CareSearch Project
Research Studies Register: Registration Proforma

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Study Title: A randomised double blind placebo controlled trial of infusional subcutaneous octreotide in the management of malignant bowel obstruction in people with advanced cancer.

Brief description of the study:

Background:

Bowel obstruction in the setting of advanced cancer is frequently encountered however there is limited evidence in the understanding of the pathophysiological processes involved and no adequately powered randomised evidence to guide pharmaco-therapeutic options to minimise gastrointestinal secretions and reduce the frequency and volume of vomiting and reduce pain, especially colicky pain caused by continuing peristalsis.

Current management options include combinations of surgery where this is clinically feasible, nil by mouth, nasogastric decompression or continuous suction, analgesia (opioids, anti-spasmotics), and medications that reduce sectretions. None of these interventions have been the subject of an adequately powered study to determine the net clinical benefit, and more aggressive interventions such as surgery may not be technically possible or best practice for someone close to the end of life.

Octreotide is a somatostatin analogue that has specific effects including the potential to inhibit the release of vasoactive intestinal peptide, gastrin, secretin, motilin and other peptide hormones. Three placebo controlled double-blind RCTs of octreotide for malignant bowel obstruction all showed a benefit favouring the use of octreotide. Other published data have been from small, underpowered studies with significant methodological limitations. Additional data are required to further define the efficacy of octreotide in the treatment of bowel obstruction in the palliative care setting. Octreotide is currently not approved for use for this indication despite widespread clinical use.

Study design:

A phase III randomised, double blind, placebo controlled trial of octreotide delivered by subcutaneous infusion used in conjunction with bolus daily parenteral (subcutaneous or intravenous) dexamethasone, ranitidine by subcutaneous infusion and parenteral hydration (10mls/kg/24hours) over a maximum of 72 hours is proposed. Hospital in-patients >18 years of age with a bowel obstruction with vomiting that precipitates a hospital admission or change in clinical care while in hospital will be included.

Objectives:

To compare the efficacy of subcutaneous octreotide relative to placebo in the setting of parenteral ranitidine, dexamethasone and hydration in the treatment of malignant bowel obstruction in people with advanced cancer in: reducing frequency of vomiting, and changes in quality of life, performance status, pain, use of other medications and health service utilisation.

Treatment schedule:

Subcutaneous infusion of octreotide/placebo delivered at 600mcg/24hrs used in conjunction with dexamethasone (8mg bolus dose given in the morning), ranitidine (200mg/24 hrs subcutaneous infusion) and parenteral hydration (10ml/kg/24hrs parenteral infusion). Treatment will be for a total of 72 hours. Treatment thereafter will be at the attending physician's discretion. Hyoscine butylbromide 20mg bolus subcutaneously up to hourly (to a maximum of 120mg in any given 24 hour period) and opioids will be administered as needed at the discretion of the treating clinician for colicky or uncontrolled pain.

Assessments:

Episodes of vomiting will be assessed by participant self-report, 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-30 and the FACIT-PAL. NCI common criteria for adverse events V3 will be used to monitor for adverse events.

Primary endpoint:

Number of days without vomiting at the end of 72 hours of treatment.

Primary Analysis

Number of days without an episode of vomiting at the start of day 4 will be compared by 2-tailed Mann-Whitney U test. A p-value of <0.05 will be taken as evidence of a difference between octreotide and control groups. A study of 92 patients (46 patients per arm) allows 80% power to detect a $x<.017$ reduction in the proportion of patients with 2 or more days without vomiting, with 5% level of significance.

Economic analysis This will estimate incremental differences in costs, effects and net benefit of Octeotride relative to placebo from patient level data collected over 28 days of follow up (survival to 28 days or death whichever is shorter) for:

resource use including bed days spent in hospital for inpatient admissions (index admission and readmissions), professional community support utilized at home after discharge from hospital, including general practitioner and palliative care service visits, and concomitant medication use and;

effects including days of survival without vomiting, pain response, toxicity, adverse events, health related quality of life, and compliance.

Bootstrapping of patient costs and effects data will be used to model decision making uncertainty related to the net benefit and acceptability of octreotide relative to placebo.

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
x	**Intervention: RCT**
	Intervention: Comparative or cohort study
	Intervention: Case series

Project details:

Funding source (Optional): Australian Government of Health and Ageing

Has the study received ethics approval?	x	Yes		No		Not applicable

Project starting date: 21 July 2008

Project completion date: May 2012

Multi site:	x	Yes		No		Not applicable

RESEARCHERS

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Associated publications / reports: None

Topics (Admin only) Bowel obstruction, Drug trials