Esmolol and its Anesthetic Implications

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York College of Pennsylvania / Wellspan Health NAP
Role of Esmolol in Perioperative Analgesia and Anesthesia: A Literature Review

Megan Harless, CRNA, MSN
Caleb Depp, CRNA, MSN
Shawn Collins, CRNA, DNP, PhD
Ian Hewer, CRNA, MSN, MA

Use of opioids to provide adequate perioperative analgesia often leads to respiratory depression, nausea, vomiting, urinary retention, pruritus, and opioid-induced hyperalgesia, with the potential to increase length of stay in the hospital. In an effort to reduce perioperative opioid administration yet provide appropriate pain relief, researchers began to study the use of esmolol beyond its well-known cardiovascular effects. Perioperative esmolol has been shown to reduce anesthetic requirements, decrease perioperative opioid use, decrease the incidence of postoperative nausea and vomiting, lead to an earlier discharge, and increase patient satisfaction. This article provides a review of the literature on the use of esmolol as an adjunct for perioperative analgesia and anesthesia.

Keywords: Esmolol, opioid sparing, perioperative analgesia and anesthesia.
Opioid Side Effects

Central:
- Hallucination
- Confusion
- Fainting
- Dizziness
- Loss of appetite
- Lightheadedness
- Drowsiness
- Headache
- Mood changes

Skin:
- Hives
- Rash
- Flushing
- Sweating
- Itching

Respiratory:
- Difficulty breathing
- Slowed breathing

Intestinal:
- Constipation

Addiction

Eyes:
- Swelling
- Smaller pupil
- Redness

Mouth, tongue or lips:
- Swelling
- Dryness

Face:
- Swelling

Throat:
- Hoarseness
- Swelling
- Difficulty swallowing

Heart:
- Fast or slow heartbeat

Muscular:
- Seizures
- Weakness

Gastric:
- Nausea
- Vomiting

Hands, feet, ankles, or lower legs:
- Swelling
Objectives

• Discuss the research and evidence on esmolol’s use as an adjunct to anesthesia

• Describe the proposed physiology and pharmacology of how esmolol may reduce anesthetic and analgesic requirements in patients undergoing general anesthesia.

• Identify patient population and procedure types in which esmolol may be useful as an adjunct.

• Determine appropriate methods of administering esmolol and address economic considerations.
Pharmacology

• Ultra-short acting cardioselective $\beta_1$-receptor antagonist
  o 34 times higher affinity for $\beta_1$ then $\beta_2$-receptor

• Loading Dose – 0.5 - 1 mg/kg

• Infusion Rate – 50 - 300mcg/kg/min

• Rapid onset and short duration
  o Peak hemodynamic effects 6-10 min
  o Distribution half life – 2 minutes
  o Elimination half life – 9 minutes
  o 55% Protein bound

• Hydrolyzed by esterases within the cytosol of RBCs

• Renal excretion of inactive metabolite (1/1500th potency)
Pharmacology

• (Classic) Clinical Indications
  o Supraventricular Tachycardia (Slows AV Node Conduction)
  o Torsade de pointes control in patients with prolonged QTc intervals
  o Medical treatment of Aortic Aneurysm or Dissection
  o Hypertensive emergency
  o Blunt stress response to laryngoscopy & intubation
  o Intraoperative and postoperative tachycardia and hypertension

• Contraindications
  o Heart block
  o Heart Failure
  o WPW
  o Severe pulmonary disease (COPD, asthma)
  o Bradycardia and hypotension not caused by RVR
  o Pheochromocytoma in absence of alpha-blockade
Multimodal Analgesia
Propofol Anesthesia

• Propofol Induction
  o 25% reduction in dose required for loss of response to command (Wilson et al. 2004)

• Maintenance of anesthesia
  o 26% reduction in propofol concentration to prevent movement in propofol / nitrous oxide / morphine based anesthesia (Johansen et al. 1998)

• Some authors attribute this to the reduction in cardiac output, redistribution rate, and reduced hepatic clearance of concurrently administered anesthetics and analgesics.
β-Blocker Effects on Pharmacokinetics

- Arm-To-Brain Circulation Time
- Cardiac output inversely related to arterial plasma concentration
- Reduced rate of redistribution
- Reduced hepatic clearance
MAC Requirements
Role of β-blockade in anaesthesia and postoperative pain management after hysterectomy

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Table 1 Patients and surgical characteristics included in the study (n=97). Values are mean (range), mean (SD) or number. The two groups were similar for all values tested; only maintained isoflurane concentration and fentanyl used showed significant differences

<table>
<thead>
<tr>
<th></th>
<th>Esmolol group</th>
<th>Control group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>49</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Age (yr) (range)</td>
<td>48.5 (30–79)</td>
<td>49.8 (27–75)</td>
<td>0.263</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>57.4 (7.2)</td>
<td>61.3 (10.6)</td>
<td>0.436</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>153.6 (5.4)</td>
<td>155.6 (4.4)</td>
<td>0.591</td>
</tr>
<tr>
<td>ASA (I/II)</td>
<td>21/28</td>
<td>24/24</td>
<td>0.481</td>
</tr>
<tr>
<td>Total esmolol (mg)</td>
<td>375.4 (143.2)</td>
<td>–</td>
<td>0.835</td>
</tr>
<tr>
<td>Total blood loss (ml)</td>
<td>421 (375)</td>
<td>325 (308)</td>
<td>0.917</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>122 (54)</td>
<td>138 (50)</td>
<td></td>
</tr>
<tr>
<td>Maintained isoflurane (%)</td>
<td>1.0 (0.3)</td>
<td>1.4 (0.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fentanyl used (µg kg⁻¹)</td>
<td>0.9 (0.2)</td>
<td>1.2 (0.5)</td>
<td>0.006</td>
</tr>
<tr>
<td>Number of patients needed ephedrine</td>
<td>1</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>Number of patients needed atropine</td>
<td>2</td>
<td>0</td>
<td>0.495</td>
</tr>
</tbody>
</table>
Intraoperative Esmolol Infusion in the Absence of Opioids Spares Postoperative Fentanyl in Patients Undergoing Ambulatory Laparoscopic Cholecystectomy

Vincent Collard, MD*
Giovanni Mistaletti, MD*
Ali Taqi, MD†
Juan Francisco Asenjo, MD*
Liane S. Feldman, MD†
Gerald M. Fried, MD†
Franco Carli, MD, MPhil*

BACKGROUND: The use of opioids during ambulatory surgery can delay hospital discharge or cause unexpected hospital admission. Preliminary studies using an intraoperative continuous infusion of esmolol in place of an opioid have inconsistently reported a postoperative opioid-sparing effect. In this study, we compared esmolol versus either intermittent fentanyl or continuous remifentanil on postoperative opioid-sparing, side effects, and time of discharge.

METHODS: Ninety patients (consisting of three groups) were enrolled in this prospective, randomized, and observer-blinded study. The control group (n = 30) received intermittent doses of fentanyl, the esmolol group (n = 30) received a continuous infusion of esmolol (5–15 \( \mu g \cdot kg^{-1} \cdot min^{-1} \)) and no supplemental opioids during surgery, and the remifentanil group (n = 30) received a continuous infusion of remifentanil (0.1–0.5 \( \mu g \cdot kg^{-1} \cdot min^{-1} \)). General anesthesia was standardized, and adjuvant medications included acetaminophen, ketorolac, local anesthetics in the skin incisions, dexamethasone, and droperidol. Postoperative analgesia included fentanyl.
### Esmolol in Absence of Opioids

<table>
<thead>
<tr>
<th>Control</th>
<th>Esmolol</th>
<th>Remifentanil</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Fentanyl 1 mcg/kg with induction</td>
<td>- Esmolol 1 mg/kg with induction</td>
<td>- Remi 1 mcg/kg with induction</td>
</tr>
<tr>
<td>- Fentanyl boluses 50mcg to keep HR within 20% of base</td>
<td>- Esmolol gtt 5-15 mcg/kg/min titrated to keep HR within 20% of base</td>
<td>- Remi gtt 0.1 – 0.5 mcg/kg/min titrated to keep HR within 20% of base</td>
</tr>
</tbody>
</table>

### Desflurane Requirements

- Titrated to keep BP within 20% of baseline and BIS < 60.
- 4 – 8% to maintain a MAC between 0.7 and 1.2

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Remifentanil</th>
<th>Esmolol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.93 ± 0.4</td>
<td>0.89 ± 0.3</td>
<td>0.95 ± 0.4</td>
</tr>
</tbody>
</table>

Collard et al. (2007)
Demographics were similar between groups

All patients received multimodal analgesia and PONV prophylaxis
  o  Acetaminophen 1.3g PR
  o  Ketorolac 30 mg
  o  Bupivacaine 0.25%/epi injected at incision sites
  o  Dexamethasone 8 mg IV
  o  Droperidol 0.625 mg
Esmolol in Absence of Opioids

<table>
<thead>
<tr>
<th></th>
<th>Control n = 27</th>
<th>Esmolol n = 30</th>
<th>Remifentanil n = 28</th>
<th>3 groups</th>
<th>Cont versus Esm</th>
<th>Cont versus Remi</th>
<th>Esm versus Remi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount of fentanyl used (μg)</td>
<td>168.1 ± 96.8 (155)</td>
<td>91.5 ± 42.7 (100)</td>
<td>237.8 ± 54.7 (238)</td>
<td>0.0001</td>
<td>0.0010</td>
<td>0.0036</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nausea in recovery room: n (%)</td>
<td>18 (66.7)</td>
<td>9 (30.0)</td>
<td>19 (67.9)</td>
<td>0.004</td>
<td>0.006</td>
<td>0.925</td>
<td>0.004</td>
</tr>
<tr>
<td>Use of ondansetron: n (%)</td>
<td>18 (66.7)</td>
<td>7 (23.3)</td>
<td>20 (71.4)</td>
<td>0.001</td>
<td>0.002</td>
<td>0.702</td>
<td>0.001</td>
</tr>
<tr>
<td>No. of patients requiring ondansetron(0/4/8 mg)</td>
<td>9/5/13</td>
<td>23/6/1</td>
<td>8/9/11</td>
<td>0.0003</td>
<td>0.0002</td>
<td>0.8146</td>
<td>0.0001</td>
</tr>
<tr>
<td>No. of patients with White-Song score &gt;12 at 1st/30th/60th/90th min or more</td>
<td>16/6/0/5</td>
<td>21/4/3/2</td>
<td>9/8/6/5</td>
<td>0.0409</td>
<td>0.3563</td>
<td>0.0963</td>
<td>0.0060</td>
</tr>
<tr>
<td>Time from arrival to the PACU to discharge home (min)</td>
<td>180 (130–210)</td>
<td>120 (100–150)</td>
<td>162.5 (110–220)</td>
<td>0.0033</td>
<td>0.0006</td>
<td>0.3900</td>
<td>0.0367</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation (median), absolute number (percentage), relative number of patients, or median (interquartile range).

P values are calculated with ANOVA one-way analysis of variance with Scheffé test for the parametric normally distributed variables, Pearson χ² test for categorical variables, Kruskal–Wallis ranked sum test for comparisons among groups for the parametric not-normally distributed variables and Wilcoxon test between groups for the parametric not-normally distributed variables. Regarding the comparison among the three groups, the Bonferroni correction was used, with the significant value set at P < 0.017. Highlighted in bold are the significant differences among or between groups.

Collard et al. (2007)
### Table 4. Postoperative Day 1 Clinical Data

<table>
<thead>
<tr>
<th></th>
<th>Control ( n = 27 )</th>
<th>Esmolol ( n = 30 )</th>
<th>Remifentanil ( n = 28 )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRS score at 24 h from discharge</td>
<td>3 (2–4)</td>
<td>2 (1–3)</td>
<td>3 (1.75–4)</td>
<td>0.2790</td>
</tr>
<tr>
<td>PONV next day: n (%)</td>
<td>6 (22.2)</td>
<td>4 (16.0)</td>
<td>5 (17.9)</td>
<td>0.589</td>
</tr>
<tr>
<td>Tylenol next day: n (%)</td>
<td>16 (59.3)</td>
<td>16 (53.3)</td>
<td>15 (53.6)</td>
<td>0.990</td>
</tr>
<tr>
<td>Tylenol next day (mg)</td>
<td>987.5 (650–1300)</td>
<td>812.5 (575–1300)</td>
<td>1150 (650–2275)</td>
<td>0.4881</td>
</tr>
<tr>
<td>Naproxen next day: n (%)</td>
<td>8 (29.6)</td>
<td>9 (30.0)</td>
<td>7 (25.0)</td>
<td>0.878</td>
</tr>
<tr>
<td>Naproxen next day (mg)</td>
<td>875 (500–1000)</td>
<td>1000 (500–1000)</td>
<td>750 (500–1000)</td>
<td>0.7399</td>
</tr>
<tr>
<td>Morphine equivalent next day: n (%)</td>
<td>17 (63.0)</td>
<td>21 (70.0)</td>
<td>17 (60.7)</td>
<td>0.519</td>
</tr>
<tr>
<td>Morphine equivalent next day (mg)</td>
<td>60 (30–80)</td>
<td>40 (20–63)</td>
<td>50 (36–80)</td>
<td>0.4106</td>
</tr>
</tbody>
</table>

Values are presented as median (interquartile range), or absolute number (percentage).

\( P \) values are calculated with Pearson \( \chi^2 \) test for categorical variables, and Kruskal-Wallis ranked sum test for parametric not-normally distributed variables; significant values are with \( P < 0.017 \) (Bonferroni correction).

VRS = Verbal Rating Scale for pain; PONV = Postoperative nausea and vomiting.
Beta-adrenergic antagonists during general anesthesia reduced postoperative pain: a systematic review and a meta-analysis of randomized controlled trials

Lasse Härkänen¹,² · Jari Halonen² · Tuomas Selander³ · Hannu Kokki¹

Received: 9 March 2015 / Accepted: 21 June 2015 © Japanese Society of Anesthesiologists 2015

<table>
<thead>
<tr>
<th>Study Author(s)</th>
<th>Study Design</th>
<th>Procedure</th>
<th>Intervention</th>
<th>Control</th>
<th>Outcome</th>
<th>p Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sale-Ahmed [18]</td>
<td>Double-blinded, active control, n = 60</td>
<td>Laparoscopic inguinal hernia repair</td>
<td>Esmolol 1 mg/kg + 5–15 µg/kg/min vs. fentanyl 1 µg/kg + 50 µg/kg per 30 min</td>
<td>Fentanyl 2.4 (µg)</td>
<td>65 vs. 100%; p = 0.0032</td>
<td>8/8</td>
<td></td>
</tr>
<tr>
<td>Ozturk et al. [11]</td>
<td>Double-blinded, placebo-control, n = 40</td>
<td>Laparoscopic cholecystectomy</td>
<td>Esmolol 1 mg/kg + 5–10 µg/kg/min vs. Ringer’s lactate</td>
<td>Need for rescue analgesia/24 h (%)</td>
<td>65 vs. 100%; p = 0.0032</td>
<td>3/5</td>
<td></td>
</tr>
<tr>
<td>Chia [5]</td>
<td>Double-blinded, placebo-control, n = 97</td>
<td>Abdominal hysterectomy</td>
<td>Esmolol 0.5 mg/kg + 50 µg/kg/min vs. saline</td>
<td>Morphine/72 h (mg)</td>
<td>37 vs. 55%; p &lt; 0.05</td>
<td>5/5</td>
<td></td>
</tr>
<tr>
<td>Coloma [13]</td>
<td>Double-blinded, active control, n = 53</td>
<td>Laparoscopic tubal ligation</td>
<td>Esmolol 1 mg/kg + 5–15 µg/kg/min vs. remifentanil 1 µg/kg + 25–125 ng/kg/min</td>
<td>Need for rescue hydrocortisone/24 h (%)</td>
<td>52 vs. 23%; p &lt; 0.05</td>
<td>3/5</td>
<td></td>
</tr>
<tr>
<td>Smith [17]</td>
<td>Double-blinded, active control, n = 97</td>
<td>Arthroscopic surgery</td>
<td>Esmolol 2 mg/kg + 25–100 µg/kg/min vs. alfentanil 16 µg/kg + 0.8 µg/kg/min</td>
<td>Need for rescue analgesia (%)</td>
<td>57 vs. 34%; p &lt; 0.05</td>
<td>4/5</td>
<td></td>
</tr>
</tbody>
</table>

PACU post-anesthesia care unit

¹ Mean value
² Median value

Härkänen et al. (2015)
Physiology and Pharmacology
Theories Behind the Mechanism of Action

1. Reduced redistribution rate and hepatic blood flow resulting in the slowed extraction of drugs

2. Improved intraoperative hemodynamics resulting in reduced opioid administration – attenuation of opioid induced hyperalgesia (OIH) and tolerance

3. Non-$\beta_1$-receptor mediated increase in inhibitory signals in the substantia gelatinosa

4. Blockade of voltage gated Na+ Channel

5. Reduced catecholamine induced inflammation and sensitization of nociceptors
Antinociceptive and cardiovascular properties of esmolol following formalin injection in rats

Elyad M. Davidson MD, Marie-Françoise Doursout PhD, Peter Szmuk MD, Jacques E. Chelly MD PhD MBA

Purpose: To assess the role of esmolol, a β₁ receptor blocker, in the modulation of pain in the absence of anesthesia.

- 25 Rats divided into three groups
  - (n = 9) Saline treated
  - (n = 7) Esmolol low – 150 mg/kg bolus followed by 40 mg/kg/hr
  - (n = 9) Esmolol high – 600 mg/kg bolus followed by 150 mg/kg/hr
- Formalin 5% was injected into rats’ hind paw to induce pain
- Measurements of paw lifting occurred in 5 minute intervals over 35 minutes

Davidson et al (2001)
Antinociception Properties of Esmolol

**FIGURE 1** Paw lifting time following saline (n=9), esmolol low (n=7) and esmolol high (n=9) in rats subjected to formalin injection. Data are presented in actual changes from ST (mean ± SEM); ST = steady state
*P < 0.05 vs ST. †P < 0.05 vs saline. ‡P < 0.05 vs esmolol low

**FIGURE 2** Cumulative paw lifting time in (early, 0-5 min) Phase 1 and paw lifting time in (late, 10-35 min) Phase 2 following saline (n=9), esmolol low (n=7) and esmolol high (n=9) in rats subjected to formalin injection; ST = steady state
*P < 0.05 vs saline

Davidson et al (2001)
Theories Behind the Mechanism of Action

1. Reduced redistribution rate and hepatic blood flow resulting in the slowed extraction of drugs

2. Improved intraoperative hemodynamics resulting in reduced opioid administration – attenuation of opioid induced hyperalgesia (OIH) and tolerance

3. Non-β₁-receptor mediated increase in inhibitory signals in the substantia gelatinosa

4. Blockade of voltage gated Na⁺ Channel

5. Reduced catecholamine induced inflammation and sensitization of nociceptors
Opioid Induced Hyperalgesia (OIH) and Opioid Tolerance

• Pneumoperitoneum causes the release of catecholamines and hormones such as NE, epi, renin, and ADH.
• Opioids inhibit the hypothalamic sympatho-adrenal response to pain
• Opioids do not, however, prevent local NE release in response to pneumoperitoneum
• Beta-blockers reduce intra-operative opioid requirements by improving autonomic stability

• Could we be blunting this physiologic response with adrenergic antagonists rather then opioids?

Conclusion: These data suggest that esmolol modulates inhibitory transmitter release in the Sp5c through a mechanism involving Ca2+ entry but in a β1-adrenoceptor-independent manner. The present results suggest that the facilitation of inhibitory transmitter release in the central nociceptive network underlies, at least in part, the antinociceptive effect of esmolol.
Esmolol vs. Control

Yasui et al. (2011)
Esmolol + or – β-agonist

A: isoproterenol (-)

B: isoproterenol (+)

Yasui et al. (2011)
Conclusion: Esmolol, but not landiolol, may have useful effects against pain related to TTX-r Na+ channel activity.
Reduced Peripheral Inflammation

Li et al. (2013)
The immunomodulatory role of esmolol in patients undergoing laparoscopic gastrectomy due to gastric cancer

Cytotoxic T cell Activation and Action

The Effects of Intraoperative Esmolol Administration on Perioperative Inflammatory Responses in Patients Undergoing Laparoscopic Gastrectomy: A Dose–Response Study

Yongsuk Kim, MD¹, Wonjung Hwang, MD¹, Mi-La Cho, PhD¹, Yang-Mi Her¹, Seulgi Ahn, MD¹, and Jaemin Lee, MD, PhD¹

Kim et al. (2015)
Clinical Impact of Selective and Nonselective Beta-Blockers on Survival in Patients With Ovarian Cancer

Median Survival
None 34 mo
β₁-selective 38 mo
Non-selective 90 mo

Using β-blockers to inhibit breast cancer progression

Desmond G. Powe and Frank Entschladden

Practice points

- Norepinephrine mediates prometastatic cell signaling in cancer cells by activating adrenergic receptors
- Laboratory research has identified a biological mechanism by which β-blockers inhibit cell migration and metastasis
- Three recent population studies show a protective role against disease progression of β-blockers prescribed during breast cancer treatment
- β-blockers are safe and cost-effective drugs that are very unlikely to cause cancer

Figure 1 | By binding to specific adrenergic receptors, β-blockers inhibit cancer cell migration and metastasis, suggesting a novel targeted therapeutic application in protecting against breast cancer disease progression.
The Role of the Perioperative Period in Recurrence After Cancer Surgery

Antje Gottschalk, MD,*† Sonal Sharma, MD,* Justin Ford, MD,* Marcel E. Durieux, MD, PhD,* and Mohamed Tiouririne, MD*
“The tantalizing possibility that anaesthetic care of the surgical oncology patient might affect long term oncologic outcome remains unproven speculation, awaiting prospective human study.”
However, there were more deaths in the metoprolol group than in the placebo group (120 [3.1%] vs 97 [2.3%] patients; 1.33, 1.03 - 1.74; p=0.0317). More patients in the metoprolol group than in the placebo group had a stroke (41 [1.0%] vs 19 [0.5%] patients; 2.17, 1.26-3.74; p=0.0053).

**Interpretation** Our results highlight the risk in assuming a perioperative β-blocker regimen has benefit without substantial harm, and the importance and need for large randomised trials in the perioperative setting. Patients are unlikely to accept the risks associated with perioperative extended-release metoprolol.
# The Safety of Perioperative Esmolol: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Savio K. H. Yu, BHSc, Gordon Tait, PhD, Keyvan Karkouti, MD, MSc, FRCPC, Duminda Wijeysundera, MD, FRCPC, Stuart McCluskey, MD, PhD, FRCPC and W. Scott Beattie, MD, PhD, FRCPC

## Table 2. Details of Reported Outcomes

<table>
<thead>
<tr>
<th>Outcome (study reference no.)</th>
<th>Studies</th>
<th>Events</th>
<th>Number of patients</th>
<th>Effect estimate (95% CI)</th>
<th>P value</th>
<th>I²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradycardia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (15–83)</td>
<td>67</td>
<td>56</td>
<td>3766</td>
<td>1.30 (0.8, 2.2)</td>
<td>0.493</td>
<td>0</td>
</tr>
<tr>
<td>Bolus (15, 16, 19, 21–24, 26, 28, 29, 30, 33, 37–39, 41–45, 50, 57, 63, 65, 66, 67–69, 72, 73, 74, 80, 81)</td>
<td>33</td>
<td>37</td>
<td>2317</td>
<td>1.35 (0.7, 2.6)</td>
<td>0.727</td>
<td>0</td>
</tr>
<tr>
<td>Infusion (17, 20, 25, 27, 31, 32, 34–36, 40, 46–49, 51–56, 58, 59, 61–62, 64, 70, 71, 75–79, 82, 83)</td>
<td>34</td>
<td>19</td>
<td>1449</td>
<td>1.23 (.41, 18)</td>
<td>0.661</td>
<td>0</td>
</tr>
<tr>
<td>Hypotension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (15–82)</td>
<td>67</td>
<td>237</td>
<td>3766</td>
<td>1.48 (1.2, 1.8)</td>
<td>0.0001</td>
<td>0</td>
</tr>
<tr>
<td>Bolus (15, 16, 19, 21–24, 26, 28, 29, 30, 33, 37–39, 41–45, 50, 57, 63, 65, 66, 67–69, 72, 73, 74, 80, 81)</td>
<td>33</td>
<td>214</td>
<td>2317</td>
<td>1.49 (1.2, 1.9)</td>
<td>0.0001</td>
<td>0</td>
</tr>
<tr>
<td>Infusion (17, 20, 25, 27, 31, 32, 34–36, 40, 46–49, 51–56, 58, 59, 61–62, 64, 70, 71, 75–79, 82, 83)</td>
<td>34</td>
<td>23</td>
<td>1449</td>
<td>1.31 (0.6, 3.0)</td>
<td>0.781</td>
<td>0</td>
</tr>
</tbody>
</table>

**Studies reporting myocardial ischemia**

| Overall | 7 | 48 | 427 | 0.17 (0.02, 0.45) | 0.002 | 21% |
| Bolus (42, 79) | 2 | 7  | 105 | 0.13 (0.03, 0.85) | 0.03  |    |
| Infusion (17, 25, 27, 58, 61) | 5 | 31  | 297 | 0.29 (0.12, 0.74) | 0.04  | 51% |

**Studies reporting on myocardial infarction**

| Overall | 7 | 6  | 297 | 0.30 (0.06, 1.55) | 0.15  | 0   |
| Bolus   |   |    |     |      |       |     |
| Infusion| 7 | 6  | 297 | 0.30 (0.06, 1.55) | 0.15  | 0   |

All studies were used to determine the incidence of hypotension and bradycardia. Kindler et al.\textsuperscript{21} is counted as 2 studies; 2 doses of esmolol were compared with control. Not all studies reported data on myocardial ischemia and infarction, and thus only those reporting on the event were included. CI = confidence interval.
Meta-analysis of 67 articles evaluating esmolol infusion

- Increased incidence of unplanned hypotension that occurred in a dose-dependent manner.
- Reduced risk when given as an infusion.
- Reduced risk of myocardial ischemia when titrated to hemodynamic end points.
- Very few studies address safety in higher-risk patients (ASA III and IV).
- More studies need to be performed to investigate safety of esmolol.

Safety Concerns

Yu et al. (2011)
Pharmacoeconomics

Esmolol 100mg/10cc
• $17.26

<table>
<thead>
<tr>
<th></th>
<th>Bolus</th>
<th>Infusion</th>
<th>Vial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5 mg/kg</td>
<td>5 - 15 mcg/kg/min</td>
<td>100 mg / 10cc</td>
</tr>
</tbody>
</table>

Weight 70 kg
Bolus 35 mg
Infusion 21 - 63 mg/hr
Duration 1 - 3 hours

Plan on 2nd Vial for:
Patients > 90 - 100 kg or
Surgeries > 2 - 3 hours

Zofran 4mg vial
• $0.56

Fentanyl 100mcg
• $1.92

Ketamine 500mg/10cc
• $4.28

Scopolamine 1 patch
• $21.40

Ofirmev 1000mg
• $42.48

Precedex 200mcg/2ml vial
• $47.52

Remifentanil 1mg vial
• $67.48

Based on AWP on 03/06/16 from http://online.lexi.com/action/home
Guidelines on the Management of Postoperative Pain

Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists’ Committee on Regional Anesthesia, Executive Committee, and Administrative Council

Roger Chou, † Debra B. Gordon, † Oscar A. de Leon-Casasola, † Jack M. Rosenberg, § Stephen Bickler, ¶ Tim Brennan, ‡ Todd Carter, ** Carla L. Cassidy, †† Eva Hall Chittenden, †† Ernest Degenhardt, §§ Scott Griffith, ††† Renee Manworren, †††† Bill McCarberg, †††† Robert Montgomery, †††† Jamie Murphy, ††††† Melissa F. Perkal, ††††† Santhanam Suresh, ††††† Kathleen Sluka, ††††† Scott Strassels, ††††† Richard Thirlby, ††††† Eugene Viscusi, ††††† Gary A. Walco, ††††† Lisa Warner, ††††† Steven J. Weisman, ††††† and Christopher L. Wu †††††
In Conclusion . . .

Anesthesia
References


Questions?