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Cochrane Database of Systematic Reviews 2018, Issue 7. Art. No.: CD010885.
DOI: 10.1002/14651858.CD010885.pub4.

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[Intervention Review]

Different infusion durations for preventing platinum-induced hearing loss in children with cancer

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Editorial group: Cochrane Childhood Cancer Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 7, 2018.

Citation: van As JW, van den Berg H, van Dalen EC. Different infusion durations for preventing platinum-induced hearing loss in children with cancer. *Cochrane Database of Systematic Reviews* 2018, Issue 7. Art. No.: CD010885. DOI: 10.1002/14651858.CD010885.pub4.

ABSTRACT

Background

Platinum-based therapy, including cisplatin, carboplatin or oxaliplatin, or a combination of these, is used to treat a variety of paediatric malignancies. Unfortunately, one of the most important adverse effects is the occurrence of hearing loss or ototoxicity. In an effort to prevent this ototoxicity, different platinum infusion durations have been studied. This review is the second update of a previously published Cochrane review.

Objectives

To assess the effects of different durations of platinum infusion to prevent hearing loss or tinnitus, or both, in children with cancer. Secondary objectives were to assess possible effects of these infusion durations on: a) anti-tumour efficacy of platinum-based therapy, b) adverse effects other than hearing loss or tinnitus, and c) quality of life.

Search methods

We searched the electronic databases Cochrane Central Register of Controlled Trials (CENTRAL; the Cochrane Library 15 March 2018), MEDLINE (PubMed) (1945 to 15 March 2018) and Embase (Ovid) (1980 to 15 March 2018). In addition, we handsearched reference lists of relevant articles and we assessed the conference proceedings of the International Society for Paediatric Oncology (2009 up to and including 2017) and the American Society of Pediatric Hematology/Oncology (2014 up to and including 2017). We scanned ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP; apps.who.int/trialsearch) for ongoing trials (searched on 12 March 2018 and 13 March 2018 respectively).

Selection criteria

Randomised controlled trials (RCTs) or controlled clinical trials (CCTs) comparing different platinum infusion durations in children with cancer. Only the platinum infusion duration could differ between the treatment groups.

Data collection and analysis

Two review authors independently performed the study selection, 'Risk of bias' assessment and GRADE assessment of included studies, and data extraction including adverse effects. Analyses were performed according to the guidelines of the *Cochrane Handbook for Systematic Reviews of Interventions*.

Main results

We identified one RCT and no CCTs; in this update no additional studies were identified. The RCT (total number of children = 91) evaluated the use of a continuous cisplatin infusion (N = 43) versus a one-hour bolus cisplatin infusion (N = 48) in children with neuroblastoma. For the continuous infusion, cisplatin was administered on days one to five of the cycle, but it is unclear if the infusion duration was a total of five days. Risk of bias was present. Only results from shortly after induction therapy were provided. No clear evidence of a difference in hearing loss (defined as asymptomatic and symptomatic disease combined) between the different infusion durations was identified as results were imprecise (risk ratio (RR) 1.39, 95% confidence interval (CI) 0.47 to 4.13, low-quality evidence). Although the numbers of children were not provided, it was stated that tumour response was equivalent in both treatment arms. With regard to adverse effects other than ototoxicity, we were only able to assess toxic deaths. Again, the confidence interval of the estimated effect was too wide to exclude differences between the treatment groups (RR 1.12, 95% CI 0.07 to 17.31, low-quality evidence). No data were available for the other outcomes of interest (i.e. tinnitus, overall survival, event-free survival and quality of life) or for other (combinations of) infusion durations or other platinum analogues.

Authors' conclusions

Since only one eligible RCT evaluating the use of a continuous cisplatin infusion versus a one-hour bolus cisplatin infusion was found, and that had methodological limitations, no definitive conclusions can be made. It should be noted that 'no evidence of effect', as identified in this review, is not the same as 'evidence of no effect'. For other (combinations of) infusion durations and other platinum analogues no eligible studies were identified. More high-quality research is needed.

PLAIN LANGUAGE SUMMARY

Different infusion durations for preventing platinum-induced hearing loss in children with cancer

Review question

We reviewed the evidence of the effects of different durations of platinum infusion to prevent hearing loss or tinnitus, or both, in children with cancer. We also looked at anti-tumour efficacy, adverse effects other than hearing loss and quality of life.

Background

Platinum-based chemotherapy, including cisplatin, carboplatin or oxaliplatin, or a combination of these, is used to treat different types of childhood cancer. Unfortunately, one of the most important adverse effects of platinum chemotherapy is hearing loss. This can occur not only during treatment but also years after the end of treatment. Although it is not life-threatening, the loss of hearing, especially during the first three years of life, may lead to difficulties with school performance and psychosocial functioning. Therefore, prevention of platinum-induced hearing loss is very important and might improve the quality of life of children undergoing cancer treatment and those who have survived treatment with platinum-based chemotherapy.

Study characteristics

The evidence is current to March 2018.

We found one study (91 participants) comparing a continuous cisplatin infusion with a one-hour cisplatin bolus infusion in children with neuroblastoma. For the continuous infusion, cisplatin was administered on days one to five of the treatment cycle but it is not clear if the infusion duration was a total of five days. Only results from shortly after induction therapy were available.

Key results

At the moment there is no evidence showing that the use of a different cisplatin infusion duration prevents hearing loss or adversely affects tumour response and adverse effects. No data were available for the other outcomes of interest (i.e. tinnitus, overall survival, event-free survival and quality of life) or for other (combinations of) infusion durations or other platinum analogues. We need more high-quality research before definite conclusions can be made about the usefulness of different platinum infusion durations to prevent hearing loss in children with cancer.

Quality of the evidence

The quality of the evidence was low.