Special Situations Amenable with TIVA
POSTOPERATIVE NAUSEA AND VOMITING
Smith I, Thwaites AJ. Anaesthesia 1999: 54; 745-52
SINGLE AGENT AMBULATORY ANAESTHESIA

Nausea
- Sevo 30%
- Prop 3%
- Prop 0%

Vomiting
- Sevo 17%
SINGLE AGENT AMBULATORY ANAESTHESIA

Mild

0%

0%

Prop 3%

Prop 0%

Prop 0%

Mod

Severe
SINGLE AGENT
AMBULATORY ANAESTHESIA

- Sevo 17%
- Prop 0%

Mild: Sevo 7%, Prop 3%
Mod: Sevo 17%, Prop 0%
Severe: Sevo 7%, Prop 0%
DAY CASE
(Ambulatory)
ANAESTHESIA
ANAESTHETIC TECHNIQUE

- no or minimal preoperative anxiety
- rapid onset and recovery
- minimal PONV
- how long before recovery is ‘safe’?
Blood alcohol concentration and psychomotor effects

Oral Dose

<table>
<thead>
<tr>
<th>Alcohol Group</th>
<th>Change in tracking performance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td>20 mg</td>
<td></td>
</tr>
<tr>
<td>50 mg</td>
<td></td>
</tr>
<tr>
<td>80 mg</td>
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</table>

Dose Levels:

- 20 mg
- 50 mg
- 80 mg

Change in tracking performance (%) range from -12 to 2.
Blood propofol concentration and psychomotor effects on driving skills

Deterioration in choice reaction time (ms)

Blood propofol concentration (µg.ml⁻¹)
Deterioration in 2\textsuperscript{nd} reaction time (ms)

Blood propofol concentration (µg.ml\textsuperscript{-1})
Secondary & Choice Reaction Time Deterioration (ms)

Alcohol Group (mg.100ml-1) & Propofol Group (µg.ml-1)
Propofol-Remifentanil Interaction

- Adequate anesthesia
- Awakening
Propofol-Remifentanil Interaction

- Adequate anesthesia
- Awakening
TIVA

THE FUTURE
FUTURE

- New drugs
- Closed loop system
- patient controlled sedation, analgesia or premedication
THRX-918661

a new hypnotic
in vivo activity of THRX-918661
a new hypnotic agent

- acts at the GABA<sub>A</sub> receptor
- produced hypnosis following iv bolus or infusion in rats, guinea-pigs, ferrets, cats, dogs and pigs
- rapid onset of action
- more rapid recovery profile than propofol
**in vivo activity of THRX-918661**

**Recovery**

- speed of recovery from hypnosis was unaffected by duration of infusion in rats
- suggests the compound has a short & constant context-sensitive half-time
- in contrast, recovery from propofol anaesthesia increased with the duration of the infusion
COMPUTER ASSISTED DRUG DELIVERY

- **Open Loop**
  - system has no sensor
  - use predictive mathematical models

- **Closed Loop**
  - system measures the signal being controlled
  - automatic drug infusion to maintain the signal close to the set point
CLOSED-LOOP
CONTROL SYSTEMS
BENEFITS of AUTOMATION

- aim is to improve patient care
- relate delivery of a drug or therapy directly to the requirements of the individual patient
- remove any observer bias in research
COMPONENTS OF A CLOSED-LOOP SYSTEM

- input signal
- comparator
- output device
INPUT SIGNAL

- the most important feature of any automated drug control system
- requires good artefact rejection
- signal response must be sufficiently rapid
APPLICATIONS OF CLOSED-LOOP CONTROL SYSTEMS

- blood pressure
- neuromuscular blockade
- general anaesthesia
- patient controlled analgesia
CLOSED-LOOP CONTROL OF PROPOFOL ANAESTHESIA

100 patients breathing spontaneously during body surface surgery

BP & HR

Before induction
5 min. post-induction
10 min. post-induction
10 min. pre-incision
5 min. post-incision
0-5 min. post-incision
10 min. post-incision
15 min. post-incision
20 min. post-incision
20 min. pre-recovery
15 min. pre-recovery
10 min. pre-recovery
0-5 min. pre-recovery
<table>
<thead>
<tr>
<th>Target ±</th>
<th>AEPex</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 %</td>
<td>65</td>
</tr>
<tr>
<td>10 %</td>
<td>90</td>
</tr>
<tr>
<td>15 %</td>
<td>99</td>
</tr>
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</table>
QUALITY OF CONTROL AS A PERCENTAGE OF TOTAL CLAN TIME

<table>
<thead>
<tr>
<th>Target ±</th>
<th>AEPex</th>
<th>BIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 %</td>
<td>65</td>
<td>34</td>
</tr>
<tr>
<td>10 %</td>
<td>90</td>
<td>57</td>
</tr>
<tr>
<td>15 %</td>
<td>99</td>
<td>75</td>
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</table>
PATIENT-CONTROLLED SYSTEMS
POSTOPERATIVE ANALGESIA

- patient controlled analgesia is a form of closed-loop control
- PCA is used widely
- perceived benefits for patient & staff
Postoperative analgesia using a computerised infusion of alfentanil following aortic bifurcation graft surgery

Davies FW, White M and Kenny GNC.

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<tbody>
<tr>
<td>Hours</td>
<td>27.6</td>
<td>10.0</td>
<td>1.4</td>
<td>0.05</td>
</tr>
<tr>
<td>Range</td>
<td>(2.8-41.8)</td>
<td>(0.25-24.25)</td>
<td>(0-10)</td>
<td>(0-0.25)</td>
</tr>
</tbody>
</table>
Patient Maintained Analgesia With Target Controlled Alfentanil Infusion After Cardiac Surgery: a Comparison With Morphine PCA

Checketts M, Gilhooly, CJ and Kenny GNC.

Br J Anaesth 1998; 80; 748-751
Extubation Times (min)
Alfentanil vs Morphine
Median Post Operative Pain Scores (VAS)

0hrs | 4hrs | 8hrs | 12hrs | 16hrs | 20hrs | 24hrs

Alfentanil
Morphine
Overall Patient Satisfaction

Alfentanil vs Morphine

<table>
<thead>
<tr>
<th>Quality</th>
<th>Alfentanil</th>
<th>Morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>61%</td>
<td>30%</td>
</tr>
<tr>
<td>Good</td>
<td>47%</td>
<td>35%</td>
</tr>
<tr>
<td>Satisfactory</td>
<td>7%</td>
<td>14%</td>
</tr>
<tr>
<td>Poor</td>
<td>2%</td>
<td>4%</td>
</tr>
</tbody>
</table>

% of Patients
Alfentanil Target Concentrations Requested by 10 of 52 Patients
REMIFENTANIL
-
the A-A gradient
Apnoea - Agony gradient
POSTOPERATIVE REMIFENTANIL INFUSION

Side-effects

- Apnoea 13%
- Rigidity 8%

Schüttler et al, 1997
POSTOPERATIVE REMIFENTANIL INFUSION

Side-effects

- Apnoea 13% 7%
- Rigidity 8%

Schüttler et al, 1997
Bowdle et al, 1996
POSTOPERATIVE REMIFENTANIL INFUSION

Side-effects

- Apnoea 13% 7% 4%
- Rigidity 8% 1%

Schüttler et al, 1997
Bowdle et al, 1996
Yarmush et al, 1997
Comparison of remifentanil and alfentanil in patients undergoing major abdominal surgery

LIFE THREATENING ADVERSE EVENTS

- 22 life-threatening events in 10 patients
- muscle rigidity and apnoea
- related to bolus doses, rapid increases in infusion rate, drug concentration
Patient-Maintained Target Controlled Remifentanil for the Transition to Early Postoperative Analgesia

Schraag S, Kenny GN, Mohl U, Georgieff M

British Journal of Anaesthesia 1998; 81: 365-8
Remifentanil Targets at Spontaneous Respiration and Adequate Analgesia
Target Remifentanil Concentrations Associated With Adequate Analgesia
CLOSED LOOP ANAESTHESIA FOR RESEARCH
PROPOFOL SPARING EFFECT OF
REMIFENTANIL
USING CLOSED-LOOP
ANAESTHESIA

Milne S, Kenny GNC, Schraag S.

Propofol-Remifentanil Interaction

Blood propofol (µg/ml)

Plasma remifentanil (ng/ml)

- Adequate anesthesia
- Awakening

Milne, Kenny & Schraag

3.0
3.5
4.9
PATIENT MAINTAINED
SEDATION
Midazolam 2mg bolus (peak effect at 13mins)

Propofol 20mg bolus (peak effect at 4mins)
Midazolam 0.05 mg/kg + 0.025 mg/kg x 2
Sedation with propofol during surgery under local blockade
Assessment of a target-controlled infusion system

Skipsey IG, Colvin JR, Mackenzie N & Kenny GN.

Anaesthesia 48:210-213, 1993
TCI FOR SEDATION UNDER LOCAL BLOCK

- 40 patients to have orthopaedic surgery performed under spinal block
- Premedicated with temazepam 20-30 mg
- Median target concentration required was 0.9 µg/ml (range 0.15-2.6)
- 87% of time spent at the desired level of sedation
TCI FOR SEDATION UNDER LOCAL BLOCK

- '...functions satisfactory in the clinical situation'
- 'allows rapidly titratable sedation to be achieved without undue oversedation.'
Propofol for sedation during endoscopy

assessment of a computer-controlled infusion system

Church JA, Stanton PD, Kenny GN & Anderson JR.

TCI FOR SEDATION DURING GASTROSCOPY

- Initial target selected of 1.5 µg/ml blood propofol concentration
- Increased by 0.5 µg/ml every 30s until the patient's speech became slurred
- Median target required was 2.5 µg/ml (range 1.5-4.0)
PROPOFOL CONCENTRATIONS REQUIRED FOR:

ANAESTHESIA

SEDATION
Patient-maintained propofol sedation as a premedication in day case surgery

Assessment of a target-controlled system

VAS - ANXIETY STATE
0 and 15 minutes

Anxiety State Score

Patient Number
PATIENT CONTROLLED TCI
PROPOFOL PREMEDICATION

Propofol target needed for maximal anxiolysis

Target propofol concentration (µg/ml)

Frequency
A partially blinded randomised controlled trial of patient maintained propofol sedation and operator controlled midazolam sedation in third molar extractions

Results - Anxiolysis

Reduction in VAS (100 mm) after sedation and before injection of LA (p=0.01)

- Midazolam – 11mm
- Propofol – 21mm
PSYCHOMOTOR PERFORMANCE

Digit Symbol Substitution Task

**Midazolam**

**Propofol**

**Pre-op**
(p=0.29)

**Pre-LA**
(p<0.001)

**Post-op**
(p=0.003)
Propofol vs Midazolam

- safety at least as good if not better
- efficacy better in terms of anxiolysis and caused less memory loss
- time to sedation longer but overall time to discharge less by ~6 minutes
- psychomotor skills retained better
- patient satisfaction at least as good
- better control of duration of sedation