Systematic review of effectiveness of different treatments for childhood retinoblastoma

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Executive summary

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Executive summary

Background

Retinoblastoma is a malignant tumour of the retina and usually occurs in children under 2 years old. It is relatively rare, with an incidence of one case per 23,000 live births, and accounts for about 3% of all cancers occurring in children younger than 15 years in the UK. It is an aggressive tumour that can lead to loss of vision, and in extreme cases death, although cure rates in developed countries can be in excess of 90%.

Objective

The objective of this study was to assess the clinical effectiveness of treatments for childhood retinoblastoma.

Methods

Search

Seventeen electronic databases were searched from inception to April 2004 for studies published in any language. Internet searches were carried out and bibliographies of included articles were searched. Two reviewers independently assessed titles and abstracts and the full paper was obtained if either reviewer considered the reference potentially relevant. Two reviewers assessed the eligibility of full papers against the review inclusion criteria, with disagreements resolved by discussion and, if necessary, a third reviewer.

Inclusion and exclusion criteria

Studies of participants diagnosed with retinoblastoma at the age of 18 years or under were eligible for inclusion. Studies of adults were only included where childhood retinoblastoma was followed up into adulthood. Studies of mixed diagnoses were included if outcomes were reported separately for children with retinoblastoma. Any intervention, or combinations of intervention, and all clinical outcomes were eligible. Where controlled trials were not available, prospective and retrospective cohort studies with clear comparisons between treatment groups were eligible.

Data extraction

Data were extracted by one reviewer into structured summary tables and checked for accuracy by a second reviewer. Any disagreements were resolved by discussion and, if necessary, a third reviewer was involved.

Quality assessment

Each included study was assessed against a checklist for methodological quality of observational studies by one reviewer and checked by a second reviewer. Disagreements were resolved by discussion and, if necessary, a third reviewer was involved.

Synthesis

A narrative synthesis was conducted. Where possible, studies assessing common interventions were grouped together, with prospective and retrospective studies grouped separately. Emphasis was placed on prospective studies.

Results

Thirty-one individual studies, from 42 publications, were included in the review. Apart from one non-randomised controlled trial, only comparative studies of observational design were available for any of the treatments. Four of the included studies were prospective and the remaining 27 were retrospective. Most of the studies were of radiotherapy or chemotherapy, with few studies available on enucleation or focal treatments such as brachytherapy, photocoagulation, cryotherapy and thermotherapy.

The methodological quality was generally poor, with a high risk of bias in all included studies. The main problems were in relation to how treatment was allocated and lack of consideration of potentially confounding factors, such as initial disease severity, in the study design and data analysis.

The evidence base for effectiveness of treatments for childhood retinoblastoma is extremely limited. Owing to the considerable limitations of the evidence identified, it was not possible to make

meaningful and robust conclusions about the relative effectiveness of different treatment approaches for childhood retinoblastoma.

Conclusion

In the authors' opinion, the evidence base is not sufficiently robust to provide clear guidance for clinical practice.

Recommendations for research

Ideally, good-quality randomised controlled trials (RCTs) assessing the effectiveness of different treatment options for childhood retinoblastoma are required. Research is required on all the treatments currently used for this condition. Where RCTs are not feasible, for ethical or practical reasons, only high-quality, prospective, non-randomised studies should be given consideration, owing to the generally higher risk of bias in retrospective studies.

To reduce the risk of confounding due to allocation by clinical indication, studies should compare patients with similar disease severity rather than compare patients of mixed disease severities.

Standardised outcomes should be agreed for use in studies assessing the effectiveness of treatment. These outcomes should encompass potential important adverse effects of treatment such as loss of visual acuity and cosmetic outcome, as well as beneficial effects.

Publication

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NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA Programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, service-users groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including service users) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or conducting a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a short time period.

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Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 03/63/01. The contractual start date was in May 2004. The draft report began editorial review in December 2004 and was accepted for publication in April 2005. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

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