Authors' objectives
To describe a meta-analysis of all known randomised clinical studies performed to date that evaluate nitroimidazoles as modifiers of hypoxia in solid tumours.

Searching
The author does not provide details of the sources searched or the strategies used.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were considered.

Specific interventions included in the review
Nitroimidazoles including: misonidazole, metronidazole, etanidazole, ornidazole, pimonidazole and nimorazole. In all but one trial the nitroimidazoles were given as a hypoxic-cell radiosensitizer. The hypoxic modification was compared to a control treatment, mainly radiotherapy.

Participants included in the review
Patients with primary solid tumours not previously treated were included. The main tumour sites were head and neck, central nervous system, lung, bladder, uterine cervix and oesophagus.

Outcomes assessed in the review
The outcomes assessed included loco-regional control and survival.

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

Assessment of study quality
The author does not report the method used to assess validity, or how the validity assessment was performed.

Data extraction
The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were grouped and discussed according to tumour site. A meta-analysis of all the RCTs was also carried out following the methods described by Stell and Rawson (see Other Publications of Related Interest). Odds ratios (ORs) and 95% confidence intervals (CIs) are presented for tumour site, on the basis of end point. Overall ORs for the different end points (locor-regional control and death) are also presented.

How were differences between studies investigated?
The author does not report any statistical testing of heterogeneity.
Results of the review
Fifty RCTs (n=7,154; median sample size 97, range: 17 to 620) were included.

The meta-analysis showed that modification of tumour hypoxia significantly improved the loco-regional tumour control after radiotherapy: OR 1.17 (95% CI: 1.06, 1.28, p=0.005). The treatment benefit could be related mainly to an improved response in head and neck tumours, OR 1.23 (95% CI: 1.09, 1.37, p=0.003), and to a lesser extent in bladder tumours, OR 1.52 (95% CI: 1.08, 2.96, p=0.05); no significant effect was observed in other tumour sites.

The overall survival rate was also improved: OR 1.13 (95% CI: 1.03, 1.23, p=0.02).

A correlation between improvement in local control, and consequently, improvement in survival, is demonstrated (slope=1.02, correlation coefficient R=0.8253).

Authors' conclusions
The findings stress the importance of improving local control and suggest that hypoxic modification, especially of epithelial tumours, may be the most relevant parameter to explore further.

CRD commentary
The review presents information on the clinical toxicity and pharmacokinetics of nitroimidazoles and hypoxia in human tumours, in addition to a systematic review examining nitroimidazoles as modifiers of hypoxia in solid tumours. The systematic review could have been greatly enhanced with the reporting of the search strategy, details of validity assessment, the methods by which relevance of primary studies was assessed and how data extraction was carried out. The review, however, provides good details of all included studies, clear results and a thorough discussion, including some of the methodological problems associated with the primary studies.

Bibliographic details

PubMedID
7620219

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Antineoplastic Agents /therapeutic use; Cell Hypoxia /drug effects; Humans; Neoplasms /drug therapy /metabolism; Nitroimidazoles /therapeutic use; Oxygen /metabolism; Randomized Controlled Trials as Topic

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**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.