Rapid Series Manual

Midazolam-Series 13

What is this series about?

Midazolam belongs to a class of medications called benzodiazepines, which produce a calming effect on the brain and nerves. It is thought to work by increasing the effect of a certain national chemical (GABA) in the brain inducing sleepiness, decreasing anxiety and causing a loss of ability to create new memories. Midazolam first came into use in 1976. It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system. Midazolam is available as a generic medication and is not very expensive.

In the final stages of end-of-life care, midazolam is routinely used at low doses via subcutaneous injection to help with agitation, myoclonus, restlessness or anxiety in the last hours or days of life. At higher doses during the last weeks of life, midazolam is considered a first line agent in palliative continuous deep sedation therapy when it is necessary to alleviate intolerable suffering not responsive to other treatments, but the need for this is rare.

Attention should be paid to dosage, reduced doses being given to the elderly, patients on opioid medication, and patients with impaired liver or renal function. Additional caution is required in the elderly, as they are more sensitive to the pharmacological effects of benzodiazepines, metabolise them more slowly, and are more prone to adverse effects, including drowsiness, amnesia (especially anterograde amnesia), ataxia, hangover effects, confusion, and falls. The risk of serious side effects (such as slow/shallow breathing, severe drowsiness/dizziness) may be increased if this medication is taken with other products that may also cause drowsiness or breathing problems.

This Series will provide us with information on the use of midazolam for agitation in the palliative population internationally, including dose ranges, benefits and harms.

Patient tracking

A log or spreadsheet should be developed in order track the patient medical record number and the study ID number allocated to each patient when commenced on a medication/intervention. This spreadsheet will be the only link between the data collected and the identity of the patient and remains the property of the participating site. This information should not be shared with the Palliative Care Clinical Studies Collaborative (PaCCSC). The spreadsheet should also contain the date and time of the data entry at each time point.

Patient PID	Patient name	Patient medical record number	Date of initial data entry	Time of data entry

Allocating Patient ID number

a) The ID number for each set of data collected is a composite number built up using a series of three codes.

i) Site identifier.

This is the number allocated to each participating site as a two digit number

ii) Medication number

The medication number for the Amitriptyline series is **13**

iii) Patient number

This is usually a three digit number e.g. **001**

Therefore the full patient ID number will be;

Site identifier/medication number/patient number e.g. 01/13/001

Time points

There are 4 main time points where data is required;

1. Commencement of the medication (baseline) (T_0)
2. 1 hour after baseline - symptomatic benefit assessment (T_1)
3. 4 hours after baseline symptomatic benefit assessment (T_2)
4. 24 hours after baseline – symptomatic benefit assessment (T_3)

Other data collection points are:

1. Toxicity at unexpected time points (T_1,T_2 and T_3):
   - There can be up to three other times where toxicity can be recorded
   - These pages can be left blank if there are no unexpected adverse events

2. Cessation of the medication
   - Complete this page if the medication/intervention of interest is ceased at any time during the data collection period for any reason
3. Date of death
   - Enter the date of death if/when known
   - If the date of death is entered during the data collection period no further prompts will be received.

Each medication/intervention of interest will have different time points for clinical benefit and adverse events according to its profile. Time points are determined by each Series subcommittee and are based on clinical experience and published product information.

For example: Oxycodone/naloxone Series

- Toxicity is assessed at both days 1 and 3
- Clinical benefit is assessed at both days 1 and 3

Adverse event assessment

Adverse events (or toxicities) are assessed using a standard scale from the National Cancer Institute Criteria for Adverse Events (NCI CTCAE). The NCI uses a scale between 1 and 5 ranging from mild to serious (resulting in death) symptoms or sequelae. The NCI criteria are provided as a reference document which is supplied separately and should be referred to for any events recorded is association with the patient's clinical course.

Each medication/intervention has a number of pre-populated expected adverse events (toxicities). These are listed at each time point, and the NCI grade is described and provided for easy reference. A grade should be provided for each listed adverse event.

If unexpected adverse events occur at any other time, either before or after any pre-determined time point, these should be recorded in the unexpected adverse event section of the CRF. Up to three other time points can be recorded.

Data entry

Login can be acquired by emailing **RAPID@uts.edu.au** and requesting the login to the series that is applicable to you.