A RAPID EVIDENCE ASSESSMENT OF THE OPTIMAL PHENOBARBITAL DOSAGE REGIMEN FOR MANAGEMENT OF INTRACTABLE AGITATION IN THE LAST DAYS OF LIFE TO PRODUCE A CLINICAL GUIDELINE

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Background Agitation is a common symptom at the end of life; without prompt assessment and management it can cause significant distress to patients and relatives. Clinical practice in the pharmacological management of intractable terminal agitation varies, particularly if the commonly used agents (benzodiazepines and antipsychotics) have failed to be effective. These difficult clinical scenarios require a robust approach to control symptoms effectively. This review aims to facilitate production of an evidence-based guideline for the use of Phenobarbital for intractable agitation at the end of life, for use within a Specialist Inpatient Palliative Care Unit.

Method A literature search was carried out through EMBASE, Medline, CINAHL and PubMed databases, using synonyms of 'Phenobarbital', 'Palliative' and 'Agitation?' as search terms.

Two researchers reviewed the search results. Articles specifying doses of injectable Phenobarbital were included for review. Additionally, in the case of review articles, the original sources stating dosage were reviewed where available.

Results 11 of the 25 articles from the initial search met inclusion criteria. Of these, 6 were excluded as they lacked sufficient detail. With the inclusion of one further source referenced in a review article, a total of 6 core sources were used. They described various doses of Phenobarbital used for end-of-life agitation.

Conclusions This review of the current evidence base provided no standard or optimal dosing regime. However, based on the available evidence, a clinical guideline would be produced for the use of Phenobarbital in intractable agitation at the end of life in our unit: with an IM loading dose of 200 mg followed by a continuous subcutaneous infusion of 800 mg-1600 mg/24 hrs. Due to the infrequency of this presentation and the use of Phenobarbital; sharing and evaluating the guideline at a regional level would facilitate more rapid efficacy assessment and refinement.

REFERENCE

VITAMIN D SUPPLEMENTATION FOR ADULTS WITH ADVANCED CANCER: IMPACT ON QUALITY OF LIFE, PAIN AND FATIGUE

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Background Vitamin D deficiency is common and can be associated with multiple symptoms including fatigue and pain. These symptoms are common in advanced cancer, and the prevalence of vitamin D deficiency in adults with advanced cancer has been estimated at 47–90%. The aim is to systematically review the available evidence for the supplementation of vitamin D for adults with advanced cancer, to assess the impact on pain, fatigue and quality of life.

Methods An electronic search (PubMed, clinical trial databases) was undertaken in October 2017, using search terms ‘Vitamin D’ and ‘cancer’, filtered for clinical trials. This was supplemented by a search of palliative and oncological journals.

Inclusion criteria:
- Population- adults with advanced/metastatic cancer;
- Intervention- systemic vitamin D, any dose;
- Comparison- placebo or other;
- Outcomes- quality of life, pain or fatigue.

Exclusion criteria:
- Conference abstracts; studies in which the effect of vitamin D could not be distinguished from another agent, because given with e.g. chemotherapy.

Results Electronic searches yielded 419 titles and abstracts (PubMed), 449 titles (journal search), 110 registered studies (trial databases), including duplicates. Of these, 79 articles were reviewed in detail. No completed randomised controlled trials were identified. One case-control study (retrospective controls) and four single-arm studies were identified. Four of these studies reported an improvement in symptoms or reduction in opioid dose, suggesting that vitamin D supplementation may have a role in symptom relief for people with advanced cancer, but there is a high risk of bias.

Two double-blind placebo-controlled RCTs (VIDAFACT, Palliative D) are ongoing.

Conclusion There is low quality evidence that vitamin D supplementation may improve pain and weakness in adults with advanced cancer. Two ongoing placebo-controlled RCTs should provide more robust evidence to guide clinical practice. In the meantime it seems reasonable to remain vigilant for vitamin D deficiency, and to recommend supplementation if deficiency appears symptomatic.