Sedation in DCCM

1. Purpose of guideline

1. To ensure the safe and effective use of sedation for patients in DCCM
2. To provide additional information regarding sedative agents, side effects and necessary monitoring to help guide prescribing decisions and administration

2. Responsibility

All medical, nursing and other allied health staff providing care and treatment for patients requiring sedation in DCCM

3. Guideline management principles and goals

Sedation is commonly required in critical care settings, particularly for patients requiring mechanical ventilation. An combination approach is commonly used, whereby sedating analgesia (typically an opioid) is used in combination with other non-analgesic sedatives to achieve an overall acceptable level of sedation.

The overarching goals for sedative use is to achieve patient comfort, minimise distress / pain whilst limiting risks and adverse drug events. This can be achieved with appropriate understanding of the agents used, their side effects and the necessary monitoring required.

This SOP will outline the recommended combinations of sedation used in DCCM and describe the different agents available, including dosing information.

As a general rule, doses of all sedative agents should be reduced for elderly or otherwise frail patients.

4. Indications

Potential indications for sedation in DCCM include:

- Improve patient comfort and minimise distress (pain, fear, delirium are common causes of distress);
- Airway manipulation (i.e. intubation);
- Transport (i.e. inter or intra-hospital, CT or MRI);
- Improve ventilator synchrony;
- Reduce oxygen demand (i.e. cerebral - to reduce intracranial pressure); and
- Other indications that the intensivist deems necessary.

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5. Recommended sedative combinations

Sedation without NMB

RASS target to be determined on ward round and entered on chart

- Opioid infusion with PRN doses if appropriate (particularly for patients expected to have pain)
- +/- Propofol or benzodiazepine (usually midazolam or diazepam)

Sedation with NMB

Ensure RASS -5 prior to initiating NMBD

Sedation **must be** continued for the duration of NMB

- Opioid infusion (and PRN doses if appropriate)
- + Propofol
- + Benzodiazepine to reduce awareness

Delirium

As per Delirium SOP

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Other indications for sedation

See relevant SOP available on Hippo intranet here on DCCM Sharepoint (i.e. Status Epilepticus SOP)

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6. Sedation agents and dosing

Sedation *with* analgesic properties

Opioids

Uses	Many patients in ICU will have pain, thus opioids are commonly required. Similar effects when given at equivalent analgesic doses. Do not prevent awareness – are not appropriate alone for sedation when patients require NMB.		
Dose	Prescribe a fixed dose infusion with option to provide PRN additional boluses. Doses should be based on patient-specific factors. The specific indication for PRN doses should be made clear to all staff to ensure appropriate administration (eg. for pain or for raised ICP).		
	Opioid	**Infusion dose**	**PRN only dose**
	Morphine	0-10mg/hr IV *Additional doses may also be prescribed PRN*	1-2mg IV
	Fentanyl	0-100mcg/hr IV *Additional doses may also be prescribed PRN*	10-20mcg IV
Renal / hepatic	Morphine is preferred in DCCM. Fentanyl should be used for renal or hepatic dysfunction.		
Adverse effects	Constipation, nausea, respiratory depression, histamine release / itch (morphine >> fentanyl)		

Methadone

Uses	May be appropriate for select patients, such as those tolerant to opioids, opioid-induced hyperalgesia or to facilitate weaning from IV opioids.
Dose	Initiation should be discussed with intensivist or fellow. **Appropriate starting doses range from 5-10mg q6-8h**; individualise to patient.
Renal / hepatic	Largely unaffected by renal dysfunction but dose with caution in hepatic failure.
Adverse effects	Has a variably long half-life and complex pharmacokinetics that can change with prolonged use. May prolong QT interval and cases of TdP have been reported. Potential for drug interactions. Other adverse effects similar to other opioids.
Monitoring	ECG may be required when initiating / adjusting doses or using other drugs that prolong QT. Weaning plan into DCCM transfer summary to guide cessation / refer to Acute Pain Service.

Central alpha-2 receptor agonists (clonidine, dexmedetomidine)

Uses	Dexmedetomidine may be used to assist weaning from mechanical ventilation. Due to cost this must be discussed with intensivist prior to initiation. Should not be used for longer than 24 hr. Clonidine may be used for delirium from alcohol or drug withdrawal, or for severe pain in addition to opioids. Clonidine patches take 2-3 days to reach steady state.			
Dose	**Alpha-2 blocker**	**IV**	**Enteral**	**Topical**
	Clonidine	25-150mcg q6-8h	25-150mcg q6-8h	Available patches 0.1mg, 0.2mg & 0.3mg/day *Prescribe as X mg/day, changed weekly*
	Dexmedetomidine	0-1.5mcg/kg/hr	N/A	N/A
Renal / hepatic	Clonidine: Use lower doses with extended dosing interval in renal dysfunction. Dexmedetomidine: Lower doses may be required in renal and hepatic failure.			
Adverse effects	Hypotension (may be of benefit in some cases), bradycardia and heart block. Withdrawal symptoms can occur with prolonged use.			

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Ketamine

Uses	May be used for procedural sedation/pain, status epilepticus or severe bronchospasm. May be useful adjuvant for severe pain in addition to opioids. Has minimal risk of respiratory depression.		
Dose	**Indication**	**Dosing ranges**	
	Pain	0-10 mg/hr	0.5-1mg/kg PRN for procedures/turns
	Status asthmaticus	0.5-2.5mg/kg/hr Bolus 0.5-1mg/kg may be required	Discuss with intensivist before initiating therapy
	Status epilepticus	Load: 2mg/kg Maintenance: 1-5mg/kg/hr	See Status Epilepticus SOP Discuss with intensivist
Renal / hepatic	Reduce doses in renal or hepatic failure.		
Adverse effects	May increase blood pressure or heart rate due to catecholamine release. Hallucinations are a common adverse effect that may limit use.		

Sedation *without* analgesic properties

Propofol

Uses	Routine sedation in DCCM. Fast onset and offset time allowing for easy titration and sedation breaks to assess neurological and respiratory status. Does not have analgesic properties – use with opioids for pain.
Dose	**Dosing range usually prescribed: 0-200mg/hr** and adjusted to required sedation level. Ongoing use should be reviewed at 48 hours by intensivist. Dosing should be based on ideal body weight in obesity. Higher doses of 300mg/hr should not be continued for >48 hours without Intensivist review.
Renal / hepatic	Dose adjustment usually not required, but use with caution.
Adverse effects	Hypotension is common, particularly with high doses. Emulsified with egg protein – avoid in severe egg allergies. Each 1mL propofol 1% contains 1.1kcal (lipid) - adjustments to nutrition may be required with high doses. Propofol infusion syndrome (PRIS) is rare but may occur with high doses/prolonged use. Therapeutic hypothermia can affect metabolism of propofol, increasing risk of toxicity. Lower doses should be used and with caution.
Monitoring	Triglycerides, liver function and CK tests may be required.

Benzodiazepines

Uses	Delirium and agitation, severe anxiety, drug or alcohol withdrawal. Often required for patients without neurological concerns that require ongoing NMB (eg. proning for ARDS) to reduce risk of awareness. Propylene glycol in lorazepam injection may limit IV lorazepam use.			
Dose	**Benzodiazepine**	**Dosing ranges**		
		General sedation	**Seizures/status**	Also see Status Epilepticus and Elevated ICP SOP for further details
	Diazepam	5-20mg q4-6h	Bolus: 5-10mg IV	
	Lorazepam	0.5-2mg q6-12h	Bolus: 4mg IV	
	Midazolam	Bolus 1-4mg q2-6h Infusion: 1-10mg/hr	Bolus: 5-10mg IV Infusion: 0.2-2mg/kg/hr	
Renal / hepatic	Use with care in renal impairment. Lorazepam preferred in hepatic failure.			
Adverse effects	Cardiac and respiratory depression, paradoxical excitation. Tolerance as a result of changes to receptor expression can occur with prolonged exposure, as can withdrawal effects. May cause delirium in some patients.			

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Barbiturates

Use	Phenobarbitone has a long half-life. It may be given enterally and thus be suitable for long-term sedation, in addition to other sedatives or status epilepticus. Patients with normal neurological function should tolerate phenobarbitone dosing as below and remain rousable. Thiopentone may be considered in addition to other sedatives for elevated ICP or refractory status epilepticus – discuss with intensivist or fellow prior to initiation. Loading doses should give burst suppression on EEG (correlates approx. thiopentone level 200-300micromol/L).		
Dose	**Barbiturate**	**Loading dose**	**Maintenance**
	Phenobarbitone	10-15mg/kg NG or slow IV	60-400mg NG q8-12h
	Thiopentone *Use must be approved by intensivist first*	3mg/kg doses - titrated to ICP *Exceptional circumstances: 100mg/kg given at rate of 1g/hr or less, prescribed only by Intensivist*	2-5mg/kg/hr
Renal / hepatic	Reduce doses in liver and renal dysfunction.		
Adverse effects	Long half-lives (phenobarbitone: 35-140 hr; thiopentone: up to 26 hr) can lead to prolonged sedation. Hypotension and immunosuppression may also occur. Thiopentone may cause hypokalaemia – replace with caution as hyperkalaemia (potentially life threatening) may occur when therapy is stopped. K^+ target 3-3.5 with thiopentone.		
Monitoring	Phenobarbitone and thiopentone levels may be required according to clinical situation.		

Atypical adjuncts

Uses	Delirium - first generation antipsychotics listed here have sedating properties that may be beneficial in some cases. Haloperidol is common in DCCM.		
Dose *See intensivist if higher doses required*	**Antipsychotic**	**Dose**	**Maximum / 24 hr**
	Haloperidol	Bolus: 0.5-10mg IV or NG Maintenance: 0.5-5mg IV or NG q4-8h	20 mg
	Chlorpromazine	25-100mg NG q4-8h	400mg
	Atypicals	No evidence to support a particular agent. See Delirium SOP	
Renal / hepatic	Reduce dosing in renal and hepatic dysfunction. Haloperidol may be preferred.		
Adverse effects	QT prolongation is a risk for both as is potential for multiple drug interactions. Haloperidol is associated with risk of EPSE. Chlorpromazine may cause significant hypotension / vasodilation, tachycardia and other anticholinergic effects. The risk of EPSE may be lower for chlorpromazine than for haloperidol.		
Monitoring	ECG monitoring		

7. Sedation breaks and monitoring

Sedation breaks should be considered daily, with RASS targets to be discussed on the morning ward round and charted on the appropriate DCCM documentation.

Ensure the plan for sedation breaks and any monitoring that may be required (eg. ECG) is communicated with the nurse in the bedspace and the Clinical Charge Nurse where appropriate.

Monitoring that may be required for specific sedatives are outlined in the relevant table in the section above. For further information on dosing or monitoring discuss with the intensivist or pharmacist.