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Royal Cornwall Hospitals NHS Trust

Ketamine as an Analgesic Agent: Acute and Perioperative Pain, Chronic Pain and Palliative Care Clinical Guideline

V5.0

March 2023

1. Aim/Purpose of this Guideline

1.1. To provide guidance to nursing and medical staff at RCHT, to support the use of ketamine as part of a patient's pain control regime in the treatment of acute, perioperative, and chronic pain or pain in palliative patients.

1.2. See also:

- RCHT Guideline for Peri and Post Operative Pain Control for Complex Patients.
- Clinical Guideline for the Nursing Care of the Patient with Intravenous Ketamine Infusion Intravenous Analgesia for Adults in Recovery Areas –The Recovery Protocol Clinical Guideline.

1.3. This version supersedes any previous versions of this document.

Data Protection Act 2018 (General Data Protection Regulation – GDPR) Legislation

The Trust has a duty under the Data Protection Act 2018 and General Data Protection Regulations 2016/679 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed, and documented. We cannot rely on opt out, it must be opt in.

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2. The Guidance

2.1. Background

2.1.1. Ketamine is an anaesthetic agent with analgesic properties (1). Its principal site of action is in the dorsal horn of the spinal cord where it blocks the N-methyl D-aspartate (NMDA) receptor.

2.1.2. Ketamine hydrochloride solution for injection is licensed in the UK as an anaesthetic agent for diagnostic and surgical procedures in children and adults. Although ketamine (in any preparation) is not currently licensed in the UK for treating pain, its use is well established.

2.1.3. Ketamine is controlled under 'The misuse of Drugs act 1971 (Schedule 2, Class B) and as such is subject to the Misuse of Drugs Regulations.

2.1.4. The drug should be prescribed appropriately on EPMA in both words and numerical value of milligrams with clarity of concentration.

2.1.5. The drug should be checked in the appropriate way in line with Hospital Policy for controlled drugs and appropriately recorded in the controlled drug book. Keys to a ketamine pump lock box should be with the controlled drug keys.

2.2. Contraindications

2.2.1. Ketamine has the potential to increase blood pressure and raise intra-cranial and intra-ocular pressures. It should be avoided or used with caution in the following:

- Significant hypertension.
- Cerebrovascular disease.
- Ischaemic heart disease.
- Raised intracranial pressure e.g. cerebral tumour (primary or secondary).
- Raised intraocular pressure.
- Known history of psychosis or hallucinations.
- Epilepsy.

2.2.2. Ketamine side effects are dose related and therefore ketamine is usually started at low dose and titrated.

2.3. Use in Acute and Perioperative Pain

2.3.1. Ketamine can be used as an adjuvant in acute pain control, in a low dose, with appropriate monitoring, in certain circumstances. Patients who may benefit include those for whom pain is inadequately controlled by opioids alone, those with acute neuropathic pain, or in opioid tolerant patients or those at risk of opioid hyperalgesia.

2.3.2. A low dose can be used as part of intraoperative analgesia in patients who the anaesthetist thinks may benefit from this as an adjunct. Example dosing regimen for 70kg patient would include: 10mg at induction, then 10mg/hr up to 40mg total. Caution with clearance in patients with liver dysfunction. Consider use of 1-2g magnesium as co-analgesic alongside this.

2.3.3. Post-operative ketamine infusions for use in acute pain should only be prescribed under the supervision of the anaesthetic or Pain Teams.

2.3.4. Ketamine may be used in priming, de-sensitisation doses prior to induction (25-50mg), or can be used in its oral form, intranasal, subcutaneous or intravenous route for the first 48 hours post operatively.

2.3.5. Ketamine preparations: 10mg/ml, (20ml vial) 50mg/ml (10ml vial) and 100mg/ml (10ml vial).

2.3.6. Where oral or intranasal or sublingual ketamine is used specific vial may be used more than once for single patient only use.

2.3.7. Post-operative low-dose ketamine infusions may be either via intravenous or subcutaneous routes.

2.3.8. If administered by infusion the drug should diluted in normal saline, clearly labelled and in a locked pump. It should be using an infusion set with an anti-syphon and anti-reflux line, ideally with a dedicated cannula.

2.3.9. Expectation management regarding ketamine infusions is important for both patients and staff. Patients may not show immediate benefit, particularly if the subcutaneous route is being used. This may be offset somewhat with a 0.1mg/kg intravenous loading dose, administered at the discretion of the anaesthetist.

2.3.10. Pain services must be informed of the commencement of an infusion as to ensure a timely review.

2.3.11. Guidelines for administration and monitoring should be followed as per RCHT “Ketamine infusion nursing care clinical guideline”.

2.3.12. Ketamine should be used in conjunction with other analgesia such as paracetamol, NSAID’s (if suitable), local anaesthetic blockade or infusions and opioids.

2.4. Ketamine Infusion Protocol:

2.4.1. The infusion used consists of 500mg Ketamine in 100mls N Saline (5mg/ml).

2.4.2. This may be administered using the designated McKinley 595 grey-fronted ‘Specialist Analgesia’ pumps and Bodyguard Microset antisyphon infusion lines, via either a dedicated intravenous cannula or a subcutaneous infusion cannula. These may be located from general recovery or ward areas.

2.4.3. The infusion range is from 1 – 5 mls/hr (5mg - 25mg/hr).

2.4.4. Rate should usually be started at 1ml per hour.

2.4.5. The infusion rate should not be increased more frequently than hourly and should never exceed 5ml per hour.

2.4.6. Pain scores together with BP, pulse and respiratory rate regularly assessed as per intravenous ketamine nursing care clinical guideline. The infusion rate should be clearly recorded on the observation chart.

2.4.7. It would not be expected that Ketamine be used without involvement of the Acute/Inpatient Pain Team.

2.4.8. It would be usual that ketamine is not used for longer than 3 days unless discussed with a member of the Acute Pain Team.

2.4.9. Needs should be reviewed daily by the Acute/Inpatient pain team where possible. Should it be felt of benefit to the patient to continue to receive Ketamine then conversion to oral or intranasal form should be considered – 25 - 50mg tds – the patient may still be nil by mouth, but this is a small volume and should be tolerated orally.

2.4.10. **Actions Required for Problems whilst using Ketamine Infusion:**

- **Hypotension and Depressed Respiratory Rate** – Unlikely to be Ketamine related, exclude all other causes prior to stopping infusion. If hypotension persistent and systolic pressures are less the 90mmHg then follow algorithm on MEWS chart and call for medical assistance.

- **Sedation** – May be caused by Ketamine, if score greater than 2, stop infusion and call for assistance, if combined with opioid infusion consider naloxone.

- **Nausea** – Give regular antiemetic and if persistent PONV after 2 drugs consider addition of dexamethasone. Avoid the use of neuroleptic drugs such as Droperidol or chlorpromazine.

- **Poor Pain Relief** – If Ketamine infusion fails to help the pain do not exceed recommended rate of infusion but exclude other reasons for severe pain e.g. surgical, tissued IV or malfunctioning epidural and call for advice from Acute Pain Team or on call anaesthetist.

2.5. Chronic Pain or Palliative Care Use

2.5.1. Ketamine can be used to treat complex pain under specialist supervision in chronic pain and palliative contexts when the pain is poorly responsive or unresponsive to standard treatment. The pain will usually have a neuropathic component. Ketamine can be used in phantom limb pain, ischaemic pain and incident pain.

2.5.2. Ketamine, for use in chronic or palliative pain, should only be prescribed under the supervision of the Pain Team or Palliative Care Team.

2.5.3. Ketamine may be prescribed in a range of routes and regimens depending on the patient's pain and other symptoms and characteristics. These brief outlines are an indication of the ways in which Ketamine is most commonly used but are not exhaustive.

2.5.4. Ketamine can be given orally as a regular medication or PRN medication.

2.5.5. Oral ketamine is available as 50mg/5ml mixture. Oral ketamine starting dose is typically 10-25mg three to four times per day and PRN. Daily dose should rarely exceed 200mg.

2.5.6. Ketamine can be given subcutaneously as a continuous infusion via syringe driver or as a subcutaneous PRN medication (off label).

2.5.7. The starting dose for continuous subcutaneous ketamine administration is 1 - 5mg/kg per 24hrs. It would normally be titrated by 50-100mg per 24hrs, depending on clinical effectiveness and side effects. (1mg/kg/24 hours is 3mg/hr for a 72kg patient.) Ketamine is usually not given long term and usually weaned down after stabilisation.

2.5.8. When Ketamine is given by continuous subcutaneous infusion using a McKinley T34 syringe driver, it should be made up with 0.9% saline to the maximum volume following 'RCHT policy and procedure for the management of subcutaneous infusions in adults. It is not normally mixed with other drugs in continuous subcutaneous infusion, but a low dose of midazolam or haloperidol may be added to mitigate adverse effects.

2.6. Legal restrictions and considerations

2.6.1. All ketamine prescriptions for chronic pain or pain in the palliative patient will be off label or unlicensed (RCHT, The Medicines Policy Chapter 6 – 6.5.3 Unlicensed medicines).

2.6.2. Ketamine is controlled under the Misuse of Drugs Act 1971 and as such is subject to the misuse of drugs (controlled drugs) regulations.

2.6.3. Ketamine is known to be a drug of abuse and a risk assessment should be done, if there is concern that the medication could be misused or diverted. This is of particular importance if the patient is being discharged home with an ongoing prescription for Ketamine. Arrangements for ongoing prescription should be discussed with the patient's GP.

Ketamine is a 'zero tolerance' drug in the current driving regulations and patients should be informed that they must take their medication as prescribed to be entitled to a 'medical defence' should they test positive for ketamine whilst driving (3).

2.7. Side Effects of Ketamine in Chronic/Palliative Usage

Side Effect	Suggested Actions
Psychotomimetic phenomena dysphoria, vivid dreams, nightmares, hallucinations, altered body image	• Nurse in an environment that minimises bright light and noise. • Review opioid dose if taking concurrently (may need to be reduced by 25%-50%). • Consider concurrent use of haloperidol (2.5mg bd) or a benzodiazepine (midazolam 2.5mg – 5mg sc stat or midazolam 5mg – 15mg sc over 24hrs via syringe driver. • Consider ketamine dose reduction.

Drowsiness	• Review opioid dose if taking concurrently (may need to be reduced by 25%-50%) and consider naloxone. • Consider ketamine dose reduction.
Hypertension and tachycardia	• Consider ketamine dose reduction or discontinuation.
Diplopia, nystagmus	• Consider ketamine dose reduction or discontinuation.
Erythema and pain at the injection site for continuous subcutaneous infusions	• Dilute ketamine to the maximum volume with 0.9% saline, as per RCHT policy and procedure for the management of subcutaneous infusions in adults (6). • Consider the addition of dexamethasone 0.5mg – 1mg.
Urinary tract toxicity (4) Urinary symptoms – frequency, urgency, urge incontinence, dysuria and haematuria. Irreversible damage leading to renal failure has occurred. This is very unlikely when medical grade ketamine is administered	• If patient has urinary symptoms with no evidence of bacterial infection, the ketamine should be stopped, and urology referral made.
Nausea	• Give regular antiemetics. • If nausea persists after two drugs consider the addition of dexamethasone. • Avoid the use of neuroleptic drugs such as droperidol or chlorpromazine.
Hypersalivation	• Consider ketamine dose reduction or discontinuation.

3. Monitoring compliance and effectiveness

Information Category	Detail of process and methodology for monitoring compliance
Element to be monitored	Review and discussion at Palliative Care MDT of patients in whom. Ketamine has been used to check compliance with policy. Pain Services review of chronic pain use.
Lead	Carolyn Campbell (Governance and audit leads for palliative care team). Keith Mitchell (Governance and Audit lead for Pain Services).
Tool	Hospital Palliative Care MDT documentation Pain Services Audit.
Frequency	Annual monitoring, and report every 3 years dependent upon number of patients affected (likely to be very small).
Reporting arrangements	Relevant Divisional Boards and Governance Committees will receive. report with advised action (if any) attached, and amendment of policy to follow agreement by the committee.
Acting on recommendations and Lead(s)	As above.
Change in practice and lessons to be shared	As the policy refers to a drug rarely prescribed, and then only by specialist practitioners, each case will be reviewed on an individual basis and used to inform practice on wards, including extra information or support to ward doctors and nurses when using this.

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the 'Equality, Inclusion and Human Rights Policy' or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Information Category	Detailed Information
Document Title:	Ketamine as an Analgesic Agent: Acute and Perioperative Pain, Chronic Pain and Palliative Care Clinical Guideline V5.0
This document replaces (exact title of previous version):	Ketamine as an Analgesic Agent in Chronic Pain and Palliative Care Clinical Guideline V4.0 And Ketamine as an Adjuvant Post-Operative Analgesic by Anaesthetists only Clinical Guideline V4.0
Date Issued/Approved:	21 March 2023
Date Valid From:	March 2023
Date Valid To:	March 2026
Directorate / Department responsible (author/owner):	Dr Carolyn Campbell, Consultant in Palliative Care Elizabeth Thomas, Specialist Nurse Palliative Care Dr Keith Mitchell, Consultant in Anaesthesia and Pain Management
Contact details:	Dr Carolyn Campbell 01726 65711 Liz Thomas 01872 258346 Dr Keith Mitchell 01872 252792
Brief summary of contents:	Guidance for nursing and medical staff at RCHT, to support the use of ketamine as part of a patient's pain control regime in the treatment of chronic pain or pain in palliative patients.
Suggested Keywords:	Chronic pain, Neuropathic pain, Care, Health care, Medical care, Patient care, Palliative care, Anaesthesia, Analgesia, Pain management, Products, Medicinal products, Drugs, Analgesics, Ketamine.
Target Audience:	RCHT: Yes CFT: No CIOS ICB: No
Executive Director responsible for Policy:	Chief Medical Officer

Information Category	Detailed Information
Approval route for consultation and ratification:	Combined Pain and Palliative Care Group
General Manager confirming approval processes:	Matthew Body
Name of Governance Lead confirming approval by specialty and care group management meetings:	James Masters
Links to key external standards:	**References:** 1. Fallon MT and Welsh J. The role of ketamine in pain control. European Journal of Palliative Care 1996 3;143-146 2. ESUOM27: Chronic pain: oral ketamine. NICE Evidence Summary, 2014. http://publications.nice.org.uk/esuom27-chronic-pain-oral-ketamine-esuom27 3. Guidance for healthcare professionals on drug driving. Department for Transport, 2014. 4. PCF4 Palliative Care Formulary Fourth Edition. 5. Pallaborative Ketamine guideline Pallaborative Ketamine guideline 6. Scottish Intercollegiate Guidelines on Ketamine Use in Palliative Care Palliative Care Guidelines Medicine Information Sheets / ketamine
Related Documents:	1. RCHT Guideline for Peri and Post Operative Pain Control for Complex Patients 2. RCHT Clinical Guideline for Nursing Care of Patient with Intravenous Ketamine Infusion 3. Intravenous Analgesia for Adults in Recovery Areas - The Recovery Protocol Clinical Guideline 4. Subcutaneous Infusions in Adults Policy and Procedure 5. RCHT, The Medicines Policy Chapter 6 – 6.5.3 Unlicensed Medicines
Training Need Identified?	No
Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet and Intranet

Information Category	Detailed Information
Document Library Folder/Sub Folder:	Clinical / Pain

Version Control Table

Date	Version Number	Summary of Changes	Changes Made by
Nov 2008	V1.0	Initial issue	Dr Rachel Newman, Consultant in Palliative Medicine Eve Thorp, Clinical Nurse Specialist in Palliative Care
01 Jan 2012	V2.0	Guideline reviewed	Dr Rachel Newman, Consultant in Palliative Medicine Eve Thorp, Clinical Nurse Specialist in Palliative Care
01 Aug 2015	V3.0	Guideline revised to include use of ketamine for pain in palliative care and chronic pain	Dr Carolyn Campbell, Consultant in Palliative Medicine Dr Melanie Huddart ST6 Palliative Medicine Dr Keith Mitchell, Consultant in Anaesthesia and Pain Management
June 2019	V4.0	Reformatted into the new Trust template	Dr Carolyn Campbell, Consultant in Palliative Medicine Dr Melanie Huddart ST6 Palliative Medicine Dr Keith Mitchell, Consultant in Anaesthesia and Pain Management

Date	Version Number	Summary of Changes	Changes Made by
March 2023	V5.0	Amalgamated with Ketamine As An Adjuvant Post-Operative Analgesic By Anaesthetists Only Clinical Guideline. Minor amendments	Dr Neil Roberts, Fellow in Pain Medicine Dr Carolyn Campbell, Consultant in Palliative Medicine Dr Keith Mitchell, Consultant in Anaesthesia and Pain Management

All or part of this document can be released under the Freedom of Information Act 2000

This document is to be retained for 10 years from the date of expiry.
This document is only valid on the day of printing

Controlled Document
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Appendix 2. Equality Impact Assessment

Section 1: Equality Impact Assessment (EIA) Form

The EIA process allows the Trust to identify where a policy or service may have a negative impact on an individual or particular group of people.

For guidance please refer to the Equality Impact Assessment Policy (available from the document library) or contact the Equality, Diversity and Inclusion Team rcht.inclusion@nhs.net

Information Category	Detailed Information
Name of the strategy / policy / proposal / service function to be assessed:	Ketamine as an Analgesic Agent: Acute and Perioperative Pain, Chronic Pain and Palliative Care Clinical Guideline V5.0
Directorate and service area:	Pain, ACCT
Is this a new or existing Policy?	Existing
Name of individual completing EIA (Should be completed by an individual with a good understanding of the Service/Policy):	Dr Keith Mitchell, Consultant in Anaesthesia and Pain Management
Contact details:	01872 252095

Information Category	Detailed Information
1. Policy Aim - Who is the Policy aimed at? (The Policy is the Strategy, Policy, Proposal or Service Change to be assessed)	Enable safe practice of administration of ketamine as an analgesic for adults with chronic pain and palliative pain at RCHT.
2. Policy Objectives	As above
3. Policy Intended Outcomes	As above
4. How will you measure each outcome?	Case discussion at Palliative MDT Pain Services audit of use in Chronic Pain
5. Who is intended to benefit from the policy?	Teams who are involved in administration of ketamine as part of a patient's pain control Any adult who requires ketamine as part of their analgesic regime for chronic or palliative pain

Information Category	Detailed Information
6a. Who did you consult with? (Please select Yes or No for each category)	• Workforce: Yes • Patients/ visitors: No • Local groups/ system partners: No • External organisations: No • Other: No
6b. Please list the individuals/groups who have been consulted about this policy.	**Please record specific names of individuals/ groups:** Consultation has taken place with the Hospital Palliative Care Team and the Pain Team via the Combined Pain and Palliative Care Team Meetings. Consultation has a wide cross setting consultation with palliative care practitioners across settings of care including Cornwall Hospice Care
6c. What was the outcome of the consultation?	Agreed
6d. Have you used any of the following to assist your assessment?	**National or local statistics, audits, activity reports, process maps, complaints, staff or patient surveys:** No

7. The Impact

Following consultation with key groups, has a negative impact been identified for any protected characteristic? Please note that a rationale is required for each one.

Where a negative impact is identified without rationale, the key groups will need to be consulted again.

Protected Characteristic	(Yes or No)	Rationale
Age	No	
Sex (male or female)	No	
Gender reassignment (Transgender, non-binary, gender fluid etc.)	No	
Race	No	
Disability (e.g. physical or cognitive impairment, mental health, long term conditions etc.)	No	

Protected Characteristic	(Yes or No)	Rationale
Religion or belief	No	
Marriage and civil partnership	No	
Pregnancy and maternity	No	
Sexual orientation (e.g. gay, straight, bisexual, lesbian etc.)	No	

A robust rationale must be in place for all protected characteristics. If a negative impact has been identified, please complete section 2. If no negative impact has been identified and if this is not a major service change, you can end the assessment here.

I am confident that section 2 of this EIA does not need completing as there are no highlighted risks of negative impact occurring because of this policy.

Name of person confirming result of initial impact assessment: Dr Keith Mitchell, Consultant in Anaesthesia and Pain Management

If a negative impact has been identified above OR this is a major service change, you will need to complete section 2 of the EIA form available here:
Section 2. Full Equality Analysis