Review of Remifentanil and its Clinical Use

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Schafer et al., Anesthesiology 1991; 74:53
London, Ontario

- Intra-op use of morphine
- Introduction of remifentanil
- Awake craniotomies
Pharmacokinetics and Pharmacodynamics of Remifentanil
Remifentanil: Molecular structure

- 1-(2-Methoxycarbonyl-ethyl)-4-(phenyl-propionyl-amino)-piperidine-4-carboxylic acid methyl ester hydrochloride
- $C_{20}H_{28}N_2O_5$ – HCl
- MW: 412.9 D
- μ–opioid receptor agonist

Remifentanil hydrochloride

- Fentanyl

1. Approved Ultiva Product Information
Remifentanil: Key pharmacokinetic and pharmacodynamic characteristics

*In-vitro/In-vivo* studies do not necessarily predict clinical effect

**Remifentanil is a short-acting opioid receptor agonist**¹⁻²:

- **Rapid onset of effect**: \( t_{1/2}k_{e0} = 1.3 \) minutes³
- The onset of analgesia is rapid, with peak effect at 1-3 minutes¹,³
- Potency twice that of fentanyl

- **Rapid offset of action**: context-sensitive half-time of 3.65 minutes, independent of duration of infusion⁴
- **Rapid offset of clinical effects** with no residual opioid activity within 5 to 10 minutes after discontinuation¹
- **Metabolised by non-specific blood and tissue esterases**¹,²
- **Metabolism results in formation of a carboxylic acid metabolite**, which is 4600 times less active than remifentanil¹

\[ t_{1/2}k_{e0} = \text{half-time for equilibration between plasma and the effect compartment} \]

Anesthetic interaction

- Decrease MAC by 60-90%
- With 1ng/cc – 3ng/cc of remi

Propofol decreases Volume distribution of remi
InCREASES remi concentration first 15min
Dose of 4ng/cc can decrease propofol needs by 2/3
Context-sensitive half-time$^{1,2}$

*In-vitro*/In-vivo studies do not necessarily predict clinical effect

![Graph showing time to 50% drop in plasma drug concentration (minutes) vs. duration of infusion (minutes) for Fentanyl, Alfentanil, and Remifentanil.]

1. Egan TD et al., Anesthesiology 1993;79:881-892,
2. Westmoreland CL et al., Anesthesiology 1993;79:893-903

Adapted from Egan TD et al, 1993
Remifentanil: Rapid offset of effect

- After a 2 hour infusion remifentanil has a markedly more rapid offset of effect than alfentanil

1. Egan TD et al., Anesthesiology 1996;84:821-33
Singapore
Local practice and population

- One ampule of fentanyl and one ampule of morphine

- Sensitivity to narcotics
  - Respiratory depression
  - Coughing

- Airway
  - More anterior larynx?
  - Hypersensitive?

- No more sufentanil
- Bucking and coughing on emergence or forever waking up
- Quit anesthesia / go home?
Intra-Operative Analgesia and Anaesthesia
Multicentre, prospective, 1:1 single-blind, randomised controlled study

156 hospitals and ambulatory surgery facilities

 Patients (n=2,438) undergoing elective surgery under general endotracheal anaesthesia with duration ≥30 minutes

remifentanil vs fentanyl as an adjunct intra-operative opioid
General surgery

• 2438 pts for general surgery
• 0.5ug/kg/min induction followed by 0.25ug/kg/min remi
• Fentanyl as per anesthesia routine
• Adjunct propofol or isoflurane +/- N20

• Lower BP lower HR
• Earlier patient verbal response, leaving OR, discharge from hospital
• Anesthesia felt titratable, predictable and better quality of anesthetic
Patients (n=30) undergoing percutaneous nephrolithotripsy

Compared propofol–alfentanil or propofol–remifentanil anaesthesia on haemodynamics, recovery characteristics and postoperative analgesic requirements
Remifentanil is associated with rapid and predictable post-operative recovery in adults\(^1\)

- Recovery times after remifentanil/propofol versus alfentanil/propofol anaesthesia:\(^2\)

Adapted from Ahonen et al., 2000

<table>
<thead>
<tr>
<th></th>
<th>Remi (n=15)</th>
<th>Alfentanil (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to awakening</td>
<td>p &lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>Time to tracheal extubation</td>
<td>p &lt; 0.01</td>
<td></td>
</tr>
</tbody>
</table>

1. Approved Ultiva Product Information
Remifentanil Provides a predictable and vital awakening

Recovery times of remifentanil-propofol vs. alfentanil-propofol

Cicek M et al., Eur J Anaesthesiol 2005;22(9):683–688
Use of Remifentanil in Different Surgery Types
Remifentanil in Neurosurgery

- Stability of intracranial pressure
- Stability of cerebral capacity
- Maintenance of CO2-reactivity
- Good haemodynamic protection, e.g. during intubation or fixation of the head
- Early and predictable postoperative neurological assessment
- Suitable for special procedures (e.g. awake craniotomy)

Wilhelm W et al., Anaesthesist 2003;52:473-494
Remifentanil in Neurosurgery (1 of 2)

• In a randomised, multicentre, double-blinded, prospective trial comparing remifentanil to fentanyl during elective supratentorial craniotomy for intracranial space-occupying lesions, remifentanil patients were 1.67 times more likely to be extubated than fentanyl patients at any given time (95%CI:1.04–2.68, p=0.035).¹

• The risk ratio indicated that Ultiva patients were 2.29 times more likely to follow commands than fentanyl patients at any given time (95% CI:1.39–3.79, p = 0.001).¹

Remifentanil in Neurosurgery (2 of 2)

Intracranial pressure (ICP), cerebral perfusion pressure (CPP) and brain relaxation scores in patients undergoing supratentorial craniotomy for space-occupying lesions with Ultiva, versus fentanyl-based anaesthesia.¹

<table>
<thead>
<tr>
<th></th>
<th>Fentanyl (n = 16)</th>
<th>Ultiva (n = 17)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICP (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>14 ± 13</td>
<td>13 ± 10</td>
<td>0.65 (NS)</td>
</tr>
<tr>
<td>Range</td>
<td>0–38</td>
<td>0–36</td>
<td></td>
</tr>
<tr>
<td>CPP (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>76 ± 19</td>
<td>78 ± 14</td>
<td>0.71 (NS)</td>
</tr>
<tr>
<td>Range</td>
<td>38–119</td>
<td>53–104</td>
<td></td>
</tr>
<tr>
<td>PaCO₂ during ICP measurement (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>29 ± 5</td>
<td>28 ± 4</td>
<td>0.35 (NS)</td>
</tr>
<tr>
<td>Range</td>
<td>23–42</td>
<td>22–33</td>
<td></td>
</tr>
<tr>
<td>Brain relaxation score* [no. of patients (%)]</td>
<td>(n = 31)</td>
<td>(n = 31)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>11 (35)</td>
<td>13 (42)</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>13 (42)</td>
<td>15 (48)</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>5 (16)</td>
<td>3 (10)</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>3 (10)</td>
<td>0 (0)</td>
<td>–</td>
</tr>
</tbody>
</table>

NS – Not significant
* Brain relaxation scores: 1 = excellent, no swelling; 2 = minimal swelling, but acceptable; 3 = serious swelling, no change in treatment required; 4 = severe swelling requiring intervention.


Adapted from Guy et al., 1997
Neuroanesthesia

- Canadian Journal of Anesthesia 2003 50:9 pg 946 -52
- Adrian Gelb et al

- Remifentanil with morphine transitional analgesia shortens neurological recovery compared to fentanyl for supra-tentorial craniotomy

- Remi : 1.0ug/kg bolus + 1.0ug/kg/min + 0.2ug/kg/min
- Fent : 1.0ug/kg bolus + 1.0ug/kg/min + 0.04ug/kg/min
- Maintenance nitrous and 0.5 MAC ISO
- 0.08 mg/kg morphine at bone flap for remi group
• Better operating conditions for surgeons
• Faster more alert neurological assessment
• Morphine provides adequate transitional analgesia without compromising neurological assessment
Neuroanesthesia

• General anesthesia
  • TIVA (TCI) vs Volatiles
  • Usually dependent on location of tumor and ICP

• Midazolam pre-induction – BIS monitor
• TCI propofol (Schnider / effect site) 3ug/cc
• + Remifentanil 0.08 – 0.2 ug/kg/min
• Ropivicaine 1% for pin sites (bolus remi 1ug/kg)
• Paracetomol 1g IV and Morphine 0.03-0.05mg/kg after bone flap
• Timed TCI ET between 1.0 ug/cc (elderly) to 1.5ug/cc (young)
• and remifentanil 0.08 to 0.14 ug/kg/min for emergence

• With 6% Desflurane and Air o2 - ET 0.6 to 1.2 for emergence
• With 3% Desflurane and N2O - ET 0.3 for emergence
• Remi 0.08 - 0.14ug/kg/min
• Sevo: < 0.1 (not enough decimal points)
• Fentanyl/lidocaine/rocuronium for induction for smoother hemodynamics
Neuroanesthesia

• Transphenoidal resection
  • Extreme prolonged hypertension with nasal septum / sphenoidal mucosal infiltration
  • Vigilance (art line) and bolus remifentanil (1-2ug/kg)

• Spine
  • TIVA to minimize interference of evoke potentials
  • Smoother intra-op wake up tests
Neuroanesthesia

• Awake (craniotomies, DBS, Burr holes,)
• Patient selection key as well as early rapport

• Induction with titrated fentanyl and midazolam
• Immediate maintenance infusions of precedex 0.3ug/kg/hr and remifentanil 0.05 – 0.08 ug/kg/min

• For catheterization, scalp blocks, head pinning
• Avoids bolus and its side effects
• Titrate precedex for LOC, titrate remifentanil via respirations
• Reduce precedex by halves for awake portions of the operation
• Paracetamol, ondansetron, morphine (1-2 mg) on closure
Sedation / Remote

- For long cases with episodes of patient cooperation
- Endovascular stenting - requires breath holding

- Titrated Midazolam (1-2 mg) and fentanyl (50 – 200ug)
- Maintenance infusions of precedex (0.3ug/kg/hr) and remifentanil (0.05 – 0.1 ug/kg/min)
- Rescue propofol standby

- Adjust precedex for level of consciousness
- Adjust remifentanil according to respiratory rate
Remifentanil in ENT Surgery

- Remifentanil-based regimen provides improved surgical conditions with regard to bleeding from the surgical field in patients undergoing endoscopic sinus surgery compared with alfentanil and fentanyl regimens.\(^1\)-\(^3\)

Haemodynamic parameters and rating of the surgical field by two blinded ENT surgeons during microscopic and endoscopic sinus surgery.\(^2\)

<table>
<thead>
<tr>
<th></th>
<th>IV anaesthesia (IVA group) (n = 45)</th>
<th>Balanced anaesthesia (BA group) (n = 43)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>65 (61/69)</td>
<td>67 (63/72)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean heart rate (beats per min)</td>
<td>55 (51/64)</td>
<td>72 (66/83)</td>
<td>p ≤ 0.001</td>
</tr>
<tr>
<td>VAS rating(^\dagger)</td>
<td>2.8 (2.0/3.4)</td>
<td>4.9 (3.5/7.7)</td>
<td>p ≤ 0.001</td>
</tr>
<tr>
<td>Rating on a 6-point scale (0–5)(^\ddagger)</td>
<td>1 (1/2)</td>
<td>2 (2/4)</td>
<td>p ≤ 0.001</td>
</tr>
<tr>
<td>Estimated blood loss (mL)</td>
<td>100 (50/240)</td>
<td>170 (100/270)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS – Not significant; The values are presented as median (25th/75th percentile).
IVA group: induction and maintenance – propofol/Ultiva; BA group: induction – propofol/alfentanil; maintenance – isoflurane/alfentanil
\(^\dagger\) 10-cm VAS (0 = best possible operating conditions and dryness of the surgical field; 10 = worst possible conditions).
\(^\ddagger\) 6-point ascending scale: 0 = no bleeding; 1 = slight bleeding; no suction of blood required; 2 = slight bleeding; occasional suctioning required. Surgical field not threatened; 3 = slight bleeding; frequent suctioning required. Bleeding threatens surgical field a few seconds after suctioning is removed; 4 = moderate bleeding; frequent suctioning required. Bleeding threatens surgical field directly after suction is removed; 5 = severe bleeding; constant suctioning required. Bleeding appears faster than can be removed by suction. Surgical field severely threatened.

Adapted from Eberhart et al 2003

ENT and the Airway

- General anesthesia / ETT
  - sometimes unable to anticipate the end of the procedure

- Resection of airway tumors
  - Enhances tolerance of awake intubation
  - Improves ability to safely and smoothly extubate patients

- FESS
  - Improves ability to safely extubate patients esp when pt must mouth breath
  - Less bucking / coughing / blood on emergence
  - Less hypertension on emergence /extubation / and potentially post–op
• My Preferred technique
• Remifentanil 0.12ug/kg/min
• Propofol induction
• Ventilate with Sevo 2% while atracurium takes effect
• Reduce remifentanil to 0.08ug/kg/min prior to intubation
• Des 3 % Insp with 50% n20
• dexamethasone

• Morphine 0.05-0.1 mg/kg  30  min pre – emergence

• ondansetron
• Time :ET des 0.3 and remi at least 0.08ug/kg/min
ENT

• ELMS ( suspension laryngoscopy )
• Remifentanil ideal for such cases
• Highly stimulating, often short procedure, not painful

• Pre-op Sleep Study
  Examination of the airway by the surgeon while patient is deeply asleep
  Combination of Midazolam / fentanyl / precedex /remifentanil /propofol
ENT and Airway

Awake intubation
Start 0.05ug/kg/min remi
In conjunction with midazolam / precedex / propofol and topicalization of the airway

• Anesthesia  2011, 66 pages 368-372
• R. Vennila et al
• Remifentanil as a sole agent to facilitate awake fiberoptic intubation in the absence of premedication

• Avoids LA toxicity and anaphylaxis
• Reduces loss of tone
• LA enhanced airway reflexes – laryngospasm / bronchospasm
awake intubation and remi

• Nasal cocaine 5%
• TCI remi (Minto – ESC)
• 1ng/cc with 0.5ng/cc increments

• Mean time to sedation 6.6 min
• Cet nasoscope 6.3 ng/cc
• Cet intubation 8.0 ng/cc

• 15/20 mild coughing
• 4/20 with no recall
Mersey regime

- bolus over 1-2 min 0.5 – 1.0 ug/kg
- bolus infusion 0.1ug/kg/min
- Increments of 0.05ug/kg/min
- Avg maintenance 0.25ug/kg/min
- Max 0.5-0.8 ug/kg/min

- Or

- TCI with CET
- Initial bolus 1.5 – 3 ng/cc
- Increments of 1 ng/cc
- Avg 5 ng/cc
- Max 8 ng/cc
Controlled hypotension has been used to reduce bleeding and the need for blood transfusions, and provide a satisfactory bloodless surgical field. It has been indicated in a variety of surgeries, including oromaxillofacial surgery, such as mandibular osteotomy and facial repair.\textsuperscript{1}

Controlled hypotension can be promptly achieved\textsuperscript{*} and sustained throughout surgery in patients undergoing maxillary and mandibular osteotomies receiving anaesthesia with remifentanil (U) in combination with either propofol (P), desflurane (D) or sevoflurane (S).\textsuperscript{2}

Intra-operative blood loss with these anaesthetic regimens was minimal and the operating field was judged to be excellent by the surgeons at all times based on the surgical field quality, blood loss and need for hypotensive drugs (see Table on the next slide).\textsuperscript{2}

\textsuperscript{*} Mean time to achieve controlled hypotension: U/P group 4 ± 1.8 min; U/D group 3.6 ± 1.7 min; U/S group 5 ± 2 min.

\begin{itemize}
\item Degoute CS. Drugs 2007; 67 (7): 1053-1076
\end{itemize}
Blood loss, surgical field quality and early recovery in patients undergoing maxillary and mandibular osteotomies.¹

<table>
<thead>
<tr>
<th></th>
<th>Group U/P (n = 40)</th>
<th>Group U/D (n = 40)</th>
<th>Group U/S (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss (mL)†</td>
<td>160 ± 39</td>
<td>156 ± 42</td>
<td>166 ± 40</td>
</tr>
<tr>
<td>Surgical field quality†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 = No bleeding</td>
<td>1.7 ± 0.3</td>
<td>1.6 ± 0.32</td>
<td>1.8 ± 0.28</td>
</tr>
<tr>
<td>2 = Mild bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 = Moderate bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 = Heavy but controllable bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 = Massive uncontrollable bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye opening (min)†</td>
<td>14.5 ± 3.4</td>
<td>7.3 ± 2†</td>
<td>13.8 ± 3.2</td>
</tr>
<tr>
<td>Squeeze fingers (min)†</td>
<td>15.2 ± 4</td>
<td>8 ± 3†</td>
<td>14.6 ± 3.8</td>
</tr>
<tr>
<td>Spontaneous breathing (min)†</td>
<td>11.2 ± 3.2</td>
<td>5 ± 2†</td>
<td>11 ± 3</td>
</tr>
<tr>
<td>Extubation (min)†</td>
<td>16 ± 3.3</td>
<td>8.3 ± 2†</td>
<td>15.2 ± 3.2</td>
</tr>
<tr>
<td>State name, birth date, age (min)†</td>
<td>17.8 ± 3.2</td>
<td>10 ± 2†</td>
<td>17 ± 3</td>
</tr>
</tbody>
</table>

Group U/P: propofol-Ultiva regimen; Group U/D: desflurane-Ultiva regimen; Group U/S: sevoflurane-Ultiva regimen.
† Values are mean ± SD;
‡p < 0.05 vs U/P and U/S groups.

Adapted from Caverni V et al 2005

Dental (maxillofacial)

- Controlled hypotension
- Less blood loss
- Controlled emergence and safer extubation
Cardiothoracic

- Tracheal Stents
- TIVA propofol/remifentanil
- Enhanced tolerance to airway manipulation
- Consistent anesthetic without pollution of unprotected airway by volatiles

- Cardiac
  - Mitral clips and TAVI
  - Mainly for tolerance of the TEE
  - Smooth hemodynamics
  - Smooth on table extubation

- CABG
  - Less fast-tracking of patients in Singapore – less need for remi
  - But allows for reduction of use of propofol - higher MAP
  - Cardiac preconditioning (1ug/kg bolus – 0.5ug/kg/min 30min pre-sternotomy
  - Plus usual 25ug/kg fentanyl total and propofol)
remifentanil in Cardiac Surgery (1 of 2)

- In patients undergoing minimally invasive coronary artery bypass surgery, an remi/propofol regimen offered shorter times to awakening and tracheal extubation ($p < 0.01$) compared to an alfentanil/propofol regimen.\textsuperscript{1}
- Remifentanil may be beneficial in patients undergoing coronary artery bypass graft (CABG) surgery by providing haemodynamic stability, reducing hypnotic drug requirements and attenuating the neurohumoral ‘stress response’.\textsuperscript{2,3}
- Despite having larger drug acquisition costs compared with fentanyl, remi does not increase the total hospital costs* associated with CABG surgery.\textsuperscript{2}

* Total hospital costs included the following cost categories: operating theatre, intensive care unit, ward nursing, pharmacy, imaging, pathology and an ‘other’ category, which included allied health and medical costs.

Intra-operative events and sedation drug requirements during CABG surgery.\(^1\)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group U (n = 29)</th>
<th>Group FLD (n = 24)</th>
<th>Group FMD (n = 24)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (mBP &gt; 90 mmHg)</td>
<td>2 (7%)</td>
<td>10 (42%)</td>
<td>9 (39%)</td>
<td>p ≤ 0.005</td>
</tr>
<tr>
<td>Hypotension (mBP &lt; 60 mmHg)</td>
<td>19 (66%)</td>
<td>6 (25%)</td>
<td>7 (30%)</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Tachycardia (HR &gt; 90 bpm)</td>
<td>12 (41%)</td>
<td>15 (63%)</td>
<td>9 (39%)</td>
<td>p = 0.20 (NS)</td>
</tr>
<tr>
<td>Bradycardia (HR &lt; 50 bpm)</td>
<td>5 (17%)</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
<td>p = 0.30 (NS)</td>
</tr>
<tr>
<td>Cortisol excretion (μmol/min)</td>
<td>0.2 (0.11–0.29)</td>
<td>1.5 (0.67–2.60)</td>
<td>0.29 (0.14–0.88)</td>
<td>U vs FLD p &lt; 0.0005, U vs FMD p = 0.21 (NS)</td>
</tr>
<tr>
<td>Average propofol infusion rate (mg/kg/h)</td>
<td>4.0 (3.6–4.3)</td>
<td>5.2 (4.4–5.7)</td>
<td>4.8 (3.9–5.2)</td>
<td>p ≤ 0.002</td>
</tr>
</tbody>
</table>

NS = not significant; Values are n (%) or median (interquartile range).
U = Ultiva \(0.83\) μg/kg/min; FLD = fentanyl bolus, small dose at 12 μg/kg; FMD = fentanyl bolus, moderate dose at 24 μg/kg.
mBP = mean blood pressure; HR = heart rate.
*Post hoc analysis

Patients undergoing carotid artery surgery under an remi-based regimen had more rapid recovery than those given a fentanyl-based regimen in regards to time to eye opening and time to extubation.\textsuperscript{1,2}

This accelerated recovery allows earlier neurological examination and is associated with rapid return of psychomotor and cognitive functions within the first hour after surgery.\textsuperscript{1}

Intra-operative haemodynamics were preserved in remi -treated patients undergoing carotid endarterectomy, and these patients had significantly fewer episodes of intra-operative hypertension than those receiving fentanyl (p <0.05).\textsuperscript{2}

Recovery times (min) after atropine-neostigmine administration in patients undergoing carotid endarterectomy:

- Time to spontaneous ventilation
- Time to eye opening
- Time to extubation

Recovery times (min) after atropine-neostigmine administration in patients undergoing carotid endarterectomy:

Ultiva (n = 34)

Fentanyl (n = 34)

P < 0.05

Adapted from Kostopanagiotou G et al., 2005

Pediatrics

• Intranasal use

• Sedation for drip setting or cooperation

• Improves intubation conditions


• Verghese et al

• 4μg/kg with Sevo 8% - excellent intubation conditions at 3 min
Obstetrics

- Journal of Obstetrics and Critical Care 2013 / 3/2/ 74-76
- Goudra and Singh
- Review on remifentanil in labour
- Can achieve high satisfaction but can be fraught with risks
- 4 cases of cardio-respiratory arrests
- Up to 10% risk of neonatal resp depression
- Requires strict protocol use
- Highly trained one to one monitoring with resus equipment readily available
- No other opioids within 6 hours of starting remifentanil
- Usual regime 20ug bolus q 3min lockout
Remifentanil and TCI*

- lack of any context sensitive half time.
- concentration will always half in 3-5 minutes independent of pathology
- if the infusion rate of remifentanil is increased, only 57% of the final concentration at the effect site is achieved after 5 minutes.
- infusion rate halved or doubled, then a stable, steady state is not achieved even after 15 minutes.
- pharmacokinetic variation with age and gender.
- 1 µg/kg remi to young, tall, slim female - peak blood concentration 13 ng/ml.
  - patient spon vent @ ESC of 2 ng/ml in about 4 minutes after
- 1 ug/kg to elderly obese short female - peak blood concentration 28 ng/ml
  - ESC of 2 ng/ml in 10 minutes after.
- greater sensitivity to remi in the elderly
- respiration may not start until the ESC 1 ng/ml in about 14 minutes after
- In anaesthesia, we wish to achieve the clinical effect as rapidly as possible so that we can titrate the drug to produce the optimum dose for the individual patient.
- rapid changes are obtained with TCI when increasing and decreasing the blood concentration and the system will achieve the most accurate and rapid change possible with the drug
- * Kenny GNC, The Society of Intravenous Anaesthesia
Post-Operative Recovery
Incidence of postoperative nausea and vomiting after paediatric strabismus surgery with sevoflurane or remifentanil–sevoflurane

A. Y. Oh, J. H. Kim, J. W. Hwang, S. H. Do and Y. T. Jeon*

Age 6-12

Sevo 1% with 50% N20 and remifentanil vs Sevo 2-3 % with 50% N20

Remifentanil 1ug/kg – 0.5ug/kg/min – 0.25ug/kg/min

No difference in nausea and vomiting
Ultiva. Provides a predictable and vital awakening

- Patients with PONV episodes up to 24 h post-operatively

ICU

• Analgesic based sedation
• Patient comfort, cooperative, better awareness of surroundings
• Reduction of time of mechanical ventilation
• Smoother extubation
• Precise analgesic control
• Use in renal/hepatic impairment
• Cost control
  • Reduced use of other sedatives
  • Reduced time on mechanical ventilation
  • Reduced time in ICU
Hyperalgesia

• For high dose remifentanil and prolonged infusions
• ATTenuated by ketamine, n20, propofol, Mgso4, paracetamol
• NSAID, COx2, beta blocker
Conclusions

- Mainstay of neuroanesthesia
- Very useful adjunct to ENT and airway
- Useful in other disciplines
- Fear of cost?
- Caution in hyperalgesia