

TOPIC: INTRAVENOUS ANAESTHETIC AGENTS/INDUCTION AGENTS

WHAT ARE IV INDUCTION AGENTS

- These are the drugs when given intravenously in an appropriate dose ,cause rapid loss of consciousness
- One arm brain circulation

They are used

- To induce anesthesia prior to other drugs being given to maintain anesthesia
- To maintain anesthesia for longer procedures by intravenous infusion
- To provide sedation

CLASSIFICATION OF IV INDUCTION AGENTS:

Barbiturates

- Thiopentone
- Methohexitone

Non barbiturates

- Propofol (2,6 di iso propyl phenol)
- Etomidate (Imidazole derivative)
- Ketamine (Phencyclidine derivative)
- Benzodiazepines

WHAT ARE BARBITURATES

- Sedative and sleep inducing drugs derived from barbituric acid
- Barbiturate is a drug that acts as central nervous system depressant
- Produce wide spectrum of effects from mild sedation to total anaesthesia

SODIUM THIOFENTONE(STP) :

- First intravenous anaesthetic agent
- 1st synthesized in 1932 by Vonwiler & Tabern but 1st used clinically by Ralph Waters & John Lundy in 1934.
- It is an ultrashort acting barbiturate

- Sulfur analogue of pentobarbitone
- Chemically sodium ethyl thiobarbiturate

Uses of Sodium thiopentone:

- Induction & maintenance of anesthesia(3-6mg/kg of STP)
- To decrease raised ICP(1-4mg/kg of STP)
- anticonvulsants responds to STP(0.5-2mg/kg)
- Focal Cerebral protect
- For Narco analysis –STP can be used for Lie detector test
- Electro convulsive therapy (Methohexitone is the agent of choice)

Physicochemical properties:

- It comes as 2.5% & 5% vial of yellow amorphous powder
- Prepared & kept in the atmosphere of N₂ to prevent the formation of free acid by CO₂ in the atmosphere
- 6% anhydrous sod carbonate is added
- Reconstituted with N.S
- STP solutions with strength >2.5% should not be used.
- PH of STP 2.5% is 10.4 highly alkaline

Mechanism of action:

It mediates their action through GABA receptors such as (GABA-A sub type)

Increasing the membrane conductance to chloride ions causing hyperpolarisation of membrane.

ANAESTHETIC PROPERTIES AND PHARMACOKINETICS:

- Unconsciousness is produced in one arm brain circulation i.e in 15 sec
- Consciousness is regained after 15 to 20 minutes because of redistribution
- At induction it causes mild hypokalemia
- Elimination t_{1/2} 10.4hrs(10-12hrs)
- Pediatric patients require more dose than adults which in turn require more dose than elderly & males requiring more dose than females
- Metabolized in liver & metabolic products excreted via kidney
- Conditions where less dose of STP is required

Malnutrition

Burns pt

Shock

Advanced malignancy

Uremia

Pregnancy

Dose of STP for various conditions:

- IV induction 2.5% soln. (3-6mg/kg)
- Sedation 2.5% soln.(0.5-1.5mg/kg)
- Raised ICP 2.5% soln(1-4mg/kg)

Systemic effects of STP:

CNS

- Unconsciousness produced in 15s, max. depth achieved in 60s
- Consciousness is regained in 15-20min
- Agent of choice for cerebral protection, effective only in focal ischemia & not in global ischemia
- Decreases CMR, CMO₂ , CBF & ICT
- Facilitates CSF absorption
- Anticonvulsant action
- It increases stage2 & decreases stage3,4 & REM of sleep cycle
- No analgesic effect & at low doses has antanalgesic effect

CVS

- Causes hypotension due to suppression of vasomotor center in medulla
- Also acts as direct myocardial depressant
- Tachycardia is probably due to central vagolytic effect
- In normal subjects both tachycardia & increased myocardial contractility as a result of Baroreceptor reflexes maintains cardiac output.

Respiratory system

- Dose related respiratory depression

- At inadequate depth of anesthesia if a painful stimulus is applied patient may go into laryngospasm & bronchospasm (Rx IPPV with small dose of scoline)
- Transient apnea usually occurs & requires no treatment

Immuno suppression

- Long term administration of high doses of STP is associated with an increased incidence of nosocomial infections

Kidneys

- STP reduces urine output by causing hypotension and by increasing ADH release

EYE

- Decreases the IOT(Intra ocular tension)
- STP relaxes the LES(Lower Esophageal sphincter) and increases the risk of aspiration
- ANTI THYROID ACTIVITY
- NOT A MUSCLE RELAXANT

General complications:

1. Laryngospasm & bronchospasm
2. Cardiovascular depression
3. Respiratory depression
4. Hiccups
5. Hypersensitivity reactions
6. Onion / garlic taste
7. Postop disorientation

Local complications:

1. **Perivenous / subcutaneous injection:** It occurs when STP gets accidentally leaked into extravascular compartment & due to its high alkalinity causes tissue necrosis & ulceration.

Treatment

Preventive:

Not to use >2.5% soln.

Inject very slowly

Immediately stop further injection if pt c/o any pain

Curative: 10ml of 1% lignocaine with 100 units of hyaluronidase is to be injected in that area

2. Intra- arterial injection

Easily preventable complication but if not diagnosed at time can lead to gangrene & loss of limb complication is commonly seen when STP is injected in antecubital vein because in 10% cases brachial a divides above elbow giving a very superficial abnormal ulnar which lies just deep to antecubital vein.

Symptomatology: severe burning pain down the injection site, pallor cyanosis, edema & gangrene of limb.

Pathophysiology: STP forms micro precipitates in acidic ph of arterial blood which blocks microcirculation. It also causes endothelial damage. Both these processes produce vasospasm leading to ischemia & gangrene of limb.

Rx

Preventive:

Curative: stop further injection

Leave the needle at site

Inject 500u of heparin

Inject Papaverine 40-80mg in 10-20ml of N.S

Tolazoline & phenoxybenzamine are other vasodilators

10ml of 1% xylocaine can be injected

Brachial plexus / stellate ganglion block

Oral anticoagulants to be used for another 2wks

Defer the elective surgery

3. Thrombophlebitis: Due to deposition of bicarbonate crystals

4. Injury to nerve

CONTRAINDICATIONS OF STP:

Absolute

- H/O previous anaphylaxis to STP
- Respiratory obstruction

Relative

1. Hypotension & shock
2. Fixed cardiac output lesions
3. Asthmatics

4. Severe hepatic and renal disease

Methohexitone:

1. Available as 500mg powder
2. Soln of 1% with ph of 11.1
3. 2-3 times more potent than STP
4. Dose 1.5mg/kg iv in adults, 1mg/kg in pediatric pts. Can be given IM in a dose of 6mg/kg to produce hypnosis in children. Can also be given rectally in a dose of 25mg/kg.
5. It is the agent of choice for ECT.
6. Histamine release is much less than STP so preferred barbiturate for asthma pts.

Rest of the pharmacology is similar to STP.

NON BARBITURATES

PROPOFOL:

- Commonly used drug
- Mechanism of action is similar to STP

PHYSICAL AND CHEMICAL PROPERTIES:

- Chemically it is 2,6 di isopropyl phenol
- Available as white milky solution in 1% & 2% concentration
- Oil based containing
 - a. Egg lecithin
 - b. Soya bean oil
 - c. Glycerol
- Injection is painful
- Containing antimicrobial agents like sodium meta-bisulphate or disodium edetate

ANAESTHETIC PROPERTIES:

- Unconsciousness is produced in one arm brain circulation in 15 seconds
- Consciousness is produced after 2 – 8 minutes due to redistribution.
- Half life 2-4 hrs
- **Dose** is 2-2.5 mg/kg BW (adults)
- 3-3.5 mg/kg BW (children's)

- Rapid and smooth recovery

- Not a muscle relaxant

METABOLISM:

- Mainly in liver but significantly (30%) extra hepatic metabolism.
- Excreted via kidneys.

SYSTEMIC EFFECTS:

CVS

- Hypotension

RESPIRATORY SYSTEM

- Apnea is higher(20-30%) than STP
- Respiratory depression is more
- Induces bronchodilation in COPD patients
- Depression of upper airway reflexes is more than STP so most preferred for surgeries done under LMA (Laryngeal Mask Airway) without muscle relaxants.

CNS

- It is also effective like STP for brain protection
- It is reliable amnestic also
- Sometimes it can produce myoclonic activities and muscle twitching

EYE

- Reduces IOP(Intra Ocular Pressure)

GIT

- Antiemetic

IMMUNOLOGIC

- Antipyretic

USES:

- Because of its early induction, early and smooth recovery and antiemetic effects it is the iv agent of choice for day care surgery
- Along with opioids(aifentanyl) propofol is the agent of choice of T.I.V.A(Total Intravenous Anaesthesia)

- Propofol infusion is used to produce sedation in ICU
- Because of its antiemetic property, it is most preferred for surgeries associated with incidence of nausea and vomiting.

CONTRAINDICATIONS:

ABSOLUTE

- Airway obstruction
- Children's less than 3 years

RELATIVE

- Hypotension

DIS-ADVANTAGES:

1. Apnea is more profound and longer
2. Hypotension is more severe
3. Injection is painful
4. Allergic reactions
5. Myoclonic activity can be produced
6. Propofol infusion syndrome

It is very rare but is a lethal complication seen if propofol is continued for more than 48 hours. It is more common in children's. It occurs because of failure free fatty acid metabolism. It is associated with metabolic acidosis, acute cardiac failure, lipaemia

ETOMIDATE

- Chemically it is Imidazole derivative
- It also acts through GABA receptors
- Dose 0.3 mg/kg Bw

ADVANTAGES:

- It is more cardiovascular stable agent among all IV agents
- Minimal respiratory depression
- No histamine release

SIDE EFFECTS:

- Nausea and vomiting incidence is 40% which is higher among all IV agents
- Injection is painful
- High incidence of Thrombophlebitis.
- Hiccups are common
- No analgesia

USES:

- IV anaesthetic of choice for aneurysm surgery and patients with cardiac disease.

KETAMINE

- First used in humans by domino and corsen in 1965
- Available as solution of 10 mg/ml and 50 mg/ml concentration
- Ph is acidic 3.5-5.5 highly lipid soluble
- Contains preservative benzethonium chloride
- It produces dissociative anaesthesia.
- Onset of action is 30-60 seconds
- Consciousness is regained in 15-20 minutes
- Half life is 2-3 hours
- Strong analgesic
- Metabolised in liver and products excreted in urine
- Not a muscle relaxant

SITE OF ACTION:

- Primary site of action is thalamo neocortical projection. ketamine inhibits cortex (unconsciousness) and thalamus (analgesia) and stimulates limbic system (emergency delirium and hallucinations).
- It also acts on medullary reticular formation and spinal cord.

MECHANISM OF ACTION

- Its effect is by inhibiting N methyl D aspartate (NMDA) receptors.

SYSTEMIC EFFECT

CNS

- Increases brain oxygen consumption and metabolic rate

- ICT is highly raised
- Strong analgesia
- Emergency reactions:-

Incidence is 10-30%, less incidence in children's and old ages. Emergency reactions include illusions, extra corporeal experiences like floating out of the body, excitement, confusion, fear.

- Hallucinations:-

Both auditory and visual (mainly auditory)

Incidence is 30-40 %

Most common effect of Ketamine

CVS

Stimulates sympathetic system causing tachycardia and hypertension. So IV agent of choice for shock

RESPIRATORY SYSTEM

- it stimulates respiration but can cause respiratory depression in children's
- It is potent bronchodilator so IV agent of choice for asthmatics
- Pharyngeal and laryngeal reflexes are preserved
- Tracheo bronchial and salivary secretions are increased, these secretions can produce upper airway obstruction and laryngospasm

EYE

- Increases IOT
- Pupils dilate moderately
- Nystagmus

GIT

- Increases intra gastric pressure
- Salivary secretions are increased

DOSE

- Can be given
- IV,IM,NASAL,RECTAL,ORAL,INTRATHECALLY
- IV dose is 2-2.5 mg/kg BW
- IM dose is 5-10 mg/kg BW

ADVANTAGES AND USES

1. Induction agent of choice for
 - Asthmatics
 - Shock
 - Children's (IM)
2. Can be use as a sole agent for minor surgeries
3. Preferred agent for patients with full stomach (because pharyngeal and laryngeal reflexes are preserved)

DISADVANTAGES

- incidence of hallucinations & emergence reactions
- Increased muscle tone
- Secretions are increased which can cause Bronchospasm and laryngospasm.
- Increased myocardial oxygen demand
- All pressures like intra cranial pressure, IOP, intra gastric pressure are markedly increased.

CONTRAINDICATIONS

- Eye surgeries
- Head surgeries
- IHD(increases myocardial oxygen demand)
- Vascular aneurysm
- Hypertensive's
- Patient with psychiatric disease and drug addicts