TIVA Versus Inhalational Anesthesia for Airway Examination

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Product Information

- **Propofol** is also indicated for paediatric anaesthesia in children 3 years of age and older. In the absence of sufficient clinical experience, propofol is not recommended for anaesthesia in children less than 3 years of age. (Hospira Healthcare Corporation monograph)

- **Remifentanil** is not recommended for use in spontaneous ventilation anaesthesia, in monitored anaesthesia care, for continuation as an analgesic in the immediate postoperative period, in neurosurgery, in cardiac surgery, or in paediatric anaesthesia. (ULTIVA monograph)

- **Dexmedetomine** should not be used in children less than 18 years of age. (Hospira Healthcare Corporation monograph)
OUTLINE

- The Ideal Agent for Airway Procedures
- Advantages of TIVA for Airway Procedures.
- Disadvantages of Inhalational technique for Airway Procedures.
CONSIDERATIONS FOR PAEDIATRIC AIRWAY PROCEDURES

- Small airways
- Shared airway with surgeon
- Risks of cough/laryngospasm/desaturation
- SV indicated in presence of foreign body to prevent ipsilateral hyperinflation and barotrauma (Zhang X et al., 2011)
- SV will maximise V/Q matching (Hemmings & Hopkins)
- Topical local anaesthesia to cords/carina
- Anticholinergic agent
THE IDEAL ANAESTHETIC FOR PAEDIATRIC AIRWAY PROCEDURES

- Adequate oxygenation & ventilation
- Maintenance of SV
- Allows assessment of dynamics of airway
- Avoids instrumentation of airway
- Adequate depth anaesthesia / amnesic
- No cough, stridor, laryngospasm
- Bronchodilator
- Protective with hypoxia
- Smooth emergence with no ED or cough
- Rapid good quality recovery
- No effect on atmospheric pollution
WHAT IS TIVA?

- Total IntraVenous Anesthesia
- Titrated infusions of Propofol & Remifentanil
- Dexmedetomidine
TIVA ANESTHESIA OF CHOICE

- Airway Intervention
- Malignant hyperthermia susceptibility
- Scoliosis surgery with SSEP / MEP monitoring
- Neurosurgery
- Patients with muscular disorders
- History of severe PONV
- Anaesthesia outside of operating room
TIVA ADVANTAGES

- Anaesthesia of choice for airway procedures
- Obtunded airway reflexes & Bronchodilatation
- Improved respiratory ciliary function
- Easily titratable
- Able to maintain SV with appropriate titration
- Not reliant on airway for anaesthesia
- No anaesthetic induction of ENT surgeon ?!
- Good quick quality of recovery
- Reduced emergence delirium
- Neuroprotection
TIVA: OTHER ADVANTAGES

- Reduced postoperative pain and PONV
- No atmospheric pollution
- Myocardial Protection
- No seizures
- No organ toxicity
- Lower cost
- Reduced awareness (Johr 2006) (0.2 vs 5%)
- Closed loop system in development
TIVA ADVANTAGES

- Choice for airway procedures
- Easily titratable
- Obtunded airway reflexes
- Improved ciliary function
- Bronchodilatation
- Not reliant on airway for anaesthesia
- Good quick quality of recovery
- Reduced pain and PONV
- Amnesia
- Reduced emergence delirium

- Neuroprotection
- Myocardial protection
- No atmospheric pollution
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- Reduced awareness
- Closed loop system in development
TIVA FOR AIRWAY PROCEDURES
IS IT SAFE?
Propofol-remifentanil intravenous anesthesia and spontaneous ventilation for airway foreign body removal in children with preoperative respiratory impairment

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**Summary**

Inhalational anesthetics traditionally used to facilitate airway maneuvers are associated with increased cardiovascular risk in children. The use of a remifentanil-propofol anesthetic technique for airway foreign body removal in children with preoperative respiratory impairment is shown to be safe.

**Use of a remifentanil–propofol mixture for pediatric flexible fiberoptic bronchoscopy sedation**

**Summary**

Background: Flexible fiberoptic bronchoscopy is an important diagnostic tool for pediatric pulmonologists. Because of its favorable side-effect profile, ketamine has become a popular sedative for this procedure, but may be associated with unpleasant emergence reactions in the older child. Remifentanil is a newer, ultra-short-acting opioid that has been shown to provide effective sedation and cough suppression for fiberoptic bronchoscopy when combined with intramuscular propofol. However, delivery of these agents as a combined, single injection has not been described.

Methods: Children ≤ 2 years of age undergoing fiberoptic bronchoscopy were enrolled. Ketamine was mixed in a single syringe with and without propofol, giving final drug concentrations of 0 mg/mL of propofol and 15-20 mg/mL of remifentanil. Sedation was induced with a bolus of approximately 0.13 mg/kg of each mixture and maintained by titrating the dose throughout the procedure. Vital signs, sedative effectiveness, recovery patterns, and complications were prospectively recorded.

Results: Patients aged 1.0 to 5.3 years were sedated. Sedation was induced with 1.2 ± 0.4 mg/kg of propofol 0.24 ± 0.18 mg/kg of remifentanil and maintained with 6.1 ± 1.8 mg/kg of propofol 0.13 ± 0.66 μg/kg/min of remifentanil. Five patients received low-dose ketamine to augment sedation. The maximal decrease in respiratory rate was 41 ± 5.3 breaths/min (27.6 ± 21.3%) and no patient became hypoxemic. All procedures were completed easily without significant complications. Patients recovered to baseline 13.3 ± 8.5 min following induction discontinuation.

Conclusions: A remifentanil/propofol mixture provided effective sedation and rapid recovery in pediatric patients undergoing fiberoptic bronchoscopy.
OBTUNDED AIRWAY REFLEXES

• Oberer C, et al., Anesthesiology 2005;103(6):1142-8
  Laryngeal and respiratory reflex responses in children aged 2-6 yr significantly worse with Sevo compared to propofol independent of the level of hypnosis.

  TIVA associated with significantly less coughing and reduced haemodynamic response during emergence from the anaesthesia when compared with volatile anaesthesia.
TIVA RESPIRATORY EFFECTS

  Bronchial transport velocity significantly reduced in SEVO group compared with TIVA group. Anesthesia with sevoflurane leads to significantly impaired bronchociliary clearance in comparison to TIVA.

  In presence of pre-op respiratory issues the subsequent anaesthetic risk of respiratory complications during anaesthesia was lower with intravenous induction compared with inhalational induction (all p<0·0001) and intravenous maintenance compared with volatile of anaesthesia (all p<0·0001).
  As well as airway management by a specialist paediatric anaesthetist compared with a registrar (all p<0·0001), and use of face mask compared with tracheal intubation (all p<0·0001).
PROPOFOL BRONCHODILATOR MECHANISM

- Plasma membranes contain specialized lipid rafts including 50-100nm invaginations called caveolae.
- Caveolae facilitate reactions between plasma membrane signalling elements and intracellular signalling cascades.
- Propofol effectively reduces intracellular calcium which leads to bronchodilatation.

- Burburan SM et al. 2007. Minerva Anesthesiology. 273:357-65
IMPROVED RESPIRATORY FUNCTION


• Significant endothelial damage associated with short term halothane.
NEUROPROTECTION

- Propofol significantly reduced hypoxia-mediated increases in lactate dehydrogenase with decreased morphological signs of cell damage
- Decreases neuronal death after O2 deprivation or cerebral ischemia
- Increases neurogenesis.

REDUCED EMERGENCE DELIRIUM

  Reduced ED with TIVA compared with sevoflurane.

- Jacob Z et al Anesthesiology 2012; 117:1062–71
  Metabolomic (Detection of Products of Metabolism) profiling of children’s brains undergoing GA with Sevoflurane or Propofol. Sevo assoc with higher concentrations of lactate and glucose in parietal cortex and correlated to postoperative incidence of ED.

TIVA FOR SV FOR AIRWAY ENDOSCOPY IN CHILDREN PROCEDURE
Total intravenous anesthesia and spontaneous respiration for airway endoscopy in children – a prospective evaluation

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Summary
Introduction: Inhalational anesthesia with spontaneous respiration is traditionally used to facilitate airway endoscopy in children. The potential difficulties in maintaining adequate depth of anesthesia using inhalational anesthesia and the anesthetic pollution of the surgical environment are significant disadvantages of this technique. We report our institutional experience using total intravenous anesthesia (TIVA) and spontaneous respiration.

Methods: We prospectively studied 41 pediatric patients undergoing 52 airway endoscopies and airway surgeries. Following induction of anesthesia, a propofol infusion was titrated to a clinically adequate level of anesthesia, guided by the Bispectral Index (BIS), and a remifentanil infusion was titrated to respiratory rate, ECG, BP, pulse oximetry, BIS level, transcutaneous CO2 (TcCO2), respiratory rate, and drug infusion rates were recorded. Adverse events and the response to these events were also recorded.

Results: Forty-one children underwent 52 airway procedures: 17 rigid bronchosopies and 35 microlaryngeal bronchosopies, including 18 LASER treatments. Performed. The mean (SD) age was 6.9 (5.8) years and weight 26.9 (21.2) kg. The mean induction time was 13 (6) min, and anesthesia duration was 49 (30) min. The mean highest TcCO2 recorded during the procedures was 62.4 ± 15.3 mmHg. Coughing occurred in 11 (27%) patients, requiring additional topical anesthesia (3), a bolus of propofol (4) or remifentanil (1), or removal of the bronchoscope (1). Desaturation below 90% occurred in 10 (19%) cases; only three required intervention in the form of temporary assisted ventilation (2) or inhaled bronchodilators (1). No laryngospasm, stridor, or arrhythmias were observed.

Conclusion: TIVA and spontaneous respiration is an effective technique to manage anesthesia for airway endoscopy and surgery in children.

Keywords: airway endoscopy; total intravenous anesthesia; spontaneous respiration; propofol; remifentanil; transcutaneous carbon dioxide.

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TIVA FOR SV FOR AIRWAY ENDOSCOPY IN CHILDREN

• Titrate Propofol to BIS, Remi to RR
  - Propofol 200-500µg/kg/min (Highest propofol – 386.5µg/kg/min)
  - BIS 40-60
  - Remifentanil 0.1-0.2µg/kg/min
  - RR 10-15 breathes/min
  - RR 50%< baseline in neonates/infants
Drug Interactions

Dose response curves
Iso-bolograms

Propofol

Apnea

Cough

Remifentanil

Too deep

Too light
α 2 Agonist Interactions

- Propofol
- Remifentanil

- Clonidine
- Dexmedetomidine

- Cough
- Apnea

- Too deep
- Too light
SV with TIVA is a true art form in paediatric anaesthesia
- Know speed of induction injections
- Maintain normal CO2 (Ansermino et al., 2009)
- Know anaesthetic doses for age range (Steur et al., 2004)
- Know targets in BIS and respiratory rate (Ansermino et al., 2005)
- Know relation of SV to age and drugs used (Barker et al., 2007)
REDUCED PONV


REduced Postop Pain

- Tan T et al.  
  Day-Surgery Patients Anesthetized with Propofol Have Less Postoperative Pain than Those Anesthetized with Sevoflurane.  

- Cheng SS et al.  
  Anesthesia Matters: Patients anesthetized with propofol have less postoperative pain than those anesthetized with isoflurane.  
IMPROVED QUALITY OF RECOVERY

REDUCED COST
The cost of TIVA drugs by age
ANESTHESIA OF CHOICE FOR NEUROSURGERY

  Cerebral blood flow velocity increases when propofol is changed to desflurane, but not when isoflurane is changed to desflurane in children.

- Kikuta et al.
  Effects of intravenous anesthesia with propofol on regional cortical blood flow and intracranial pressure in surgery.
  *Surgical neurology* :2007:(4) pg:421 -4
NEUROPROTECTION

• Cerebral Vasoconstrictor
  • Reduces CBF
  • Lowers CMRO$_2$
  • Dose dependant in children

• Preserves cerebral autoregulation

• Preserves cerebral reactivity to CO$_2$
NEUROPROTECTION

IN VIVO
• Ergun et al. Neurosurgical Review. 2002; 25:95-8
• Bayona et al. Anesthesiology. 2004; 100:1151-9
• Engelhard, K et al. Anesthesiology. 2004;101:912-917

IN VITRO
• Rossaint et al. Critical Care. 2009;13:R61
• Velley et al. Anesthesia. 2003;99:368-75
• Wu et al. Brain Research. 2011;1384:42-50
MYOCARDIAL PROTECTION

RELATIONSHIP BETWEEN AGE AND SV WITH TIVA

• Strabismus surgery – 3 groups
  • I (6months – 3 year). II (3-6 year). III (6-9 year)
  
Doses ($\mu g/kg/hr$) I – 0.192 II – 0.095 III – 0.075

• <3years tolerate higher dose of remifentanil and maintain SV

• Relationship of Remifentanil dose, age and weight or height is NOT linear

DISADVANTAGES OF TIVA

- Pain on injection
- Tissused/Disconnected IV
- Bacterial Contamination
- No effect site monitor
- No reliable TCI monitor
- Long context sensitive half life
- Interindividual variability in clearance
- Age related changes in propofol requirements
DISADVANTAGES OF TIVA

• Propofol infusion syndrome
• Not anaesthesia of choice for long neuro cases
• Not anaesthesia of choice for neonates or exprem babies
• Disposables costly
• Disposables not environmentally friendly
• ? Neurotoxicity to developing brain
PAIN ON INJECTION

- Prevention
- Use of medium-chain triglyceride/long chain triglyceride solvent versus long chain triglyceride solvent significantly reduces pain (Rochette et al 2008)
- Lidocaine mixed with mct/lct -propofol eliminates pain on injection (Rochette et al 2008)
- Lidocaine 2mg/kg pre propofol injection eliminates pain (Billoata et al 2006)
- Ketamine pretreatment
CLOSED LOOP SYSTEM IN DEVELOPMENT

- TIVA adjusted continually according to effector site clinical effect using EEG based depth of anesthesia monitor
- Major advantage will be measuring effector site effect and minimizing large inter individual age, culture and genetic related pharmacokinetic and pharmacodynamic effects.
- Improved respiratory and cardiovascular stability
- Reduced dependant dosing errors

- West, N et al. 2013. BCCH Vancouver Canada.
PROPOFOL INFUSION SYNDROME
Propofol Infusion Syndrome

21 (14) deaths reported in children (2006) [new cases 5(12)]

Unpublished ICU study

Impaired fatty acid metabolism (failure of tissue oxygenation)

Failure of mitochondrial metabolism

< 4mg/kg/hr (2g/kg/day)

Suppress fat metabolism (acyl-carnitine)

Inherited defects in beta oxidation?
NOT ANESTHESIA OF CHOICE FOR LONG NEURO CASES
NOT ANESTHESIA OF CHOICE FOR NEONATES OR EXPREM BABIES
NEONATAL PHARMACOKINETICS

• Non-linear changes in volume of distribution and clearance
• Pharmacokinetics of propofol in neonates is highly variable

– Allegart K et al. 2007. BJA. 99:864-70
Scatter plot showing relationship between propofol clearance and (A) PMA (weeks), (B) GA (weeks), (C) P (days), and (D) body weight (kg) of the basic model.


Copyright restrictions may apply.
Simulated population propofol concentrations - in neonates aged 27, 38, and 43 weeks PMA and <10 days and >=10 days PNA after a bolus dose of 9 mg in 10 s.

DISPOSABLES COSTLY
Cost of TIVA

Extensions
$1.48

Syringes
20cc 20c
60cc 38c

Pumps
WASTE..
ENVIRONMENTAL IMPACT OF PROPOFOL
DISPOSABLES NOT ENVIRONMENTALLY FRIENDLY
AWARENESS
**General Anesthetic**

- **High risk for AWR**
  - **Potent volatile as primary anesthetic?**
    - **NO**
      - or compared to routine care
        - **Set BIS alarm**
          - **B-Aware**\(^{14}\) shows BIS protocol prevents AWR compared to routine care in high-risk patients.
          - More than 40% of patients in B-Aware had TIVA.
    - **YES**
      - or compared to routine care
        - **Set ETAC alarm**
          - **B-Unaware**\(^{17}\) & **BAG-RECALL**\(^{20}\) show BIS protocol not superior to ETAC protocol in high-risk patients.
          - **MACS**\(^{11}\) detects no difference between protocol based on BIS or anesthetic concentration in an unselected population.
- **General population**
  - **Potent volatile as primary anesthetic?**
    - **NO**
      - or compared to routine care
        - **Set BIS alarm**
          - **MACS**\(^{11}\) shows BIS protocol prevents definite or possible AWR compared to routine care.
          - **TIVA trial**\(^{22}\) shows BIS protocol prevents AWR compared to routine care.
Lactic Acidosis

Case report
Lactic acidosis after short-term infusion of propofol for anaesthesia in a child with osteogenesis imperfecta

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Pancreatitis

Case report

Acute pancreatitis induced by short-term propofol administration

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Pediatric Anesthesia 2005 15: 1006–1008
Effects of short-term propofol administration on pancreatic enzymes and triglyceride levels in children

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within normal limits. No significant changes in serum pancreatic-amylase levels were seen (p = 0.127). In two (5%) children, pancreatic enzymes and in four (10%) children triglyceride levels were raised above normal limits; however, no child showed clinical symptoms of pancreatitis. We conclude that even short-term propofol administration with standard doses of propofol may have a significant effect on serum triglyceride and pancreatic enzyme levels in children.

Anaesthesia, 2005, 60, pages 660–663
Propofol anaesthesia and metabolic acidosis in children

Paediatric Anaesthesia 2003 13: 53–57

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Results: There was no difference in lactate dehydrogenase, myocardial creatininephosphokinase, aspartate aminotransferase, alanine aminotransferase and cholesterol levels between and within the groups. All postoperative triglyceride levels were higher and pH levels were lower in group P than group H (P < 0.05) and there was no difference within the groups.

Conclusions: In these healthy patients, short-term use of propofol did not result in significant acidaemia, nor alterations in hepatic or myocardial enzyme levels.
Other effects

Renal Failure
Dystonia
Memory Loss

Case report
Death after re-exposure to propofol in a 3-year-old child: a case report

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Pediatric Anesthesia 2004 14: 265–270
SUMMARY

• TIVA anesthesia of choice for airway procedures.
ANY QUESTIONS?