

What is the optimum thiamine dose?

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Introduction and Aims: Wernicke Korsakoff's syndrome (WKS) is a neuropsychological condition resulting from thiamine deficiency, most commonly associated with alcohol misuse. It results in neurological abnormalities including ataxia, ophthalmoplegia, and confusion with associated cognitive impairment. Whilst observational studies show parenteral thiamine administration results in drastic reduction in morbidity and mortality, relevant treatment trials have never been conducted. We aimed to determine the optimum thiamine dose for the treatment and prevention of WKS.

Design and Methods: Two double-blind, parallel, randomised controlled trials were conducted at the Alice Springs Hospital. In study one, asymptomatic 'at-risk' patients (N = 393) received either 100mg daily, 100mg thrice daily, or 300 mg thrice daily for 3 days. In study two, symptomatic patients (N=127) received either 100mg, 300mg or 500 mg thrice daily for five days. Primary analyses examined cognitive (Rowland Universal Dementia Assessment Scale (RUDAS), two Cogstate subtests, and a Story Memory Recall test) and neurological function (ataxia, ophthalmoplegia and confusion).

Results: Story Memory Recall was marginally significantly different between the high and mid dose groups in the 'at risk' arm. Primary analyses showed no other significant differences. Having a clinically unwell target population with high comorbidity and multiple presentations, coupled with challenges in cross cultural assessment likely limited study findings.

Discussions and Conclusions: Reasons for the null effect may include low power, poor sensitivity of the cognitive and neurological assessments, sub-optimal timing of assessments, insufficient treatment duration, interaction with stat dose effect on admission, non-linear effect or ineffectiveness of the treatment.

Implications for Practice or Policy (optional): While findings suggest no significant difference between high and low dose thiamine for the treatment and prevention of cognitive and neurological abnormalities related to WKS, further research is required prior to implementing any changes to clinical guidelines given the study's limitations.

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