Minocycline-induced lupus: a systematic review

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Authors' objectives
To identify the scope of minocycline-induced lupus and to characterise its' typical features.

Searching
MEDLINE and EMBASE were searched from 1966 to October 1999 for English and non-English literature. The exploded search terms 'minocycline' combined with 'arthritis' or 'arthralgia', or 'lupus' or 'systemic lupus erythematosus' were used to identify relevant articles. Bibliographies of all retrieved articles were screened for additional references.

Study selection
Study designs of evaluations included in the review
Published case reports were included.

Specific interventions included in the review
Minocycline therapy, given at doses ranging from 50 to 200 mg/day (where stated).

Participants included in the review
Participants included in the review had to have been treated with minocycline, and to have developed minocycline-induced systemic lupus erythematosus (SLE) based on the consensus of two raters and defined as: no history of SLE before minocycline therapy was started; positive antinuclear antibodies (ANA) along with at least one clinical feature of SLE; and recovery after minocycline withdrawal (with or without anti-inflammatory drug therapy). Most patients received minocycline for acne, one patient for 'hot spots' and one for rosacea.

Outcomes assessed in the review
The outcomes assessed were the features of minocycline-induced SLE: clinical manifestations and demographics (age and sex distribution).

How were decisions on the relevance of primary studies made?
Inclusion decisions were based on the consensus of two raters.

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

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the extraction. All cases meeting the inclusion criteria were analysed, even if the data presented were not complete. Data were extracted on: patient demographics (age, sex), time to onset of symptoms, description of symptoms, dose at onset, cumulative dose, ANA, erythrocyte sedimentation rate (ESR), presence of antibodies, and clinical and laboratory outcomes after discontinuation.

Methods of synthesis
How were the studies combined?
Descriptive statistics were applied to characterise the patients' demographics, onset time, dose at onset and cumulative dose. Other information was reported as a narrative synthesis.

How were differences between studies investigated?
Results of the review
Twenty-seven publications were included with a total of 57 cases.

Median time of exposure prior to clinical manifestation of SLE was 19 months (range 3 days to 6 years).

Of the included participants, 84% were female and 14% were male; no details were provided of the remaining 2%. The mean age at onset of reaction was 21.6 plus or minus 8.6 (standard deviation) years (range: 14 - 59 years).

All 57 patients showed the clinical features of polyarthritis or polyarthritis often accompanied by liver abnormalities. Twelve patients had evidence of dermatological manifestations (rash, livedo reticularis, oral ulceration, subcutaneous nodules, alopecia). Pleuropulmonary symptoms with or without pulmonary infiltrates were described in 8 patients and haematological abnormalities in 5 patients. ESR increased in 38 out of 40 patients and C-reactive protein in 17 out of 19 patients.

All patients were dechallenged, which resulted in improvement of the clinical condition. Time to resolution of clinical symptoms varied from 3 days to 2 years.

Authors' conclusions
There is increasing evidence that minocycline can induce a variety of immunological reactions including drug-induced lupus that may overlap.

Long-term exposure to minocycline may be associated with drug-induced lupus. If symptoms of minocycline-associated drug-induced lupus occur along with positive ANA, the treatment should be stopped. Baseline and periodic liver function and ANA tests accompanied by appropriate clinical monitoring are suggested for patients receiving long-term minocycline therapy.

CRD commentary
This systematic review did not question whether minocycline could induce SLE or the incidence of drug-induced SLE, but systematically summarised the features of the identified cases. Inclusion criteria for the review are not stated clearly in terms of study design. The literature search seems comprehensive and is not restricted to English language publications. No attempt was made to search for unpublished material.

No validity assessment was undertaken. Study details were well-presented and a narrative synthesis was appropriate. No mention was made of differences between included studies, but since the included participants seemed very similar from the description this might not have been necessary.

The authors' conclusions seem appropriate based on the results.

Implications of the review for practice and research
Practice: The authors state that baseline and periodic liver function and ANA tests accompanied by appropriate clinical monitoring are suggested for patients receiving long-term minocycline therapy.

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

Bibliographic details
Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Age of Onset; Anti-Bacterial Agents /adverse effects; Antibodies, Antinuclear /analysis; Female; Humans; Lupus Erythematosus, Systemic /chemically induced /immunology /pathology; Male; Middle Aged; Minocycline /adverse effects

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.