CareSearch Project Research Studies Register: Registration Proforma	0072

Study Title:

A randomised, double-blind placebo controlled study of subcutaneous ketamine in the management of cancer pain

Brief description of the study:

Background: Ketamine is a parenteral general anaesthetic agent, indicated for the induction and maintenance of anaesthesia. Ketamine at low or sub anaesthetic doses has been used for the provision of analgesia in a wide range of clinical situations and also as an adjuvant medication with analgesics, particularly opioids. The evidence available through a wide range of clinical audits and case reports supports a role for low dose ketamine in the management of refractory or neuropathic pain. The published evidence to date is generally of low level however and is subject to bias. It is apparent that additional clinical studies would be necessary to support a palliative care indication for access to ketamine on the Pharmaceutical Benefits Scheme. This study will assess the benefits of ketamine within the context of a randomised controlled trial.
Study design: A phase III randomised, double blind, placebo controlled trial of ketamine delivered by subcutaneous infusion over a maximum of 5 days. Hospital in-patients >18 years of age with chronic pain secondary to cancer and/or its treatment with a Brief Pain Inventory average pain score of ≥3 despite adequate treatment with opioids and co-analgesics for at least 5 days will be included.
Objectives: To compare the efficacy of parenteral ketamine versus normal saline when used in conjunction with opioids and standard adjuvant therapy in the management of chronic uncontrolled pain related to cancer or its treatment in terms of: pain relief, adverse events, quality of life, performance status, health outcomes and health service utilization.
Treatment schedule: Step 1 :100mg ketamine/placebo, delivered by subcutaneous infusion over 24 hours. If responding, the infusion will be continued for another 4 days (total 5 days treatment), then stopped. If there is no response at 24 hours and no unacceptable toxicity, the patient will proceed to steps 2 (300mg ketamine/placebo) and 3 (500mg ketamine/placebo). All treatment will be for a total of 5 days. Treatment thereafter will be at the attending physician's discretion. Patients' usual medications and analgesics, including breakthrough medications will be continued throughout the study period. Haloperidol and/or midazolam will be used "as required" for the treatment of psychomimetic events.
Assessments: Pain will be assessed using the Brief Pain Inventory and a Global Impression of Change measure. Quality of life will be assessed by the EORTC QLQ-C30 and the FACIT-PAL. Caregiver QOL will be assessed using the Caregiver Quality of Life Index-Cancer. NCI Common Terminology Criteria for Adverse Events V3, the Nursing Delirium Screening Scale and Clinician Administered Dissociative States Scale will monitor toxicity.
Definition of response: Reduction in Brief Pain Inventory average pain score by at least 2 points from baseline after 24 hours, irrespective of worst, and best pain scores and in the absence of any increase in baseline opioid dose and with ≤ 4 breakthrough doses of opioids/24 hours.
Primary endpoint: Brief Pain Inventory average pain score at start of day 6
Analysis : Ketamine will be considered superior to placebo if the response rate at start day 6 is 25% greater then that of placebo (assuming a placebo response rate of 30%). With a type 1 error of 0.05 at approximately 85% power, 75 patients will be required per patient arm (150 patients total complete data)**.**
Economic analysis This will utilise data relating to days spent in hospital, time to readmission, number of in-patient admissions to death, community support, General Practitioner visits, home care palliative care team review, care giver impact, concomitant medications and drug compliance as well as the pain response, toxicity, quality of life, drug usage and compliance measured beyond the 5 day study period until death.
Substudy: A substudy will also be conducted to assess the pharmacokinetics and pharmacogenetics of ketamine and to relate these to variability in the effectiveness and side effects of ketamine.

Study Methodology: (Please mark with an x which type of study methodology)

	Epidemiology
	Health Services / Health Economics / Quality Improvement
	Qualitative, Observational or Descriptive
	Mixed Method
	Systematic Review

✘	**Intervention: RCT**						
	Intervention: Comparative or cohort study						
	Intervention: Case series						
Project details:							
Funding source (Optional): Australian Government Department of Health and Ageing							
Has the study received ethics approval?	✘	Yes		No		Not applicable	
Project starting date: 1 July 2008							
Project completion date: February 2011							
Multi site:	✘	Yes		No		Not applicable	
RESEARCHERS							
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Associated publications / reports: None							
Topics (Admin only) Cancer, Pain, Drug trials							