A systematic review of treatment modalities for primary basal cell carcinomas

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Authors' objectives
To systematically review all prospective studies from 1970 to 1997 to compare the recurrence rates of the five most commonly used treatment modalities for basal cell carcinoma (BCC). The literature was also analysed for two investigational treatment modalities (immunotherapy with interferon alpha and/or beta or fluorouracil, and photodynamic therapy). Explanations for variation and controversies in study results were sought.

Searching
MEDLINE standard and advanced databases, EMBASE and Cancerlit were searched from 1970 to 1997. Keywords are listed. The yearbooks of dermatology that were published between 1978 and 1996 were manually screened for studies. Textbooks, reviews, editorials, existing guidelines and references of the studies found were checked for further information. Duplicate publications were excluded. Studies published in English, French, German, Dutch, Spanish or Italian were included.

Study selection
Study designs of evaluations included in the review
Prospective studies of 50 patients (and tumours) or more with at least 5 years follow up. Studies were excluded if they reported on combinations of 2 or more therapies, reported on therapies other than those listed in the inclusion criteria, combined results of different types of cancer or reported results only for effectiveness as proved by excision and histopathology a few months later, or cosmetic results only.

All studies included seem to be prospective case series.

Specific interventions included in the review
Surgical excision (SE), cryosurgery (CS), curettage and electrodessication (CE), radiotherapy (RT) and Mohs micrographic surgery (MMS) were included as the five most commonly used treatment modalities. Immunotherapy (with interferon or fluorouracil) and photodynamic therapy were also reviewed, but no appropriate studies were found on photodynamic therapy.

Participants included in the review
Patients with previously untreated primary basal cell carcinomas of all subtypes (superficial, nodular, micronodular, adenoid, morphea and metatypical).

Outcomes assessed in the review
Recurrence rate at follow-up of 5 years or more.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that validity was assessed.

Data extraction
For each patient series included the treatment modality, number of BCCs treated, recurrence rates and duration of follow-up were initially recorded. The authors state that secondarily the histologic subtype, size and location of tumours, number of tumours per patient, and number and reasons for drop-outs were analysed; however, these do not
Methods of synthesis
How were the studies combined?
The studies were categorised into 3 groups according to the number of tumours treated (50-99, 100-250 and >250). If possible the study size-weighted recurrence rates for all groups of tumours were calculated by dividing the total number of recurrences by the total number of tumours treated (raw recurrence rate) and the total number of patients observed for at least 5 years (5 year recurrence rate). The mean weighted recurrence rates for each treatment modality were also calculated two ways. Finally the life-table cumulative 5 year recurrence rates were either recorded from the articles or calculated in cases in which insufficient data for these calculations were available.

How were differences between studies investigated?
The authors state an objective to explain variation and controversy among study results with regard to study design, statistical methods and tumour and patient characteristics but do not address this objective in the analysis, simply reporting where these objectives were addressed by the included studies.

Results of the review
Eighteen patient series were included (n=9930).

The authors state that the real recurrence rate will be somewhere between the estimated weighted strict and raw recurrence rates. Because most studies used different statistical methods for calculating their results, overall mean recurrence rates were not calculated for every treatment modality.

Mohs micrographic surgery (3 studies, n=2660): Mean raw recurrence rate 0.8 (21/2660); Mean strict recurrence rate 1.1 (21/1989).

Surgical excision (3 studies, n = 1303): Raw recurrence rate was 1.4 in one study and 2.9 in another. Strict recurrence rate was 8.1 in one study. Mean cumulative 5 year rate (all 3 studies) was 5.3.

Cryosurgery (4 studies, n=796): Mean raw recurrence rate 3.0 (24/798); mean strict recurrence rate 4.3 (24/556); cumulative 5 year rate (3 studies) ranged from 0 to 16.5.

Curettage and desiccation (6 studies, n=4212): Raw recurrence rate (5 studies) ranged from 4.3 to 18.1; strict recurrence rate was given in one study as 8.5; cumulative 5 year rate ranged from 5.7 to 18.8.

Radiotherapy (1 study, n=862): Cumulative 5 year rate 7.4.

Immunotherapy (1 study, n=95): Raw recurrence rate 12.6, strict recurrence rate 21.4.

Authors' conclusions
Recurrence rates for different therapies could not be compared because of a lack of uniformity in the method of reporting, so evidence-based guidelines could not be developed. We surmise that Mohs micrographic surgery should be used mainly for larger, morphea-type BCCs located in danger zones. For smaller BCCs of the nodular and superficial types, surgical excision remains the first treatment of choice. Other treatment modalities can be used in patients in whom surgery is contraindicated. Immunotherapy and photodynamic therapy are still investigative.

CRD commentary
A good review of the area: the research question is clear and simple, inclusion criteria are stated and the literature search is comprehensive and includes searches for unpublished material. There are some language restrictions but quite a number of languages are included. Data is appropriately combined, given the heterogeneity in statistical methods used between studies, and results are clearly presented. More study details could have been presented (such as patient...
characteristics) and no validity assessment of the included studies was undertaken, preventing any narrative weighting of less biased studies above more biased studies (although all included studies were of a similar design). No details are given of the number of reviewers or processes involved in screening studies for relevance and data extraction. It should also be noted that the review was undertaken by members of the reference centre for Mohs micrographic surgery in the Netherlands. The authors’ conclusions seem to be based on expert opinion rather than the evidence presented and should therefore be treated with some caution.

Implications of the review for practice and research
Practice: The authors state that treating all BCCs with MMS should lead to overtreatment especially in patients with smaller (<2cm) BCCs of the nodular type located outside the H region of the face. These BCCs can be treated successfully with primary SE. Radiotherapy should not be used as primary treatment in relatively young patients because of the less favourable cosmetic results more than 5 years after therapy.

Research: The authors state that large prospective comparative studies should be performed to analyse whether small tumours with less aggressive histologic subtypes localised on some areas of the body are treated better with CS or CE.

The authors also state that because the number of dermatologic surgeons capable of performing MMS is still low, special training in this surgical technique should be an important consideration for dermatologic surgeons.

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