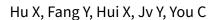


Cochrane Database of Systematic Reviews

Radiotherapy for diffuse brainstem glioma in children and young adults (Review)



Hu X, Fang Y, Hui X, Jv Y, You C. Radiotherapy for diffuse brainstem glioma in children and young adults. *Cochrane Database of Systematic Reviews* 2016, Issue 6. Art. No.: CD010439. DOI: 10.1002/14651858.CD010439.pub2.

www.cochranelibrary.com



[Intervention Review]

Radiotherapy for diffuse brainstem glioma in children and young adults

Xin Hu¹, Yuan Fang¹, Xuhui Hui¹, Yan Jv¹, Chao You¹

¹Department of Neurosurgery, West China Hospital, Sichuan University, Chengdu, China

Contact: Chao You, Department of Neurosurgery, West China Hospital, Sichuan University, No. 37, Guo Xue Xiang, Chengdu, 610041, China. youchao_nswc@163.com, doctoryouchao@163.com.

Editorial group: Cochrane Childhood Cancer Group.

Publication status and date: New, published in Issue 6, 2016.

Citation: Hu X, Fang Y, Hui X, Jv Y, You C. Radiotherapy for diffuse brainstem glioma in children and young adults. *Cochrane Database of Systematic Reviews* 2016, Issue 6. Art. No.: CD010439. DOI: 10.1002/14651858.CD010439.pub2.

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Background

Diffuse brainstem glioma is a devastating disease with very poor prognosis. The most commonly used radiological treatment is conventional fractionated radiation. So far, there is no meta-analysis or systematic review available that assesses the benefits or harms of radiation in people with diffuse brainstem glioma.

Objectives

To assess the effects of conventional fractionated radiotherapy (with or without chemotherapy) versus other therapies (including different radiotherapy techniques) for newly diagnosed diffuse brainstem gliomas in children and young adults aged 0 to 21 years.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE/PubMed, and EMBASE to 19 August 2015. We scanned conference proceedings from the International Society for Paediatric Oncology (SIOP), International Symposium on Paediatric Neuro-Oncology (ISPNO), Society of Neuro-Oncology (SNO), and European Association of Neuro-Oncology (EANO) from 1 January 2010 to 19 August 2015. We searched trial registers including the International Standard Randomised Controlled Trial Number (ISRCTN) Register, the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP), and the register of the National Institutes of Health to 19 August 2015. We imposed no language restrictions.

Selection criteria

All randomised controlled trials (RCTs), quasi-randomised trials (QRCTs), or controlled clinical trials (CCTs) that compared conventional fractionated radiotherapy (with or without chemotherapy) versus other therapies (including different radiotherapy techniques) for newly diagnosed diffuse brainstem glioma in children and young adults aged 0 to 21 years.

Data collection and analysis

Two review authors independently screened studies for inclusion, extracted data, assessed the risk of bias in each eligible trial, and conducted GRADE assessment of included studies. We resolved disagreements through discussion. We performed analyses according to the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions.

Main results

We identified two RCTs that fulfilled our inclusion criteria. The two trials tested different comparisons.

One multi-institutional RCT included 130 participants and compared hyperfractionated radiotherapy (six-week course with twice a day treatment of 117 cGy per fraction to a total dose of 7020 cGy) with conventional radiotherapy (six-week course with once a day treatment of 180 cGy per fraction to a total dose of 5400 cGy). The median time overall survival (OS) was 8.5 months in the conventional group and 8.0



months in the hyperfractionated group. We detected no clear evidence of effect on OS or event-free survival (EFS) in participants receiving hyperfractionated radiotherapy compared with conventional radiotherapy (OS: hazard ratio (HR) 1.07, 95% confidence interval (CI) 0.75 to 1.53; EFS: HR 1.26, 95% CI 0.83 to 1.90). Radiological response (risk ratio (RR) 0.94, 95% CI 0.54 to 1.63) and various types of toxicities were similar in the two groups. There was no information on other outcomes. According to the GRADE approach, we judged the quality of evidence to be low (i.e. further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate) for OS and EFS, and very low (i.e. we are very uncertain about the estimate) for radiological response and toxicities.

The second RCT included 71 participants and compared hypofractionated radiotherapy (39 Gy in 13 fractions over 2.6 weeks, 3 Gy per fraction) with conventional radiotherapy (54 Gy in 30 fractions over six weeks, 1.8 Gy per fraction). This trial reported a median OS of 7.8 months for the hypofractionated group and 9.5 months for the conventional group. It reported a progression-free survival (PFS) of 6.3 months for the hypofractionated group and 7.3 months for the conventional group. We found no clear evidence of effect on OS (HR 1.03, 95% CI 0.53 to 2.01) or PFS (HR 1.19, 95% CI 0.63 to 2.22) in participants receiving hypofractionated radiotherapy when compared with participants receiving conventional radiotherapy. The mainly observed adverse effect was local erythema and dry desquamation especially behind the auricles. There were some other toxicities, but there was no statistically significant difference between treatment groups. There was no information on other outcomes. We judged the quality of evidence to be moderate (i.e. further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate) for OS, and low for PFS and toxicities. It should be mentioned that the sample size in this RCT was small, which could lead to insufficient statistical power for a clinically relevant outcome.

Authors' conclusions

We could make no definitive conclusions from this review based on the currently available evidence. Further research is needed to establish the role of radiotherapy in the management of newly diagnosed diffuse brainstem glioma in children and young adults. Future RCTs should be conducted with adequate power and all relevant outcomes should be taken into consideration. Moreover, international multicentre collaboration is encouraged. Considering the potential advantage of hypofractionated radiotherapy to decrease the treatment burden and increase the quality of remaining life, we suggest that more attention should be paid to hypofractionated radiotherapy.

PLAIN LANGUAGE SUMMARY

Radiotherapy for diffuse brainstem glioma in children and young adults

Review question

To assess the effects of conventional radiotherapy (with or without chemotherapy) versus other therapies (including different radiotherapy techniques) for newly diagnosed diffuse brainstem gliomas in children and young adults aged 0 to 21 years.

Background

Diffuse brainstem glioma typically occurs in the pons (part of the brainstem) and expands and infiltrates at least 50% of the pons, with a characteristic appearance on magnetic resonance imaging (MRI). The prognosis is very poor, with a median overall survival (OS; time from cancer diagnosis, or treatment, to death from any cause) ranges from 8 to 11 months. So far, there is no analysis or review available that assessed the benefits or harms of radiation for newly diagnosed diffuse brainstem glioma in children and young adults aged 0 to 21 years.

Study characteristics

Through comprehensive search and screening of medical databases, we found two clinical studies that tested different treatments. One study, with 130 participants included, compared hyperfractionated radiotherapy (six-week course with treatment twice a day) with conventional radiotherapy (six-week course with treatment once a day). The second study, with 71 participants included, compared hypofractionated radiotherapy (three-week course with treatment once a day) with conventional radiotherapy.

Key results

For the comparison of hyperfractionated radiotherapy and conventional radiotherapy, there was no clear evidence of effect on OS, event-free survival (EFS; time from diagnosis, study entry, or treatment to disease progression, disease relapse, a second tumour, or death), radiological response (a reduction in tumour size of more than 50%), and toxicities (damage to the body due to radiotherapy).

For the comparison of hypofractionated radiotherapy and conventional radiotherapy, there was no clear evidence of effect on OS, progression-free survival (PFS; time from diagnosis, study entry, or treatment to disease progression), and side effects.

Quality of the evidence

For the hyperfractionated radiotherapy, when compared with conventional therapy, the quality of evidence was low for OS and EFS, and very low for radiological response and toxicities.



For the hypofractionated radiotherapy, when compared with conventional therapy, the quality of evidence was moderate for OS, and low for PFS and toxicities.