A systematic review of treatment options for dermal photosensitivity in erythropoietic protoporphyria

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CRD summary
This review assessed treatment options for dermal photosensitivity in erythropoietic protoporphyria and concluded that available data were insufficient to prove the efficacy of any treatment options. The authors' assertion that there was insufficient evidence from which to draw any firm conclusions appears to be reliable.

Authors' objectives
To assess the various treatment options for dermal photosensitivity in erythropoietic protoporphyria (EPP).

Searching
PubMed was searched from 1972 to May 2008 for studies in English, German or French; search terms were reported. Reference lists of relevant articles were searched to identify additional articles.

Study selection
Studies that evaluated treatments for EPP were eligible for inclusion. Excluded studies were: case reports with less than three patients; studies that summarised statements on treatment effects; studies on identical patients or patient cohorts (the study with the most detailed information was included); and studies that dealt with treatment of EPP-related liver disease. Evaluated treatments included: beta-carotene (at doses from 25mg/day to 300mg/day, with lower doses for children and doses from 100mg/day for adults); n-acetyl-cysteine; cysteine; dihydroxyacetone/Lawson (henna); vitamin C; canthaxanthin; and ultraviolet B treatment. Most studies dealt with the application of beta-carotene and change in EPP symptoms or sunlight tolerance; efficacy criteria were not standardised. Included studies were in adults and children. Concentrations of protoporphyrin IX (PPIX) in patients ranged from 2.1μmol/L to 75μmol/L; mean concentrations in trials ranged from 10μmol/L to 23μmol/L.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Two reviewers (except one study), independently assessed study quality using 13 criteria; disagreements were resolved through consensus. The number of criteria fulfilled was divided by the total number of criteria; maximum quality score was 1.

Data extraction
Data for efficacy endpoints were extracted as percentages.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Studies were combined in a narrative synthesis, arranged by treatment.

Results of the review
Twenty five studies were included in the review (n=454, range three to 80). Five studies were randomised controlled trials. The other studies were either open-label, uncontrolled studies or retrospective case reports.

Within studies that dealt with the application of beta-carotene (16 studies; n=337), 54% of patients reported a strong improvement in in EPP symptoms, 28% reported moderate improvement and 18% no improvement. Reactivity in phototesting (two studies) yielded a strong effect in 15% of patients, moderate effect for 56% and no effect in 29%.
Four of the five well-designed studies suggested lack of efficacy of beta-carotene; efficacy was inversely correlated with study quality.

Results for additional interventions were reported, but not synthesised.

**Authors’ conclusions**
Available data were insufficient to prove efficacy of any treatments in EPP.

**CRD commentary**
The review question was clear and included broad (but reproducible) inclusion criteria. The authors only searched one database, which together with some restrictions on language and uncertainty over whether unpublished sources were searched may have led to the exclusion of some relevant studies and the possible introduction of publication and language biases. Methods used for study selection and data extraction were not reported and it was unclear whether any methods were used to minimise error and bias. Appropriate criteria were used to assess the quality of the included studies, but the findings were not reported in the review; most appeared to be of poor quality. Sample sizes were generally small. Given the heterogeneity between the studies, the decision to employ a narrative synthesis was appropriate. There was a lack of clarity of parts of the review process, but the authors’ cautious conclusion that there was insufficient evidence from which to draw any firm conclusions appears reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that a careful risk/benefit assessment should be undertaken before long-term beta-carotene therapy was instituted in EPP.

**Research:** The authors stated that high-quality efficacy studies in porphyrias were required.

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