narrative synthesis.

Results of the review
Thirty studies were included in the review (n=1,950, range one to 185). Average follow-up duration ranged from four weeks to five years. Six of the studies were SORT category class A, 14 were class B and 10 were class C.
Imiquimod: Clearance rates ranged from 43% to 100% for superficial BCC (15 studies, 27 data sets), 42% to 100% for nodular BCC (11 studies, 22 data sets), 56% to 63% for infiltrative BCC (one study, two data sets), 73% to 88% for SCC in situ (five studies, five data sets) and 71% for invasive SCC (one study, one data set).

Fluorouracil: The clearance rates were 90% for superficial BCC (one study, one data set) and ranged from 27% to 85% for SCC in situ (five studies, five data sets).

At least one adverse event was experienced by both groups (up to 100% of the imiquimod group and up to 97% of the fluorouracil group). Intensity ranged from mild to severe and erythema, pruritis and pain were commonly reported.

Authors’ conclusions
Evidence supported use of topical imiquimod as monotherapy for superficial BCC and topical fluorouracil as monotherapy for superficial BCC and SCC in situ. Recommendation for use of these as primary treatment was weak. The authors recommended that use should be limited to patients with small tumours in low-risk locations who would not or could not undergo treatment with better-established therapies for which long-term clearance rates had been determined.

CRD commentary
The review question was supported by inclusion criteria for participants, intervention and study design. Only English-language studies were sought and no searches of unpublished data were reported; therefore, the review may have been prone to language and publication biases. Study selection and data extraction processes were not described, so it was unknown whether steps were taken to reduce reviewer error and bias. Methodological quality was not assessed. Most studies appeared to be of less robust designs. Few details of study design were reported, but the sample sizes were generally small. Narrative synthesis appeared appropriate given the diversity of patients, methodology and intervention regimens.

The authors’ conclusions should be interpreted with caution as the evidence base seemed to be generally poor quality and there was a possibility of publication, language and reviewer biases.

Implications of the review for practice and research
Practice: The authors stated that use of topical imiquimod and topical fluorouracil should be limited to patients with small tumours in low-risk locations who would not or could not undergo treatment with better established therapies for which long-term clearance rates had been determined. Long-term follow-up was essential for patients treated with topical imiquimod and topical fluorouracil. Use of topical therapy was not recommended in cosmetically sensitive areas, such as the embryonic fusion planes of the face.

Research: The authors did not state any implications for research.

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