Treatment with UV-B for psoriasis and nonmelanoma skin cancer: a systematic review of the literature


Authors' objectives
To quantify the excess incidence (IDD) of nonmelanoma skin cancer (NMSC) in patients treated with UV-B phototherapy for psoriasis, as a function of the total dose of UV-B, specific for time since first exposure, age at first treatment, and other treatments for psoriasis used.

Searching
MEDLINE, BIOSIS Previews, and ONLINE CONTENTS were searched for articles published between 1980 and 1996. Combined search terms were 'UV light (UV-B)', 'phototherapy', 'psoriasis', 'skin cancer/carcinoma'. Free text searches and thesaurus and index words were used. Reference lists of retrieved articles were screened for additional studies.

Study selection
Study designs of evaluations included in the review
Two cohort studies and two case-control studies are included. Case series, case reports, reviews with no original data, and animal studies were excluded. Only studies published in English, French, German or Dutch were included.

Only studies that presented original data, adequately adjusted for confounders, that were unlikely to included selection or information bias were included in the meta-analysis.

Specific interventions included in the review
UV-B phototherapy. Interventions used in the included studies were UV-B monotherapy, and UV-B plus coal tar. Treatment dose and time since first exposure were not sufficiently specified in the included studies. The number of treatments, where reported, ranged from 100 or more to 300 or more. Studies of psoralen-UV-A photochemotherapy (PUVA) were excluded from this review.

Participants included in the review
Patients with psoriasis. Control group participants were psoriasis patients or from the general population.

Outcomes assessed in the review
Incidence of histopathology reported nonmelanoma skin cancer (NMSC) as a function of UV-B therapy. Studies that presented insufficient data to calculate the IDD of NMSC were excluded from the analysis. Outcomes reported in the included studies were prevalence of NMSC, cumulative incidence of NMSC, cumulative incidence of genital squamous cell carcinoma (SCC). Average follow-up in the included studies ranged from 2.7 to 20.1 years.

How were decisions on the relevance of primary studies made?
The relevance of all retrieved articles was evaluated by the first author on the basis of title, abstract, and keywords. Articles were retrieved only if they satisfied the inclusion criteria. A second reviewer evaluated a sample of all references to examine the reproducibility of the selection procedure (this was reported to be 99%). Both reviewers then read the selected articles and their relevance was assessed again. Disagreement was resolved between the two reviewers.

Assessment of study quality
Articles were assessed for various sources of bias (no further information was given) and how this was done was not explained. Articles were included in the meta-analysis only if selection and information bias were deemed unlikely by one author who was an epidemiologist.

Data extraction
Data were extracted independently by two reviewers.

**Methods of synthesis**

How were the studies combined?

A narrative synthesis is presented. The authors assumed constancy of the incidence to calculate excess incidence in each study, and also assumed absence of bias or confounding. Meta-analysis was conducted of the excess incidence per year of NMSC, estimated for each included study.

How were differences between studies investigated?

A table shows the differences between the four studies included in the meta-analysis for study design, population and control group characteristics, outcome measures, intervention, follow-up duration and results (IDD). Each study is described in more detail in the text, followed by a narrative summary in which possible causes of variation between the results obtained in each study is discussed, such as the dose of UV-B and co-interventions for psoriasis used. No formal test for heterogeneity was done.

**Results of the review**

A total of 104 potentially relevant articles were identified, and 91 were retrieved. Only 10 articles contained information about the incidence of NMSC in patients with psoriasis following UV-B phototherapy. One study was considered ineligible for inclusion in the meta-analysis due to confounding, and five others contained insufficient information to calculate the excess incidence of NMSC. This left four studies which were included in the meta-analysis. The total number of patients in the treatment group in the 4 included studies was 2195, the number of control participants is not reported for all 4 included studies.

The estimated excess incidence of NMSC per 100 patients with psoriasis treated with UV-B phototherapy per year in the four included studies was: -0.04 (n=85); 0.01 (n=892); 1.8 (n=958); and -0.58 to 0.06 (n=260). The risk of excess incidence due to a certain total number of UV-B treatments could not be determined as all four included studies lacked information about the total dose of UV-B received. The estimates of excess incidence were calculated under the assumption that the incidence of NMSC was constant across studies and that sources of bias and confounding were absent. Construction of a dose-response model specific for time since exposure or age at first treatment was not possible using reported data. Concomitant exposure to coal tar (in three of the four included studies) was not taken into account in the calculations of excess incidence. Lack of sufficient information in the included studies made it impossible to control for bias resulting from the effects of exposure to other treatments for psoriasis.

**Authors’ conclusions**

The available evidence is insufficient to quantify the excess incidence of NMSC in patients with psoriasis treated with UV-B. Empirical data are inadequate to estimate a dose-response relationship. It seems unlikely that the excess risk exceed 2% per year. It is not possible to assess from published data at what level of exposure this excess incidence occurs in humans, or how long after exposure excess risk is present.

**CRD commentary**

The review addresses a clear question in terms of participants, intervention and outcomes of interest. More than one database was searched. There may be language bias as articles published in four languages only were included. The possibility of publication bias is not addressed. A systematic procedure involving more than one reviewer was used to select studies for inclusion and to extract data from the included studies. How specific types of bias were investigated was not clearly specified. The four included studies are well described in the text and tables. Differences between studies are discussed and the narrative synthesis is appropriate. For the meta-analysis, calculation of the results involved several assumptions which are described clearly and the likely impact of this on the findings is discussed. Due to the limitations of the published data the authors’ conclusion that it is unlikely that the excess risk exceeds 2% should be interpreted with caution.
Implications of the review for practice and research

Practice: The authors do not discuss implications for practice.

Research: Further research is necessary to construct a valid dose-response relation on the basis of epidemiological data. Such research may be problematic because multiple treatments are used in patients with psoriasis, and treatment tends to be individualised according to a patient’s perceived susceptibility to NMSC. An RCT of UV-B versus a non-carcinogenic alternative is needed. The authors report that they are conducting an RCT to compare UV-B phototherapy with anthralin, including a cost-effectiveness analysis.

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