Midazolam Subcutaneous and Nasal- Palliative Care (Adults)

Contents

1. Overview

Purpose

This protocol outlines the administration, prescribing and monitoring of subcutaneous and nasal midazolam at Waitemata District Health Board.

Scope

All medical and nursing staff

⚠ This guideline is for use in Palliative Care ONLY.

⚠ There is variable sensitivity to midazolam which is often unpredictable.
Intravenous midazolam has a high risk of apnoea and is rarely used in palliative patients.[1]
Administration by subcutaneous, buccal or intranasal routes is preferred.

2. Presentation

Midazolam 5mg/5ml and Midazolam 15mg/3ml ampoules
Midazolam nasal spray 5mg/ml (15ml) (Manufactured by WDHB inpatient pharmacy)

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3. Indications

Licensed:

- Sedation, induction and maintenance of anaesthesia

Unlicensed:

- Restlessness, anxiety, respiratory distress, terminal agitation, seizures, myoclonic jerks, intractable hiccup, skeletal muscle relaxant[2, 3]

Unlicensed route of administration:

- Subcutaneous

4. Dose

4.1 Subcutaneous Midazolam

Indication	Starting and PRN doses	Initial Infusion Rate per 24 hours	Dose Range per 24 hours
Anxiety **Restlessness** **Respiratory distress/agitation** **Muscle tension/spasm** **Multifocal myoclonus** **Intractable hiccup**	2.5 mg stat 2.5 - 5 mg q30min PRN	10mg	10 – 20 mg higher doses may be used (up to 60 mg/24 hours)
Seizures	10mg stat and q30min PRN (use 5mg in older/frail patients)	15 - 30mg	30 – 60mg
Prevention of benzodiazepine withdrawal in patients no longer able to swallow oral medications	2.5 - 5 mg stat and q30min PRN	10 mg	

Note: There is no maximum dose for midazolam however the dose should be titrated carefully according to the response. If doses in excess of 30mg / 24 hours are required, seek advice from the Palliative Care team.

4.2 Midazolam Nasal Spray

The main indication for midazolam nasal spray is anxiety-related dyspnoea.

There is no commercial preparation of midazolam nasal spray available in New Zealand. It must be compounded for each patient by the pharmacy. The amount delivered by each spray depends on the spray bottle used. The spray bottles used at WDHB dispense 0.1ml of solution = 0.5mg of midazolam per spray. The spray may also be administered via the buccal route.

The dose required is patient and indication dependant. Prescribe as **'1 spray into each nostril q1h PRN'**

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4.3 Dose Conversion

Midazolam is the recommended benzodiazepine for subcutaneous use. Patients on oral benzodiazepines should be converted to midazolam if a benzodiazepine is to be used in a continuous subcutaneous infusion (CSCI). To switch from an oral benzodiazepine or intranasal midazolam to CSCI midazolam, use the table below to convert the amount of benzodiazepine used in the last 24 hours to the subcut midazolam equivalent. Round up or down to the nearest multiple of 2.5mg if necessary. Also prescribe PRN midazolam for breakthrough symptoms.

Subcut Midazolam Dose Equivalencies of Commonly Used Benzodiazepines		
Benzodiazepine	**Dose and Route**	**Equivalence**
Diazepam	**10mg PO/PR**	**2.5mg subcut midazolam**
Clonazepam	**1mg PO/SC**	
Lorazepam	**1mg PO/IV**	
Oxazepam	**15 to 30mg PO**	
Temazepam	**10mg PO**	
Midazolam Nasal Spray	**5 sprays (=2.5mg)**	

Example: A patient has been taking 1 mg lorazepam PO (equivalent to 2.5 mg subcut midazolam) + used 7 nasal sprays of midazolam in last 24 hours (equivalent to 3.5 mg subcut midazolam) = total midazolam equivalent 6 mg. Round *down* to 5 mg midazolam via CSCI over 24 hours.

5. Administration

5.1 Diluent

- For subcutaneous bolus administration midazolam does not need to be diluted.
- When added to a syringe driver the recommended diluent is water for injection.[2]

5.2 Additional Equipment

- Subcutaneous Saf-T-Intima single lumen [ADM140] (*refer WDHB Policy Palliative Care- Subcutaneous Site Selection, Insertion and Monitoring of BD Saf-T-Intima Cannula*)
- Continuous subcutaneous infusion pump (Niki T34) if required

5.3 Compatibility

Compatible with:

Water for injection, 0.9% sodium chloride, morphine sulfate, morphine tartrate, haloperidol, hyoscine hydrobromide, metoclopramide, ketamine, methadone, fentanyl, oxycodone, levomepromazine, hyoscine butylbromide, octreotide, glycopyrrolate, ondansetron, tramadol[2, 3, 4, 5]

Concentration dependent *in*compatibility with:

Cyclizine, Dexamethasone[4, 5]

⚠ Do not use if the solution is cloudy or a precipitate is present.

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5.4 Administration Procedure

Subcutaneous administration

- Use 15mg/3ml ampoules to reduce the volume administered.
- Inject through a Saf-T-Intima (butterfly) or directly via subcutaneous needle.
- The Saf-T-Intima should be flushed with 0.2ml of water for injection after administration of medication.
- Can be administered via a continuous subcutaneous infusion pump (Niki T34).

Intranasal administration

- Ensure patient is seated upright with head upright. Avoid tilting head back if possible as this can cause solution to be swallowed.
- Hold the bottle upright and instil one spray into one or both nostrils. There is no need to breathe/inhale the dose in.
- Dose can be given q1hourly PRN with the response closely monitored.
- Dose may be up-titrated according to response.
- Can be administered via the buccal route (squirt dose between the lower gum and the cheek).

6. Observation and Monitoring

Observe patient for excessive sedation

7. Mechanism of Action

Midazolam is a short-acting benzodiazepine with GABA potentiating actions in the central nervous system (CNS).[2]

It relieves anxiety, is a sedative, an anticonvulsant and a muscle relaxant.[1]

8. Contraindications and Precautions

Contraindications

- Patients with known hypersensitivity to midazolam or other benzodiazepines[1]
- Unless imminently dying:[2, 6]
    - Acute or severe pulmonary insufficiency
    - Severe respiratory depression
    - Untreated sleep apnoea syndrome
    - Severe liver disease
    - Myasthenia gravis

Precautions

- Chronic respiratory insufficiency
- Hepatic failure
- Impaired cardiac function
- Chronic renal failure[1, 6]

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9. Possible Adverse Effects

- Excessive sedation
- Hypotonia
- Ataxia
- Confusion
- Dizziness
- Respiratory depression
- Amnesia
- Fatigue
- Skin rash
- Pruritis
- Hypotension
- Hallucinations
- Paradoxical reactions (especially in elderly) e.g. agitation, delirium, insomnia, excitement, involuntary movements, rage[1, 6]

10. Drug Interactions

Medications which increase midazolam plasma concentrations

- Cimetidine, erythromycin, clarithromycin, diltiazem, verapamil, HIV protease inhibitors, ketoconazole, fluconazole, voriconazole and itraconazole can inhibit hepatic metabolism of midazolam resulting in a prolonged and more pronounced effect. [1, 6]
- Sodium valproate can displace midazolam from its binding sites and may increase the response to midazolam.[1]

Medications which reduce midazolam plasma concentrations

- Carbamazepine and rifampicin[2, 6]

Other

- CNS depressants – increased effect with midazolam[1]
- Phenytoin – unpredictable response[2, 6]

11. Half-lives of Commonly Used Benzodiazepines

Drug	Half life
Diazepam	1-2 days
Clonazepam	30 – 40 hrs
Lorazepam	12 – 16 hrs
Oxazepam	3 – 21 hrs
Temazepam	5 – 15 hrs
Midazolam nasal spray	1.5 – 2.5 hrs

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12.References

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