Meta-analytic re-evaluation of misonidazole in the treatment of high grade astrocytoma

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Authors' objectives
To assess the effectiveness of misonidazole in the treatment of high-grade astrocytoma.

Searching
MEDLARS was searched using the MeSH terms 'glioma' and 'brain neoplasms'. Subheadings searched included 'therapy', 'drug therapy', 'radiation therapy', and 'surgery'. The MeSH term 'combined modality therapy' was also used. The electronic databases of Cancerlit, EMBASE, and Current Contents were also searched. The searches included publications in English, French, German, Spanish and Italian and covered the years 1970 to 1996. In addition, all Proceedings of the American Society of Clinical Oncology and the American Association for Cancer Research were reviewed back to 1985 since they are no longer indexed by the electronic databases.

Study selection
Study designs of evaluations included in the review
Published randomised controlled trials (RCTs) which reported data on misonidazole dose and dose schedule as well as details of radiation therapy delivered, and which enrolled at least 10 patients per treatment arm.

Specific interventions included in the review
A radiation sensitiser (misonidazole, 0.6-3.0 g/m² per dose) in addition to radiation therapy with or without chemotherapy.

Participants included in the review
Adult patients (18 years of age or older) with primary intracranial anaplastic astrocytoma (AA) or glioblastoma multiforme (GBM).

Outcomes assessed in the review
One-year survival was the outcome of interest.

How were decisions on the relevance of primary studies made?
The initial citations (in the form of abstracts) were screened by a physician investigator.

Assessment of study quality
The author does not state that they assessed quality.

Data extraction
Two research physicians (one of whom was an oncologist) extracted the data using a custom-designed data extraction form. Differences in data extraction forms were resolved in a consensus conference.

Methods of synthesis
How were the studies combined?
The studies were combined in a summary odds ratio (OR) with 95% confidence intervals (CIs) using a fixed-effect model according to procedures developed by Peto.

How were differences between studies investigated?
The Q-test for homogeneity was performed. Sensitivity analyses were also performed to assess the possible effects of radiation therapy treatment schedule on the outcome of interest.
Results of the review
Nine RCTs with 10 treatment arms (711 participants) and 14 control arms (1086 participants).

There is no statistically significant heterogeneity across studies (p > 10%).

The results suggest an improved 1-year survival among patients treated with misonidazole compared to the control groups, OR 0.92 (95% CI: 0.77, 1.09) but this is not statistically significant. Average median survival was 40.6 weeks in the misonidazole group and 38.7 weeks in the control group.

Authors’ conclusions
The author states that the results of the present meta-analysis provide evidence that misonidazole sensitised radiation therapy may result in an 8-13% improvement in 1 year survival. These findings are comparable or superior to the survival impact demonstrated for the addition of chemotherapy to post-operative radiation in this disease.

CRD commentary
The author has clearly stated the review question and has made a good search of the literature. Inclusion and exclusion criteria are stated and data is reported on who selected the studies for inclusion and who extracted the data. The author did not report any quality assessment of the included studies.

The statistical analysis is appropriate and the author did test for homogeneity and performed sensitivity analyses to assess different treatment schedule effects on the results. The author did not present the data on the principal outcome (1-year survival), therefore it is impossible to check the results.

The author's conclusion, that there may be an improvement following the use of misonidazole, does not follow from the results since the results were not statistically significant. An 8% improvement in odds of 1-year survival should not be misunderstood as an 8% improvement in 1-year survival rate.

Implications of the review for practice and research
Practice: The author does not state any implications for practice.

Research: The author states that further evaluation of the risk-benefit characteristics of radiation sensitisers versus other chemotherapeutics appears warranted. The author further states that studies examining the toxicity profile and impact of treatment schedules on "quality of life" may provide important information for setting future research priorities and guiding clinical trial design.

Bibliographic details

PubMedID
9677447

Indexing Status
Subject indexing assigned by NLM

MeSH
Astrocytoma /drug therapy /mortality /radiotherapy; Brain Neoplasms /drug therapy /mortality /radiotherapy; Humans; Misonidazole /therapeutic use; Radiation-Sensitizing Agents /therapeutic use; Survival Analysis; Treatment Outcome

AccessionNumber
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.