TIVA & TCI Workshop
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ASPAAN National President
House-keeping

- PLEASE SET ALL PAGERS, MOBILE PHONES & ELECTRONIC DEVICES TO SILENT MODE.
- AMMENITIES
- EVACUATION
- ASSESSMENT AND CERTIFICATES
- INTRODUCTIONS
About your facilitator

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Session Plan

This seminar will include:

- **Session one:** The Theory of TIVA
- **Session two:** The Theory of TCI
- **Session three:** Syringe driver familiarity
- **Session four:** Simulated learning activity
TIVA (60 minutes)

At the conclusion of this session participants should be able to:

• Provide an explanation of TIVA
• Discuss the advantages, limitations and precautions with TIVA
• Discuss the considerations for PACU
What do these guys have in common?
What do these guys have in common?

• In the 17c. Christopher Wren first demonstrated the administration of Intravenous opium.
• He devised an apparatus using a pig’s bladder and a goose quill
• Upon injecting the opium into his dog, the animal was said to be “Stupefied”
• And so began the evolution of Intravenous Anaesthesia
1930’s Hexobarbital and Pentothal were introduced

1960’s Pharmacokinetic models and equations for IV infusions introduced

1980’s Computer controlled IV infusions systems introduced

1996 The first TCI system “Diprifusor” was introduced
TIVA Theory
TIVA Theory

Safety features of recognition capability

- Operates in ‘Diprifusor’ TCI mode only with tagged ‘Diprivan’ PFS – no other drugs
- Confirms ‘Diprivan’ concentration (1% or 2%) for correct infusion at requested target concentration
- Erases tag when PFS is nearly empty and prevents refilling/reuse

‘Diprifusor’ TCI Software and microprocessors
- Control unit for syringe pump when in ‘Diprifusor’ TCI mode
TIVA Theory

Today...
Today there is a society of Intravenous anaesthesia enthusiasts **The World Society of Intravenous Anaesthesia**

75 articles related to propofol/TIVA in last 5 years just in Paediatric populations.

Same number as the ten years preceding (Growing enthusiasm?)
TIVA Theory
TIVA Theory
So What is TIVA?
TIVA Theory
TIVA Theory

How is TIVA Performed?

Can be performed by manual injection
- Endoscopy
- Bronchoscopy

or by programmable mechanical syringe-drivers
- These have calculated dosing algorithms (TCI)
TIVA Theory

TIVA advantages

- Simple delivery systems
- No pollution
- Portable
- PONV
- PAED
- MH proof
- Spinal surgery (controlled hypotension)
- Neurosurgery (ICP, Cerebral metabolic protection)
- Shared airway procedures (eg. bronchoscopy)
- Cheaper?
- Less airway spasms
TIVA Theory

TIVA advantages

A meta-analysis of nausea and vomiting following maintenance of anaesthesia with propofol or inhalational agents

J. R. Sneyd, A. Carr, W. D. Byrom* and A. J. T. Bilski*

Department of Anaesthesia, Derriford Hospital, Derriford Road, Plymouth PL6 6DH, UK
* Zeneca Pharmaceuticals, Mereside, Alderley Park, Macclesfield, Cheshire, UK

70 trials (57 adult, 13 children)
Considered studies & used 3 end points: vomiting alone (n=4075); nausea alone (n=3516); N&V (n=742)

“3.5 and 5.7-fold reductions in vomiting in adults and children respectively when propofol used at induction and maintenance”
16 retinoblastoma kids 1-5 yo
All had Sevo induction
Randomised to Sevo or Propofol
<table>
<thead>
<tr>
<th>Study design</th>
<th>Population</th>
<th>Premedication</th>
<th>Analgesia</th>
<th>EA incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sevoflurane only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sevoflurane vs propofol induction/halothane maintenance</td>
<td>322 children, Age 3-12 y Day surgery or ENT surgery</td>
<td>None</td>
<td>Alfentanil, fentanyl, or regional blocks</td>
<td>Sevoflurane 25.7%, Propofol/halothane 9.4%</td>
</tr>
<tr>
<td>Sevoflurane vs sevoflurane induction, isoflurane maintenance</td>
<td>128 children, Age 1-6 y Subumbilical surgery</td>
<td>None</td>
<td>Penile, caudal, or ilioinguinal/iliohypogastric block</td>
<td>Sevoflurane 51.8%, Sevoflurane/isoflurane 32.1%</td>
</tr>
<tr>
<td>Sevoflurane only</td>
<td>68 children, Age 1-6 y Circumcision</td>
<td>Midazolam 0.5 mg/kg, or clonidine 2 or 4 μg/kg</td>
<td>Penile block and rectal paracetamol 30 mg/kg</td>
<td>Sevoflurane 60%, Clonidine 2 μg/kg 40%, 4 μg/kg 25%</td>
</tr>
<tr>
<td>Total intravenous anesthesia (TIVA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sevoflurane vs propofol TIVA</td>
<td>53 children, Age 2-3 y Mo Ambulatory surgery</td>
<td>None</td>
<td>Fentanyl 2 μg/kg or caudal block</td>
<td>Sevoflurane 23.1%, Propofol 3.7%</td>
</tr>
<tr>
<td>Sevoflurane vs propofol TIVA</td>
<td>186 children, Age 2-11 y ENT surgery</td>
<td>None</td>
<td>Fentanyl 2 μg/kg</td>
<td>Sevoflurane 20%-42%, Propofol 5%-11%</td>
</tr>
<tr>
<td>Sevoflurane vs propofol TIVA</td>
<td>88 children, Age 2-6 y MRI</td>
<td>None</td>
<td>None</td>
<td>Mean PAED scale score significantly lower for propofol group</td>
</tr>
<tr>
<td>Sevoflurane vs propofol TIVA</td>
<td>60 children, Age 3-10 y Tonsillectomy</td>
<td>None</td>
<td>Alfentanil 20 μg/kg, acetaminophen 20 mg/kg, or ibuprofen 10 mg/kg, and local infiltration at site</td>
<td>Sevoflurane 48%, Propofol 9%</td>
</tr>
<tr>
<td>Sevoflurane vs propofol TIVA</td>
<td>16 children, Age 1-5 y Eye surgery</td>
<td>Midazolam 0.5 mg/kg PO</td>
<td>Acetaminophen 30 mg/kg prn</td>
<td>Sevoflurane 38%, Propofol 0%</td>
</tr>
<tr>
<td>Propofol as adjunct to sevoflurane</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propofol 1 mg/kg vs saline</td>
<td>80 children, Age 2-6 y Strabismus surgery</td>
<td>Midazolam 0.5 mg/kg PO</td>
<td>Paracetamol 15 mg/kg IV</td>
<td>Propofol 19.5%, Saline 47.2%</td>
</tr>
<tr>
<td>Propofol 1 mg/kg vs saline</td>
<td>84 children, Age 2-7 y MRI</td>
<td>None</td>
<td>Nitrous oxide</td>
<td>Propofol 4.8%, Saline 26.8%</td>
</tr>
</tbody>
</table>

Table 3. Emergence Agitation (EA) Studies Divided by Anesthetic Technique With EA Incidence

ENT indicates ear, nose, and throat; PAED: Pediatric Anesthesia Emergence Delirium; MRI: magnetic resonance imaging; crn. as
Advantages for types of surgery: Neuro

- Maintain CO2 /Cerebral Blood Flow coupling
- Avoid BP fluctuations
- Clear-headed emergence
- Avoid coughing/ICP surges
- (TIVA interferes with mapping for epilepsy surgery)
Bronchoscopy

• Shared airways = variable inhaled agent

• Propofol + remi suppress cough = reduced incidence of laryngeal trauma & spasm

• Can continue to spont. Breathe
Tonsillectomy

- 4 Main Post-op considerations
  - Vomiting
  - emergence delirium
  - laryngospasm
  - Pain

- **Remi + Propofol** = Decreased coughing at emergence = Reduction of pain. Inhaled agents are airway irritating therefore increase coughing at emergence & as discussed reduction in spasm

- **Propofol** = reduction in P.A.E.D.
- **Propofol** = reduction in PONV
TIVA Theory

Radiology/ catheter lab
Procedural sedation
Burns bathing & dressing changes
Hospital transfers/Retrieval Services
ICU
In fact most surgery & Procedures
TIVA Theory
**Propofol** aka Diprivan

- Liquid form, white in colour, [lethicin] derivative.
- Painful on injection
- Respiratory depressant
- Can be used as a sedative and for deeper planes of anaesthesia
- 200mg in 10mls ampules
- 60-200mg given to produce induction of anaesthesia
- Some reported cross-sensitivity with Egg, Soy
- Systolic Shear
- No reversal other than time
- Traditional practice involved calculating the infusion regimen for propofol by the Roberts method. A 1.5 mg/kg loading dose is followed by an infusion of 10 mg/kg/hour that is reduced to rates of 8 and 6 mg/kg/hr at ten minute intervals.
Propofol aka Diprivan

- Traditional practice involved calculating the infusion regimen for propofol by the Roberts method:
  - A 1.5 mg/kg loading dose
  - followed by an infusion of 10 mg/kg/hour that is reduced to rates of 8 and 6 mg/kg/hr at ten minute intervals.
Plasma concentrations of propofol following a single bolus dose
TIVA Theory

This graph illustrates the time lag between blood and effect site concentration.
Remifentanil
Newer ultra short acting agent
Infusion – also great for cough suppression
1mg, 2mg and 5mg powdered form
Bolus can = asystolic arrest-seen it!
TIVA Theory

Minutes since bolus injection

Percent of peak effect site opioid concentration

fentanyl
alfentanil
remifentanil

0 2 4 6 8 10

0 20 40 60 80 100

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TIVA Theory
TIVA Theory

TIVA disadvantages

• Needs to be considered in the context of available alternative techniques
• Awareness
• Vagal responses
• Involuntary movements
• Pain on injection
• Anaphylactoid/Anaphylactic reactions are rare (what do we do with egg, peanut and food allergies?)
• PRIS
• Infection of infusion solutions
• Line dead space, Anti-reflux, flow rates, excess fluid loads in small patients
Propofol Infusion Syndrome

Rare
Develop fatty liver, lactic acidosis & complete heart block
Potentially fatal
May be preventable
Is it the drug or the carrier vehicle?
Mitochondria: respiratory chain inhibition or impaired fatty acid metabolism
*Anaesthesia* 2007; 62 p690-701
TIVA Theory

Questions on TIVA?
TIVA (60 minutes)

At the conclusion of this session participants should be able to:

• Provide an explanation of TIVA
• Discuss the advantages, limitations and precautions with TIVA
• Discuss the considerations for PACU
Morning Tea (20 minutes)
TCI (60 minutes)

At the conclusion of this session participants should be able to:

• Provide an explanation of TCI
• Discuss the common protocols
So What is TCI?
TCI Theory

- Infusions that are attempt to achieve a clinician defined drug concentration in a body compartment (Blood/Plasma) or effect site.

- By using such a technique, anaesthetists are able to set and change a desired concentration based on the clinical observations of the patient.

- TCI is a logical (Arithmetical) approach to lessen the peak trough impact observed in bolus administration and achieve a steady state based on an understanding of a drug’s pharmacokinetic profile.
TCI Theory
TCI Theory

- Central compartment = Blood or plasma
- Second compartment = highly perfused tissues
- Third compartment = poorly perfused tissues
How does it work?

- When the target concentration is increased, the system will administer a bolus to rapidly fill the central compartment producing a step-wise increase in blood concentration.
TCI Theory

This is calculated according to the estimated central compartment volume (Wt, Ht, sometimes age) and by calculating the difference between the current calculated concentration and the target concentration.

Once the new target blood concentration has been reached, the infusion stops and commences at a lower rate to replace drug that is lost by distribution and elimination. The TCI systems repeat the calculations and alter the rate of infusion every 10 seconds.
Two Mainstay models for Propofol TCI are Marsh and Schnider.

Schnider estimates body fluid on lean weight (Total wt in Kg - % body fat in kg), Marsh on total body weight.

Schnider uses less propofol and is probably gentler on the elderly, Marsh is easier to calculate however runs the risk of overdosing in bariatric populations.

Irrespective of the model, Plasma concentration of propofol required to produce loss of consciousness is about 5 to 6 mcg/ml. This may vary up-to 8 mcg/ml in young fit un-premedicated adults. In premedicated patients it is 4-5 mcg/ml.
TCI Theory

• The machine provides an estimated time for the patient to be awake, corresponding to a blood concentration of around 1.5mcg/ml for propofol.
• The mainstay model for Remifentanil is Minto

• Adequate analgesia with remifentanil is achieved with 3-8 ng/ml and may require concentrations up to 15 ng/ml, for stimulating procedures.

• A remifentanil infusion of 0.25-0.5 mcg/kg/min in 70kg, 170cm, 40 yr old man produces a blood concentration of around 6ng/ml after 25 minutes.
### TCI Theory

<table>
<thead>
<tr>
<th>TCI</th>
<th>MANUAL</th>
<th>INHALATIONAL</th>
</tr>
</thead>
</table>
| **PROS** | • Convenient to use  
• Easy to titrate the level of anaesthesia  
• Displays calculated blood concentration  
• Manipulating effect site concentration results in faster blood concentration levels  
• Predicts patient waking time  
• Quicker patient recovery  
• Compensates for interrupted infusion  
• Avoids the need for time-consuming calculations  
• Good control of depth of anaesthesia  
• Stability of anaesthesia  
• Avoids exposure to inhalational agent  
• Portable  
• Data storage and retrieval  
• Less incidence of nausea and vomiting  
• Cardiovascularly stable – lower heart rate, less stress hormones  
• Improved ciliary function post op  
• Reduced intracranial pressure with propofol due to reduced cerebral blood flow and cerebral metabolic rate  
• Predictable anaesthesia with shared airway  
• Airway manipulation facilitated | • Haemodynamic stability equivalent to TCI  
• Reduced intracranial pressure with propofol due to reduced cerebral blood flow and cerebral metabolic rate  
• Quicker patient recovery  
• Improved ciliary function post op  
• Avoids exposure to inhalational agents  
• Portable  
• Less incidence of nausea and vomiting  
• Predictable  
• Anaesthesia with shared airway | • Does not require any calculations  
• Easy to administer to the patient  
• May be used as an induction and maintenance agent  
• Adequate depth of anaesthesia in patients |
## TCI Theory

<table>
<thead>
<tr>
<th><strong>CONS</strong></th>
<th><strong>TCI</strong></th>
<th><strong>MANUAL</strong></th>
<th><strong>INHALATIONAL</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Concentrations are calculated and subject to error in those patients that do not match the model profile population</td>
<td>• Requires complicated calculation</td>
<td>• Environmental work place pollution</td>
<td></td>
</tr>
<tr>
<td>• Awareness possible especially when used with muscle relaxants</td>
<td>• Awareness possible especially when used with muscle relaxants</td>
<td>• Special equipment eg. vapouriser</td>
<td></td>
</tr>
<tr>
<td>• Requires a dedicated iv cannula for administration</td>
<td>• Requires dedicated cannula for administration</td>
<td>• Increased post op nausea /vomiting, emergence dysphoria, raised icp/iop</td>
<td></td>
</tr>
<tr>
<td>• IV access constantly needs to be checked for tissueing</td>
<td>• IV access needs to be checked for tissueing</td>
<td>• Reduced ciliary function post op</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Does not indicate the blood concentration levels</td>
<td>• Trigger of MH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Takes longer to achieve clinical effect</td>
<td>• Unpredictable level of anaesthesia during shared airway</td>
<td></td>
</tr>
</tbody>
</table>

Aspaan
TCI Theory

The Future?
TCI (60 minutes)

At the conclusion of this session participants should be able to:

• Provide an explanation of TCI
• Discuss the common protocols
Syringe Driver Familiarity  (60 minutes)

At the conclusion of this session participants should be able to:

• Identify the features and functions of the Syringe Driver
• Program TCI using Marsh, Schnider & Minto
TCI Theory

Features of the Pump
TCI Theory
TCI Theory

TIVA Mode

- Pump Status
- Drug Name and Concentration
- Pressure Information
- Flow Rate and Dose Rate
- Dose and Volume Infused
- Operations During Use

INFUSING

Remifentanil 50.0 μg/ml

Dosage:

- 16.8 ml/h
- 0.20 μg/kg/min

Dosage Information:

- DOSE 80.0 μg
- 1.63 ml
- 1 h 59 m 28 s

Cp/Ce
TCI Theory

TCI Mode

Pump Status

Drug Name and Concentration

Induction Duration

Pause Before Maintenance

Remifentanil 50.0 µg/ml

ON HOLD

INDUCTION 0.24 µg/kg 10.0 µg 0.005

MAINTENANCE 123 ml/h 0.3 ml 16.7 ml/h

CONFIRM + TIME

Plasma Concentration

Plasma Target

Initial Induction Dose

Initial Induction Rate

Initial Induction Volume

Time of Induction

Initial Maintenance Rate

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TCI Theory

**TCI Mode - MORE Information Screen**

Selecting the **MORE** softkey will display the following additional information:

- Drug Name and Model
- Elapsed Time
- Volume and Dose Infused
- Patient Parameters
- Time to End of Infusion at Current Rate
- Decrement Time
- Decrement Concentration

Press the **BACK** softkey to return to the TCI screen. The display will automatically revert to the TCI screen after approximately 20 seconds.
TCI Theory
Malignant Hyperthermia:
Staying cool when the Heat is on
Malignant hyperthermia is a rare pharmacogenetic disorder.

rare¹ /reə/ adj 1 seldom occurring or found
Unquantifiable Rare Things

Hen’s Teeth

Honest politicians
Quantifiable Rare Things

Chance of Winning Oz Lotto 1: 8,000,000

Risk of Death by Lightning Strike 1: 1,000,000

Risk of an MH Reaction: 1: 50,000 GA’s
Think you will not see it??

“You’ve got to ask yourself one question: Do you feel lucky .....Well do yah”

- Harry Callahan (Dirty Harry)
Let’s play the MH numbers game!!!
In a busy Sydney Surgi-centre

115 general Anaesthetics per day

Operating 5 days per week

Operating 47 Weeks of the year

Yields 27,025 General Anaesthetics per year

Incidence of MH case 1: 50,000 GA’s

Therefore ~ 1 MH case every 2 years.
MH Presentation

- Important to note: no single cluster of S & S identify MH.
- MH is a clinical chameleon
- All MH Signs are nonspecific and may arise from multiple causes
MH Presentation

• Historical hallmarks of MH:
  – Progressive Pyrexia & muscle rigidity
  – 1°C / 5min to 45°C
  – Mortality up to 80% (Fulminant Reactions)

• Improved investigations suggest MH as “Malignant Hypermetabolism”
Masseter Spasm – prolonged, intense

Hypermetabolism as evidenced by:
- Increased ETCO2, tachypnoea
- Increased Sympathetic outflow - tachycardia
- Mixed Metabolic & Respiratory acidosis
- Increased Core Temperature (often relatively late)

Presence of Myoglobinuria

(Investigation of choice : ABG)

Muscle Rigidity & Breakdown

DIC, Renal Failure

Death
• Hypermetabolism may be present within minutes or be delayed hours (Hommertzheim & Steinke, 2006)
• Increased Day Surgery =? increased mortality rate from MH
• Previous triggering GA without reaction does not exclude MH susceptibility
• Agents differ in their ability to trigger MH
  – Halothane + Sux
  – Halo > Sevo > Iso > Des
• Regardless of onset time fulminant reactions are qualitatively similar in that signs of hypermetabolism will always be present
So how is this relevant to TIVA & TCI?:

Participant Activity
The Case

- 24 year old male undergoing a Lap-Hernia Repair.
- Induced with 180mg Propofol, 100mcg Fentanyl, 3mg Midazolam and 50mg Esmeron.
- Intubated and Ventilated, maintained on inhalation anaesthesia (Sevoflurane with end tidal at 4%)
- 10 minutes into the case the Anaesthetist is alarmed......
The Anaesthetist informs the Surgeon: “I think we have a problem, possibly MH!!!”

The alarm is raised.

Draft a list of actions that need to occur.
DECLARE AN EMERGENCY

- Notify your ICU
- Cease inhalation agents start Propofol TCI
- Coordinate Dantrolene Admin.
- BVM 100% O2 ↑Min Volume X3
- ABG sample
- Assist with CVC, Art line & IDC insertion