The role of steroids in the management of brain metastases: a systematic review and evidence-based clinical practice guideline


CRD summary
The authors concluded that insufficient evidence existed to make a recommendation for use of steroid therapy in patients with a symptomatic brain metastases without mass effect. The reliability of the authors’ conclusions is uncertain given the risks of language and publication biases, unclear study quality and the small number of patients included.

Authors’ objectives
To assess the effects of steroids compared to no treatment (or different doses) on neurologic symptoms in patients with metastatic brain tumours.

Searching
MEDLINE, EMBASE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL) and DARE were searched for peer-reviewed studies published in English (1990 to September 2008). Search terms were not reported. Reference lists of included articles were handsearched.

Study selection
All comparative study designs (randomised controlled trials (RCTs), non-randomised trials, cohort studies, case-control studies) were eligible for inclusion. Studies needed to compare steroid therapy to no treatment or different doses of steroid therapy in adult patients with brain metastases. Eligible studies had to enrol at least five patients with brain metastases in at least two study arms and provide baseline information on eligible participants by treatment group.

Included studies assessed different doses of dexamethasone (4mg, 8mg and 16mg per day). Mean age of included patients ranged from 56 to 65 years. Included patients had various types of tumour. Outcomes included Karnofsky performance scores (KPS), adverse events (Cushingoid changes and extremity oedema), survival and neurological function class.

Two reviewers independently selected studies for inclusion; disagreements were resolved by a third reviewer.

Assessment of study quality
The quality of RCTs was assessed using the PEDro scale. The quality of non-randomised studies was assessed using eight items selected and modified from existing scales (details were reported in a linked web appendix).

The authors did not state how many reviewers assessed study quality.

Data extraction
Data was extracted by one reviewer and checked by a second reviewer.

Methods of synthesis
Study results were described narratively.

Results of the review
Two RCTs were included (n=101 participants). PEDro scores were not reported.

One RCT found no significant differences on effects of different dexamethasone doses (4mg, 8mg and 16mg per day) on Karnofsky performance scores at days seven and 28. The 16mg/day dose was associated with a significantly greater number of side-effects (Cushingoid changes and extremity oedema) compared with the 4mg/day dose (p<0.03).
The second RCT compared 4mg/day oral dexamethasone every six hours to no steroid therapy during radiotherapy. No statistical analyses were made due to the small sample size (n=12).

**Authors' conclusions**
The authors stated that corticosteroids were recommended to provide temporary symptomatic relief of central nervous system symptoms related to increased intracranial pressure and oedema secondary to brain metastases. They further stated that insufficient evidence existed to make a recommendation for use of steroid therapy in patients with a symptomatic brain metastases without mass effect.

**CRD commentary**
The review addressed a clear question with well-defined inclusion criteria. Three major databases were searched. Only published studies in English were sought, so relevant studies may have been missed. Database searches were restricted by date of publication and limited efforts were made to search for unpublished studies, so publication bias was likely. Steps were taken to minimise reviewer error and bias in study selection and data extraction, but not explicitly with quality assessment. Study quality assessment criteria appeared appropriate. The quality of the included studies was unclear as no results of quality assessments were reported. The decision to describe results narratively appeared appropriate given the small number of studies and their heterogeneous nature.

The reliability of the authors' conclusions is uncertain given risks of language and publication biases, unclear quality of the included studies and the small number of patients included.

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

**Practice:** The authors stated that corticosteroids were recommended to provide temporary symptomatic relief of central nervous system symptoms related to increased intracranial pressure and oedema secondary to brain metastases. They stated that dexamethasone was the corticosteroid of choice. They further stated that a starting dose of 4mg to 8mg per day of dexamethasone should be considered for patients who were symptomatic from metastatic brain disease unless they exhibited severe symptoms consistent with increased intracranial pressure (where higher doses such as 16mg/day or more should be considered).

**Research:** The authors stated that further randomised controlled trials were needed to investigate steroid dosing and toxicity in patients with brain metastases.

**Funding**
Not stated.

**Bibliographic details**

**PubMedID**
19957014

**DOI**
10.1007/s11060-009-0057-4

**Original Paper URL**
http://www.springerlink.com/content/n11832031700653r/

**Other URL**
http://ukpmc.ac.uk/abstract/MED/19957014& quot;& gt;http://ukpmc.ac.uk/abstract/MED/19957014
Indexing Status
Subject indexing assigned by NLM

MeSH
Brain Neoplasms /drug therapy /secondary; Databases, Factual /statistics & numerical data; Evidence-Based Medicine; Humans; Practice Guidelines as Topic; Steroids /therapeutic use; Treatment Outcome

AccessionNumber
12010001790

Date bibliographic record published
21/07/2010

Date abstract record published
31/08/2011

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.