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BMJ Support Palliat Care. 2023 Feb 17;spcare-2022-004119. doi: 10.1136/spcare-2022-004119. Online ahead of print.

Acetazolamide versus placebo for cerebral oedema requiring dexamethasone in recurrent and/or progressive high-grade glioma: phase II randomised placebo-controlled double-blind study

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PMID: 36807048 DOI: 10.1136/spcare-2022-004119

Abstract

Objectives: Symptoms of raised intracranial pressure (ICP) in recurrent high-grade glioma (HGG) generally require corticosteroid treatment, often causing toxicity with variable effects on ICP symptoms. Acetazolamide reduces ICP when used in other clinical non-cancer settings. The aim of the study was to explore whether the addition of oral acetazolamide enables safe dexamethasone dose reduction in management of raised ICP in recurrent HGG.

Methods: Participants had recurrent HGG with any of dexamethasone recommencement, dose increase or dependency; prior/current bevacizumab was an exclusion. Eligible participants were randomised 1:1 to acetazolamide or placebo for 8 weeks. Standardised protocols were used for dexamethasone dosing, with planned dose decrease from day 5 once ICP symptoms were stable. The primary endpoint was a composite of dexamethasone dose reduction and stable Karnofsky Performance Status Secondary endpoints included toxicity and feasibility.

Results: Thirty participants (15 per group) were enrolled (mean age 58 years) from seven Australian sites. The mean baseline dexamethasone dose was 6.2 mg. Mean duration on study treatment was 38 days (placebo group) and 31 days (acetazolamide group) with nine participants (30%) completing all study treatments (six placebo, three acetazolamide). Study withdrawal was due to adverse events (n=6; one placebo, five acetazolamide) and disease progression (n=6 (three per arm)). Four participants (13%) (two per arm) were stable responders. Ten participants experienced a total of 13 serious adverse events (acetazolamide arm: five participants (33%), six events, two related).

Conclusions: The study closed early due to poor accrual and increasing availability of bevacizumab. The addition of acetazolamide did not facilitate dexamethasone reduction.

Trial registration number: ACTRN12615001072505.

Keywords: brain; quality of life; supportive care.

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