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[Intervention Review]

Intracystic bleomycin for cystic craniopharyngiomas in children

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ABSTRACT

Background

Craniopharyngiomas are the most common benign histological tumours to involve the hypothalamo-pituitary region in childhood. Cystic craniopharyngiomas account for more than 90% of the tumours. The optimal treatment of cystic craniopharyngioma remains controversial. Radical resection is the treatment of choice in patients with favourable tumour localisation. When the tumour localisation is unfavourable, a gross-total or partial resection followed by radiotherapy is the main treatment option in adults. However, it presents a risk of morbidity, especially for children. Intracystic bleomycin has been utilised potentially to delay the use of radiotherapy or radical resection, to decrease morbidity. This review is the second update of a previously published Cochrane review.

Objectives

To assess the benefits and harmful effects of intracystic bleomycin in children from birth to 18 years with cystic craniopharyngioma when compared to placebo (no treatment), surgical treatment (with or without adjuvant radiotherapy) or other intracystic treatments.

Search methods

We searched the electronic databases CENTRAL (2016, Issue 1), MEDLINE/PubMed (from 1966 to February 2016) and EMBASE/Ovid (from 1980 to February 2016) with pre-specified terms. In addition, we searched the reference lists of relevant articles and reviews, conference proceedings (International Society for Paediatric Oncology 2005-2015) and ongoing trial databases (Register of the National Institute of Health and International Standard Randomised Controlled Trial Number (ISRCTN) register) in February 2016.

Selection criteria

Randomised controlled trials (RCTs), quasi-randomised trials or controlled clinical trials (CCTs) comparing intracystic bleomycin and other treatments for cystic craniopharyngiomas in children (from birth to 18 years).

Data collection and analysis

Two review authors independently performed the study selection, data extraction and 'Risk of bias' assessment. We used risk ratio (RR) for binary data and mean difference (MD) for continuous data. If one of the treatment groups experienced no events and there was only one study available for the outcome, we used the Fischer's exact test. We performed analysis according to the guidelines in the *Cochrane Handbook for Systematic reviews of Interventions*.

Main results

We could not identify any studies in which the only difference between the treatment groups was the use of intracystic bleomycin. We did identify a RCT comparing intracystic bleomycin with intracystic phosphorus^{32} (^{32}P) (seven children). In this update we identified no additional studies. The included study had a high risk of bias. Survival could not be evaluated. There was no clear evidence of a difference between the treatment groups in cyst reduction (MD -0.15, 95% confidence interval (CI) -0.69 to 0.39, P value = 0.59, very low quality of

evidence), neurological status (Fisher's exact P value = 0.429, very low quality of evidence), third nerve paralysis (Fischer's exact P value = 1.00, very low quality of evidence), fever (RR 2.92, 95% CI 0.73 to 11.70, P value = 0.13, very low quality of evidence) or total adverse effects (RR 1.75, 95% CI 0.68 to 4.53, P value = 0.25, very low quality of evidence). There was a significant difference in favour of the ^{32}P group for the occurrence of headache and vomiting (Fischer's exact P value = 0.029, very low quality of evidence for both outcomes).

Authors' conclusions

Since we identified no RCTs, quasi-randomised trials or CCTs of the treatment of cystic craniopharyngiomas in children in which only the use of intracystic bleomycin differed between the treatment groups, no definitive conclusions could be made about the effects of intracystic bleomycin in these patients. Only one low-power RCT comparing intracystic bleomycin with intracystic ^{32}P treatment was available, but no definitive conclusions can be made about the effectiveness of these agents in children with cystic craniopharyngiomas. Based on the currently available evidence, we are not able to give recommendations for the use of intracystic bleomycin in the treatment of cystic craniopharyngiomas in children. High-quality RCTs are needed.

PLAIN LANGUAGE SUMMARY

Intracystic bleomycin for children with cystic craniopharyngiomas

Craniopharyngiomas are rare, slow-growing, benign tumours in the hypothalamic-pituitary region of the brain. Although they are benign, i.e. the tumour lacks the ability to invade neighbouring tissue or metastasise (spread to other sites), there is considerable morbidity and disability even when the tumour can be resected completely. Cystic craniopharyngiomas are the most common type of craniopharyngiomas. They consist of a solid portion that contains fluid-filled balloon-like structures (cysts). Cysts are a problem because secretion of fluid into them allows the tumour to increase in size, which puts pressure on parts of the brain and can cause damage. Radical resection (removal by surgery) alone is not sufficient because the rate of recurrence is high and this procedure has a high risk of endocrinological/neurological deficits such as blindness; loss of control of appetite, urine production, emotional behaviour and physical co-ordination; memory loss; sleep disturbances; cessation of growth and sexual development; low thyroxine levels; hydrocephalus (high pressure inside the skull); and death. While in adults radiotherapy represents a valid postoperative adjunctive (additional) therapy, in children it has a high risk of side effects including further damage to any remaining sight, with reduction of intelligence quotient (IQ) and ability to perform complex tasks in later life. Intracystic bleomycin (i.e. a type of chemotherapeutic agent injected into the cyst) has been used to potentially decrease the damage associated with cystic craniopharyngioma.

This systematic review focused on (randomised) controlled studies. We could not identify any randomised controlled trials (RCTs), quasi-randomised trials or controlled clinical trials (CCTs) in which the only difference between the intervention and control group was the use of intracystic bleomycin. However, we did identify one RCT comparing intracystic bleomycin with intracystic phosphorus^{32} (^{32}P), which is a radioactive isotope of phosphorous used for intracystic irradiation. Only seven children were included in this study. The study has a high risk of bias and the sample size is too small to detect a difference in outcomes. The therapeutic use of intracystic bleomycin in children with cystic craniopharyngiomas currently remains uncertain. Although there was no significant difference in total adverse effects between the two treatment groups, there was a significant difference in both headache and vomiting in favour of the ^{32}P group. The quality of the evidence is, however, very low. More high-quality studies are needed but will be difficult as so few children get these tumours.