Guidance for analgesia and or safe conscious sedation for patients undergoing planned minor procedures within the Department of Clinical Haematology

Overview
Analgesia and or conscious sedation is used within Clinical Haematology in clinically stable patients for undertaking minor procedures, which are defined as: bone marrow biopsy (BMB) procedures, lumbar puncture, and for the insertion of central lines by the Vascular access team. Analgesia and or sedation are provided in order to render an uncomfortable procedure more tolerable and are not an alternative to general anaesthesia. Appendix 1 outlines the local issues which have led to the introduction of Entonox® use in this setting.

Purpose
To ensure that sedation that is undertaken in Clinical Haematology clinical areas is appropriate, safe and effective.
That all staff undertaking these procedures are appropriately trained, competent and working to the OUH NHS Trust policy ‘Safe Sedation by Non-Anaesthetists’ (2012).

Scope
This guidance applies to:
- Haematology Consultants, Specialist Registrars/Speciality Trainees and Advanced Nurse Practitioners performing bone marrow biopsy (BMB) procedures and lumbar punctures.
- Haematology Consultants, Specialist Registrars/Speciality Trainees prescribing analgesia/sedation.
- Day Treatment Unit, Haematology Ward and Wytham private patient nursing staff (Haematology focus), who administer Entonox or Midazolam during bone marrow biopsy procedures, lumbar punctures and central line insertions by the OUH Vascular access team.

Responsibilities
Clinical Director
To ensure that medical staff and advanced nurse practitioners undertaking the described procedures are appropriately trained and competent in the use of minimal and moderate sedation. To ensure the department is aware of and adheres to the OUH policy and local guidance and ensure regular audit of this guidance.

Ward Sisters
To ensure that nurses supporting and or undertaking minimal and or moderate sedation of patients are trained and competent in these aspects of care.

Analgesia and conscious sedation cascade
- **Level 1**: Local anaesthesia with Paracetamol pre and post procedure as necessary (As per Bone Marrow Aspirate/Trephine document). If the patient is unable to tolerate the procedure, move to level 2.
- **Level 2**: As above plus Entonox (minimal sedation). If the patient is unable to tolerate the procedure, re-schedule procedure and move to level 3.
- **Level 3**: As Level 1 plus Midazolam (moderate sedation).
Level 1: Local Anaesthesia plus Paracetamol
See Bone marrow aspirate and trephine procedure document for local anaesthesia dose. Patients should be advised to take Paracetamol as appropriate one hour before the procedure and then follow post procedure guidance.

Level 2 Minimal sedation: Entonox®

Introduction
The aim of this section of the guideline is to facilitate safe administration of Entonox® to adults. Entonox® is designed for self-administration by the conscious patient. This guideline covers the administration of Entonox® within the Clinical Haematology department at Oxford University Hospitals NHS Trust for procedures as defined above.

Entonox® is a pre-prepared gaseous mixture of 50% Oxygen and 50% Nitrous Oxide (N2O), which may be supplied in blue cylinders with blue and white quarters on the neck. Nitrous oxide is a rapidly acting inhalation agent which is tasteless and colourless. Entonox® has a rapid onset and offset and is a powerful analgesic which is safe and simple to use. It is commonly known as and may be familiar to patients as “laughing gas” or “gas and air”. Entonox® is classed as a minimal sedation agent that may be administered by a single doctor or nurse who has competencies in Hospital Life Support (HLS). National guidance recommends pulse oximetry is available.

The apparatus has a “demand valve”, that allows the Entonox® gas to flow when the patient exerts a negative pressure through inhalation. The patient either holds a tight fitting mask to their face or applies the necessary suction via a mouthpiece. This demand system makes overdose virtually impossible, as once the patient’s conscious level falls the mask or mouthpiece will no longer be retained in position, causing room air to be inhaled.

Aim
- To ensure appropriate use of Entonox® after assessment of the patient and their analgesia requirements.
- To ensure safe and appropriate administration of Entonox®.

Indications for Use
- Bone Marrow Biopsy
- Lumbar Puncture
- Patients must be give valid consent but a written consent form is not required. Consent must be documented in the patient medical record.
- Patients must be able to understand and comply with administration of Entonox® and be able to self-administer.
- Fasting is not required prior to use of Entonox.

Contraindications
- Nitrous oxide diffuses into cavities so it should not be used if any of the following are suspected:
  - Pneumothorax
Bowel obstruction, if there is abdominal distension
- Air embolism
- Decompression sickness
- Bullous lung disease
- Intracranial air collection
- Women including staff, in the first two trimesters of pregnancy, should not be given Entonox® nor be in the vicinity when it is being administered to another person
- Known B12 or folate deficiency
- Significant cardiac failure
- Any patient unable to use the self-administration system.

**Side effects**

**General:**
- At high concentration can cause sedation, unconsciousness and hypoxia
- Pulmonary toxicity in patients who have received Bleomycin.
- Caution with patients on opioids or benzodiazepines as it may increase respiratory depression or potentiate sedation.
- Dry mouth, disorientation, dizziness, euphoria, loss of inhibition, feeling floaty, blurring vision, tingling sensation lips, fingers, nose (harmless and will stop when inhalation of Entonox® is discontinued) and less commonly, nausea and vomiting, excessive sedation.
- Nitrous oxide inactivates vitamin B12 and can also interfere with folate metabolism and DNA synthesis which can impair bone marrow function. Such effects are of significance if the therapeutic exposure to Entonox® exceeds 6 hours.
- Routine blood checks should be performed for evidence of megaloblastic change in red cells and hyper-segmentation of neutrophils if Entonox® is administered more frequently than every 4 days.

**Staff Training and Competence**
- Entonox® administration must be supervised by a qualified healthcare professional. This may be a doctor or a registered nurse.
- In the case of bone marrow biopsies and lumbar punctures, the doctor and/or advanced nurse practitioner carrying out the procedure may also be responsible for supervising the Entonox®. In this case a clinical support worker should be present for patient safety and comfort during the procedure.
- All staff involved in the administration of Entonox® must complete their Hospital Life Support training on a yearly basis.
- Staff supervising Entonox® administration must receive training in the use of Entonox® and be assessed as competent in its administration, including its uses, contraindications and side effects.
- Registered Nurses must complete a Safe Conscious Sedation Competency (Entonox).
- Clinical support workers (CSW) who are involved in supporting patients during Entonox® administration must receive appropriate training as included in the CSW competency package.
Management of Entonox®

Assessment
- Assess patient to ensure no contraindications for Entonox®.
- Assess patient’s level of understanding and ability to self-administer Entonox®.
- Explain procedure and use of Entonox®.
- Gain consent, verbal or written, document in patient medical record.
- Baseline O₂ Saturations, Respiratory rate, Heart rate and Blood pressure

Administration
- Entonox® must be prescribed by a doctor or non-medical prescriber on a drug chart.
- Show the equipment to the patient and ask patient to select to use the mouthpiece or facemask. If the patient chooses to use the mask, explain that they should hold it over their mouth and nose, maintaining an airtight seal, and that they should breathe normally. If the patient chooses to use the mouthpiece, explain that they should hold the mouthpiece between their teeth and that they should breathe through their mouth only.
- Explain the procedure to be carried out and how Entonox® will be used, including information regarding side effects.
- Explain that only the patient should apply and hold the apparatus in position.
- Encourage the patient to practice the technique of Entonox® inhalation, by self-demand, before the commencement of the procedure.
- Allow the patient to practice using the apparatus for at least 30 seconds, ideally 1-2 minutes before commencing any painful procedure.
- Encourage the patient to breathe normally throughout the procedure and to inform staff if they experience pain. If the patient hyperventilates they should be encouraged to exhale slowly.
- If the patient experiences any Entonox® related side effects reassure the patient and cease inhalation until the side effects have worn off and the sensation of pain starts to return.

Monitoring
- Continually assess the patient during the procedure, check if he/she is comfortable with the Entonox® equipment and if experiencing any pain.
- Check for drowsiness/nausea. If the patient drops the mask/mouthpiece remember that the effects of Entonox® wear off quite quickly and the patient may need to use the equipment again.
- According to OUH policy there is no mandatory monitoring required during mild sedation with Entonox®. It is advised that pulse oximetry is used during Entonox® administration and until the patient has recovered from the sedation.
- Facilities for non-invasive blood pressure monitoring and ECG must be available.

Post sedation monitoring and Discharge criteria
- Inform the patient not to walk around unaided until dizziness or disorientation has subsided
• Observe the patient until the effects of the gas have worn off and they have returned to their normal mental state. Following this, patients should remain in the department for 30 minutes.
• Patients may drive themselves home if they feel competent to do so.
• Document the use of Entonox® and its effectiveness in the patient medical record.

Equipment
• Check equipment is in good working order before each use and that there is sufficient gas in the cylinder.
• An Entonox® cylinder; white in colour with blue and white shoulders. "Entonox" is clearly written on the side of the cylinder.
• Demand valve, inhalation tubing, individual patient filter and either a mask or individual patient mouthpiece, and is stored in the Day Treatment Unit. The demand valve ensures that the gas does not flow unless a negative pressure is achieved.
• Entonox® cylinders are ordered from the porters.
• Departmental resuscitation equipment should be available.

Health and Safety
• Entonox® cylinders must be stored in accordance with the BOC data information sheet in the Day Treatment Unit ‘Drug preparation room’.
• Entonox® is excreted unaltered via the patient’s breath so administration must take place in a well ventilated area to prevent others inhaling the Entonox®. Ventilation may be provided by air conditioning or an open window.

References/Resources
• BOC Medical Gas Data Sheet (2011)
• Safe Sedation by Non-Anaesthetists (2012) Oxford University Hospitals NHS Trust
• The supply/administration of Entonox® to manage the pain of intermittent procedures during medical or surgical care (2011) Salford Royal NHS Foundation Trust.
• Administration of Entonox®. Salisbury NHS Foundation Trust.

Author: Helen Moxey, RN, DTU Practise development nurse (2014)
Level 3 Moderate sedation: Midazolam

Introduction
Midazolam is a drug which can be used for intravenous sedation and its use is governed by the OUH Trust ‘Safe Sedation for non-Anaesthetists’ policy (2012). All staff performing BMB and lumbar procedures under sedation or administering sedation for BMB, Lumbar puncture, Line insertion should be familiar with the contents of the Trust policy and local guidelines. Midazolam is only to used where patients have failed to manage under level 1 and level 2 of the analgesia/conscious sedation cascade. The pharmacy drug monograph details specific drug information.

Description
1. Training requirements
   1.1. All staff must be trained in hospital life support; all staff must be familiar with the OUH Trust resuscitation policies and local procedures.
   1.2. When patients are receiving moderate sedation a member of staff with Advanced Life Support/Intermediate Life Support certification or have attended Trust advanced life support update and refresher training should be present in the clinical area.
   1.3. Nursing staff should be competent to manage IV access and administer intravenous medication according to OUH policy. They will have undertaken the Safe Conscious Sedation Competency (Midazolam) and be competent to monitor conscious sedation patients.
   1.4. Clinical staff performing BMB/Lumbar punctures (LP) and/or sedation will be trained and assessed as competent.

2. Booking of the outpatient
   2.1. The patient should be booked into an appointment for a BMB/LP with the day treatment unit staff. The last sedation appointment is 1500.

3. Assessment of the patient for sedation
   3.1. The requirement for midazolam sedation should be discussed with patients for whom BMB/LP is planned prior to the day of the procedure, where they have failed to tolerate the procedure with level 1 and 2 interventions. Patients should understand that the intention of the sedative is to decrease the discomfort of a BMB/LP procedure and that sedation to the point of unconsciousness is neither intended nor desirable.
   3.2. Suitability for intravenous sedation should be assessed prior to the procedure. The following are contraindications to intravenous sedation:
      • Airway compromise or sleep apnoea
      • Moderate to severe pulmonary disease
      • Moderate to severe cardiovascular disease
      • Previous significant reactions to sedation, general anaesthesia or benzodiazepines
   3.3 Intravenous sedation should be used with caution in:
      • Patients over the age of 60.
      • Patients taking protease inhibitors, azole anti-fungals, macrolide antibiotics, diltiazem and verapamil, all of which can prolong sedation.
3.4 A pre-procedure checklist is available as an appendix to this guideline copied from the Trust guideline “Safe Sedation for Non-Anaesthetists”

3.5 For an emergency procedure in patients who have not been fasted the urgency of the procedure must be weighed against the risk of aspiration and should be discussed with the consultant in charge.

4. Preparation of the patient for sedation

   4.1. The patient should have fasted for a minimum period of 6 hours for solid food and milk; and 2 hours for clear fluids prior to receiving intravenous sedation, as per current OUH Trust policy.

   4.2. Outpatients should be advised that they should not drive or operate machinery for the remainder of the day following sedation. They should be accompanied by a relative or friend who should escort them home following the procedure.

   4.3. It is not necessary to have written consent for sedation itself, as process of consent is most important. This should include discussion of the risks of cardiovascular and respiratory suppression. Consent should be documented in the patient medical record.

   4.4. The patient should be assessed as fit for intravenous sedation by the doctor performing the procedure.

   4.5. A wristband should be in situ.

5. Preparation of the environment.

   5.1. Sedation should only be administered in a safe appropriate environment with working bedside oxygen and suction. The resuscitation trolley must be available, as must an emergency call bell system.

   5.2. Equipment for the monitoring of patient blood pressure, continuous respiratory rate and oxygen saturations will be used. Electrocardiogram will be available as required.

6. Care of the conscious sedated patient.

   6.1. IV access will be established as per Trust guidelines. If the patient has a central line, this may be used.

   6.2. A sedated patient should never be left unattended. The IV sedation provider will remain in the area/room during the procedure. The prescribing doctor should remain in the area/room while the patient is receiving IV sedation.

   6.3. The operator carrying out the procedure cannot also be the person responsible for monitoring the patient.

   6.4. The individual responsible for administering intravenous sedation should have no other responsibilities during the case other than to monitor the patient and administer IV conscious sedation as prescribed.

   6.5. Baseline observations of pulse rate, respiratory rate, blood pressure and oxygen saturations should be recorded using the OUH Trust Track and Trigger observation chart. The patient should not be sedated if systolic BP is less than 90mmHg, oxygen saturations are less than 95% on air or if pulse rate is less than 50bpm or greater than 110bpm.

   6.6. Monitoring observations should be recorded every 5 to 15 mins depending on the patient’s condition.
6.7. Oxygen saturations and respiratory rate should be monitored continuously during the procedure. Supplemental oxygen should be given if saturations fall below 95% on air.

6.8. If the procedure lasts more than 15 minutes blood pressure should then be monitored until the conclusion of the procedure.

7. **Dosing and administration of Midazolam.**

7.1. Midazolam comes pre-diluted in vials at a concentration of 1mg/ml. All syringes will be labelled. For patients over the age of 60, or for debilitated or chronically ill patients, not more than 5mg of Midazolam should be drawn up pre-procedure. For other patients up to 7.5mg of Midazolam may be drawn up pre-procedure but see section 7.4 below.

7.2. Flumazenil (the benzodiazepine antagonist used for reversal of sedation) should be available at the bedside but need not be drawn up pre-procedure.

7.3. For fit patients under the age of 60 an initial dose of 1-2.5 mg Midazolam should be given. Further doses can be given by titration in 1mg boluses. Boluses should not be given more frequently than 1mg per minute. A total dose of more than 5mg is usually not required, however it is accepted that some patients will require higher doses.

7.4. Higher doses must be given by slow titration and close observation of conscious level should be maintained. Doses above 10mg should not be routinely used. If in doubt please discuss with your consultant.

7.5. For patients over the age of 60, or for debilitated or chronically ill patients, an initial dose of 0.5-1mg should be given and titration should be in 0.5-1mg boluses. A total dose of greater than 3.5mg is not usually required.

7.6. Reversal of sedation with Flumazenil should not be routinely performed. Flumazenil is indicated if respiratory or cardiovascular compromise occurs during sedation.

7.7. If Flumazenil is used then staff should be aware that Flumazenil has a shorter half life than Midazolam and patients may suffer a further reduction in conscious level despite an initial response to Flumazenil.

7.8. If Flumazenil reversal of sedation is required then the BMB/LP procedure should be abandoned and a Datix submitted.

8. **Recovery post sedation.**

8.1. Recovery should occur in the clinical area where the sedation was performed with the responsible staff member remaining within the area until the patient is sufficiently recovered to be discharged.

8.2. Oxygen saturations and respiratory rate should be monitored until the patient is able to maintain saturations above 95% on air and the effects of the sedation have worn off.

8.3. Conscious level should be monitored until the patient is able to respond to verbal stimuli.

8.4. For inpatients normal ward nursing may resume once saturations are above 95% on air and the patient is able to respond to verbal stimuli (provided Flumazenil reversal has not been used).
8.5. Outpatients may be discharged once the above conditions have been met and once they are able to walk safely. They should be accompanied home by a friend or relative.

8.6. Patients who have Flumazenil reversal of sedation should be observed for 2 hours prior to discharge to ensure re-sedation does not occur.

8.7. A summary of the procedure, the conscious sedation and any issues including the use of Flumazenil, will be documented in the medical notes.

9. Audit

9.1. Adherence to this policy should be the subject of regular audit.

9.2. The use of Flumazenil to reverse excessive sedation should be included as an outcome measure in any audit conducted.

Documents

- Midazolam. - OUH Trust Pharmacy drug monograph
- Oxford University Hospitals NHS Trust, Safe Sedation by Non-Anaesthetists (2012)
- Clinical Haematology Competency: N.29f Safe Conscious sedation (Midazolam)

Authors: Dr Patrick Medd, Specialist Haematology Registrar. Dr Tim Littlewood, Consultant Haematologist (2010).

Circulation: NSSG website.

Review

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Appendix 1.

Local Issues with Midazolam sedation
1. Not all patients are appropriate for midazolam sedation according to OUH Trust guidelines (e.g. those over 60, with cardiac, renal or hepatic dysfunction or sleep apnoea etc.)
2. Bone marrows with sedation take longer and require more nursing input during the procedure
3. ALS/ILS/Trust update refresher course is a necessary requirement for the sedationist or there has to be someone in the immediate vicinity. This may not be current for SpR’s
4. Post-procedure monitoring - it is, given the nature of the Day Unit, difficult to always maintain one-to-one nursing ratio for patients who are deeply sedated after bone marrow procedures

Potential Benefits of Entonox® in Bone marrows
1. Provides a halfway-house between local anaesthetic only and midazolam sedation for anxious patients
2. Less nursing time required
3. Quicker recovery without potential for overdose/need for reversal
4. Potential for the patients to be managed on the routine list.

Summary of the evidence for:
1. Entonox® use in bone marrow procedures
2. Entonox® vs Midazolam use in bone marrow procedures
The use of Entonox® in bone marrow procedures has been subject to limited research, including randomised controlled trials and one systematic review. There is however no clear conclusion as to its place. A systematic review, written from a nursing perspective, states that "evidence is inconclusive and provides little guidance for practice" (Watmough and Flynn, 2011).

Entonox® and local anaesthetic was compared to local anaesthetic alone in 136 patients undergoing bone marrows and this study showed a trend towards lower pain scores but this was not significant (Steedman et al, 2006). Importantly there were no adverse events in the Entonox® arm. Entonox® was used in a randomised controlled trial (Johnson et al, 2008) versus placebo (oxygen) to assess its effects in bone marrow examination and was found to have significantly lower pain scores in men but not women (p=0.069). Again this study is limited by low numbers (48) and also found men used more Entonox than women.

In a comparison study of a small number of patients (16) who had previously had a bone marrow with IV midazolam had a further bone marrow with Entonox® (Gudgin et al, 2008). In this small study 15/16 of patients stated that Entonox® was equivalent or superior to midazolam. Again no adverse events with Entonox® were noted.

One randomised controlled trial directly compared iv midazolam to Entonox® in 46 patients (Chakupurakal et al 2008). In this study 46 patients were randomised either to receive 2-10mg midazolam as tolerated (24 patients) or Entonox® (22 patients) and were given pain questionnaires 15 minutes and 24 hours after the procedure. There

This is a controlled document and therefore must not be changed
was a significant difference between patients' pain scores at both points and their experience of the procedure. Respiratory depression (oxygen saturation <90%) occurred in 4/22 of cases who had midazolam (none in the Entonox® arm) and flumazenil was administered in 10/22 of cases (3 for oxygen desaturation and 7 for prolonged sedation). This is certainly higher than we are used to in day unit (we have not had to give flumazenil over the past 2 years).

In conclusion, the use of Entonox® in bone marrow procedures has been investigated using trials of small numbers of patients and caution must be used in interpreting the results. Entonox® is, however, a safe and well-tolerated intervention with some units discharging patients 15 minutes after the procedure.

The evidence comparing Entonox® to midazolam in patients who require/request sedation is even sparser and somewhat conflicting. One very small study (Gudgin et al, 2008) suggests that Entonox® may be a reasonable alternative to patients who have previously had iv midazolam sedation which would reduce workload. It is unclear if Midazolam is more successful at reducing pain but comes with a small but significant risk of respiratory depression and the need for longer monitoring and specific equipment and training, i.e. a higher burden on staff.

References

Author: Dr David Bruce, Haematology SpR, August 2014.

Appendix 2.
Nursing competencies are held on the Haematology NSSG website.