



Health
South Western Sydney
Local Health Network

Drug Guideline Title: Thiopentone

Summary:

Thiopentone sodium is a short acting barbiturate with sedative, hypnotic, anaesthetic and anticonvulsant properties.

Approved by: ICU Director

Publication (Issue) Date: June 2013

Next Review Date: June 2016

Replaces Existing Drug Guideline: Thiopentone 2004.

Previous Review Dates: 2002, 2004

1. Introduction:

The risk addressed by this policy:

Patient Safety

The Aims / Expected Outcome of this policy:

Thiopentone should be administered safely and appropriately without any adverse side effects

Related Policies

- C3.00 Drug prescribing
- C3.01 Drug administration
- C3.012 Administration of IV medications

2. Policy Statement:

- All care provided within Liverpool Hospital will be in accordance with infection control, manual handling and minimisation and management of aggression guidelines.
- Medications are to be prescribed and signed by a medical officer/authorised nurse practitioner (NP) unless required during an emergency.
- All drugs administered during an emergency (under the direction of a medical officer/authorised nurse practitioner) are to be documented during the event, then prescribed and signed following the event.
- Medications are to be given at the time prescribed (as close to the time as is possible when multiple drugs require 'same time' administration and, when the nurse is caring for more than one patient, recognition is given to a possible short delay to administration – antibiotics and other lifesaving drugs are to be prioritised) and are to be signed by the administering nurse.
- Parenteral medication prescriptions and the drug are to be checked with a second registered or endorsed enrolled nurse prior to administration. The "rights of drug administration" must be followed: right: patient, drug, dose, route, administration, time, reason for the drug, documentation, education and evaluation/outcome.

- Adverse drug reactions are to be documented and reported to a medical officer.
- Medication errors are to be reported using the hospital electronic reporting system: IIMS.
- Guidelines are for adult patients unless otherwise stated.
- Thiopentone may only be given via a secure intravenous line.
- Potassium levels must be closely monitored during therapy with barbiturates and for 72 hours post cessation as hypokalemia is frequently associated with induction of thiopentone barbiturate coma and hyperkalemia is associated with abrupt cessation of thiopentone barbiturate coma⁶.

3. Principles / Guidelines

Actions^{1,2,3,4}

Thiopentone is a short acting barbiturate, CNS depressant that induces hypnosis and anesthesia, but not analgesia. Hypnosis occurs within 30 to 40 seconds of an IV single induction dose. Consciousness returns after 20 to 30 minutes. Recovery after a small dose is rapid, with some somnolence and retrograde amnesia. It has sedative, hypnotic and anticonvulsant properties.

- Thiopentone may act by enhancing responses to gamma-aminobutyric acid (GABA), diminishing glutamate responses, and directly depressing excitability by increasing membrane conductance, thereby producing a net decrease in neuronal excitability to provide anesthetic action.
- As sedative hypnotics, the barbiturates appear to act at the level of the thalamus where they inhibit ascending conduction in the reticular formation, thus interfering with the transmission of impulses to the cortex.
- It reduces intracranial pressure, cerebral metabolic rate and oxygen consumption.
- Promotes or induces hypothermia.
- It has a dose related depression of respiration and respiratory and laryngeal reflexes.
- Depresses the myocardium and decreases cardiac output as plasma levels rise.
- It may decrease lower esophageal sphincter tone and impair gastrointestinal motility.
- It will lead to prolonged anesthesia due to storage of the drug in fatty tissue with repeated IV doses or infusion. Concentrations of 6 to 12 times plasma levels occur with slow release, prolonging anesthesia. The $\frac{1}{2}$ life of the elimination phase after a single IV dose is 3 - 12 hours.

Indications^{1,2,3,4}

- Anesthetic agent for brief surgical procedures.
- Induction of anesthesia prior to the administration of other anesthetic agents.
- Refractory status epilepticus and non-convulsive status epilepticus.
- Supplementary agent in the management of intractable raised intracranial pressure.

Contraindications^{1,2,3,4}

- Known hypersensitivity to thiopentone and other barbiturates.
- Status asthmaticus or when adequate airway cannot be maintained.
- Variegated or acute intermittent porphyria.
- Constrictive pericarditis, severe cardiovascular disease.
- Uncorrected hypovolaemia, hypotension or shock is a relative contraindication.
- Addison's disease, myxoedema, myasthenia gravis.
- Hepatic or renal dysfunction.
- Severe anaemia.

Precautions^{1,2,3,4}

- Causes hypotension – use with caution in hemodynamically unstable patients.
- Thiopentone should only be administered with resuscitative, endotracheal intubation equipment and oxygen readily available as it causes respiratory depression.

- Use with caution in patients with asthma or COPD as it may cause laryngospasm or bronchospasm.
- May cause paradoxical stimulatory response, including agitation and hyperactivity, particularly in patients with acute pain.
- Avoid extravasation as it may cause tissue necrosis.
- Use with caution in the following conditions as it can potentiate the hypnotic effect. The conditions include Addison's disease, anemia, aneurysms, hepatic impairment, myasthenia gravis, myxedema, dystrophia myotonica and renal impairment.

Significant Interactions^{1,2,3,4}

- Benzodiazepines have a synergistic action when used with thiopentone.
- Ethanol increases the CNS depressant effects of thiopentone and ethanol and diazepam increase its hypotensive effects.
- Rapid or high doses of ketamine will increase the incidence of hypotension and respiratory depression.
- Magnesium sulphate IV increases CNS depressant effects.
- Phenothiazines potentiate hypotensive and CNS excitatory effects.
- Aminophylline antagonizes thiopentone.
- Thiopentone is incompatible in solution with many drugs – flush well and use a dedicated line for infusions.

Adverse Effects^{1,2,3,4}

- Hypotension, myocardial depression reduced cardiac output
- Respiratory depression, apnea.
- Bronchospasm, laryngospasm.
- Hypersensitivity reactions – sneezing, urticaria.
- Tissue necrosis with extravasation.
- Shivering (increased sensitivity to cold) and hypothermia.
- Excitatory phenomena - involuntary muscle movements, coughing, hiccups have been reported.
- Potassium disturbances with infusion– measure levels regularly. It causes hypokalemia on maintenance infusion and rebound potentially life-threatening hyperkalemia on cessation of therapy.

Presentation

Thiopentone 500mg ampoule (powder) with 20mL sterile water ampoule for reconstitution

Administration Guidelines^{1,2,3,4}

- Thiopentone is administered by the intravenous route only.
- Patients receiving thiopentone for the management of raised intracranial pressure should have continuous EEG monitoring where available, as the dose is titrated to produce a burst-suppression pattern.

Induction of anesthesia for intubation: via secure IV line

Dilute 500mg thiopentone with 20mL sterile water to arrive at a concentration of 25mg/ml Dilute 2 grams of thiopentone with 50mL sterile water for injection to give a concentration of 40mg/ml.

- Bolus dose of 1-3mg/kg (eg: For a 70kg patient this would be 70mg – 210mg = 3-8ml)
- Flush the line well, post administration.

Monitor blood pressure and treat hypotension with a fluid bolus and/or vasoconstrictor.

Management of Raised Intracranial Pressure: via secure Central Venous access

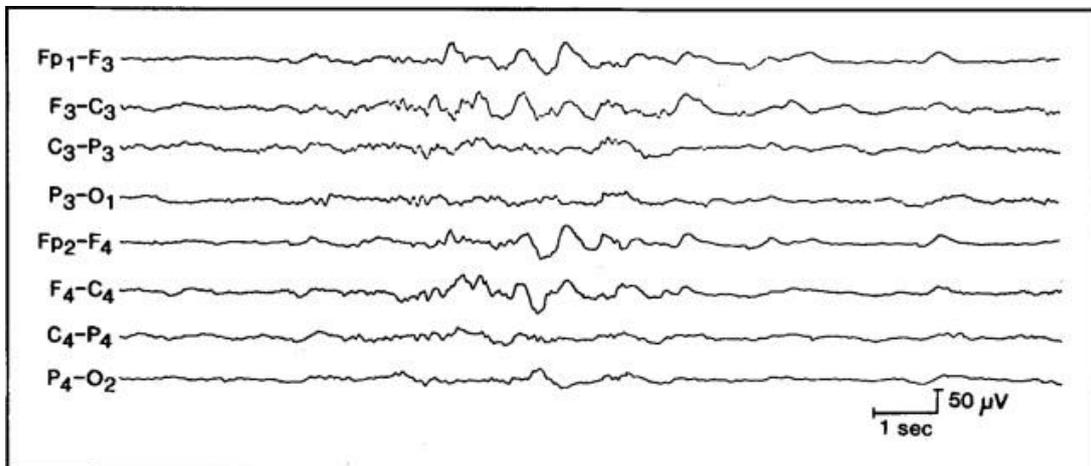
Dilute 2 grams of thiopentone with 50mL sterile water for injection to give a concentration of 40mg/mL.

1. Loading Dose (2gm /50ml = 40mg/ml):

- Administer a loading dose of 5-20mg/kg of thiopentone over 1 hour. (eg: for a 70 kg patient = 350mg to 1.4gm loading dose = 8ml to 35ml).

2. Infusion to achieve and maintain burst suppression (2gm /50ml = 40mg/ml):

- Commence infusion at 1 – 4 mg/kg/hr. (eg: for a 70kg patient this will be 2-7ml/hr)
- A smaller or greater volume of drug may be required due to individual response and differences in fat deposit uptake of the drug.
- When EEG monitoring is utilised, a burst: suppression ratio is prescribed. The aim is generally 1 to 2 seconds of bursts and 5 to 10 seconds of suppression on the EEG. The initial dose of infusion may be reduced once burst suppression is achieved, and maintained at a rate to achieve the desired burst suppression.
- Burst suppression appears as segments of activity surrounded by flat line (suppression), indicating absence of brain waves (resting of the cell) with allowance for some electrical breakthrough.



Note: It is not recommended to continue thiopentone for raised intracranial pressure beyond 4 days.

Management of convulsive states: via secure Central Venous access

Bolus Dose: Dilute 500mg thiopentone with 20mL sterile water to arrive at a concentration of 25mg/mL

- Dose for treatment of convulsive state is 75mg – 125mg (3-5ml of the 25mg/ml solution) given over 1 hour.

Infusion to cease seizure activity: Dilute 2 grams of thiopentone with 50mL sterile water for injection to give a concentration of 40mg/ml.

- Commence at 1mg/kg/hr.
- Titrate the infusion of thiopentone to control EEG monitored seizure activity. EEG pattern should change from epileptiform patterns to either burst suppression or electrocerebral inactivity.

Clinical Considerations

- Patients receiving thiopentone infusions are to receive vigilant attention to all aspects of infection control due to their increased susceptibility to opportunistic infection.
- Thiopentone does not have analgesic properties.
- Serum levels are required to assess for a return of possible consciousness /responsiveness. A zero level is required before responsiveness is likely.

- For patients receiving large doses of thiopentone, concomitant use of paracetamol must be regulated and liver enzymes assessed regularly.
- Potassium levels are known to fall with maintenance thiopentone infusions. Hypokalaemia is acceptable and any potassium replacement must be with extreme caution because of the risks of rebound hyperkalaemia on cessation⁶.
- Use caution when weaning or ceasing infusions as rebound hyperkalaemia may result. Always monitor potassium levels regularly during weaning and for 72 hours post cessation of drug therapy⁶.
- EEG monitoring with the bed side monitor should be set up. The EEG is utilized for titrating the infusion dose to achieve the prescribed burst suppression pattern. Formal EEG should also be done.

4. Performance Measures

All incidents are documented using the hospital electronic reporting system: IIMS and managed appropriately by the NUM and staff as directed.

5. References / Links

1. MIMS Online, CIAP: NSW Health Department, Copyright MIMS Australia Pty Ltd. August 2012. <http://www.use.hcn.com.au>
2. The Society of Hospital Pharmacists of Australia 2011, The Australian Injectable Drugs Handbook, 5th Edition, SHPA publications, Australia.
3. eTherapeutic Guidelines: CIAP 2012, <http://www.tg.org.au/>
4. UpToDate, 2013. Thiopental: Drug Information, <http://www.uptodate.com> , viewed 11th June 2013.
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6. Ng, S.Y., Chin, K.J., & Kwek, T.K. 2011. Dyskalemia associated with thiopentone barbiturate coma for refractory intracranial hypertension: a case series, *Intensive Care Medicine*, 37: 1285 – 1289.
7. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, Tesoro EP and Elswick RK. 2002. The Richmond agitation-sedation scale. Validity and reliability in adult intensive care unit patients. *American Journal of Respiratory and Critical Care Medicine* 166:1338-1344.

Author: CNC – ICU (S. Shunker)

Reviewers: ICU – CNC, CNE, NM, NUM, Staff Specialists, CNS 's, Medical Director, Pharmacist

Endorsed by: A Prof M. Parr, Director ICU.

APPENDIX 1: Richmond Agitation-Sedation ScoreInstructions

- Obtain a sedation score goal at handover/ward round; document this in the health care record.
- Assess a sedation score every 2-4 hours and as clinically indicated. Conduct a sedation score even if there is no apparent drug in use that would contribute to sedation.
- A 'sedation – vacation' from sedative drugs must be prescribed when the sedation score is deemed 'moderate sedation: '- 3', and this degree of sedation is not the goal of therapy.

Assessment

The use of a sedative aims to:

- Enable the patient to cooperate with ventilation and treatments, and
- Produce a desired amnesia to the Intensive Care environment.
- Document which drugs the patient is taking to produce a sedative effect

Richmond Agitation-Sedation Score (RASS) ⁷

Score	Term	Description	Stimulus
+ 4	Combative	Overtly combative, violent, immediate danger to self, staff, others	-
+ 3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	-
+ 2	Agitated	Frequent non-purposeful movement, fights ventilator	-
+ 1	Restless	Anxious but movements are not aggressive/vigorous	-
0	Alert and calm		-
- 1	Drowsy	Not fully alert, has sustained awakening (eye-opening/eye contact) to voice (≥ 10 seconds)	Verbal
- 2	Light sedation	Briefly awakens with eye contact to voice (< 10 seconds)	Verbal
- 3	Moderate sedation	Movement or eye opening to voice (but no eye contact)	Verbal
- 4	Deep sedation	No response to voice but movement or eye opening to physical stimulation	Physical
- 5	Unroutable	No response to voice or physical stimulation	Physical

Procedure

- Observe patient
 - Patient is alert, restless or agitated (score 0 to + 4)
- If not alert, state patient's name and say to open eyes and look at speaker
 - Patient awakens with sustained eye opening and eye contact (score - 1)
 - Patient awakens with eye opening and eye contact, but not sustained (score - 2)
 - Patient has any movement in response to voice but no eye contact (score - 3)
- When no response to verbal stimulation, physically stimulate the patient by shaking shoulder and / or using the trapezius pinch or applying supra-orbital pressure, as appropriate
 - Patient has any movement to physical stimulation (score - 4)
 - Patient has no response to any stimulation (score - 5)

