

# **AMBULATORY SURGERY: OPIOID FREE ANESTHESIA?**

**Xavier Falières**

*Anesthesiologist.*

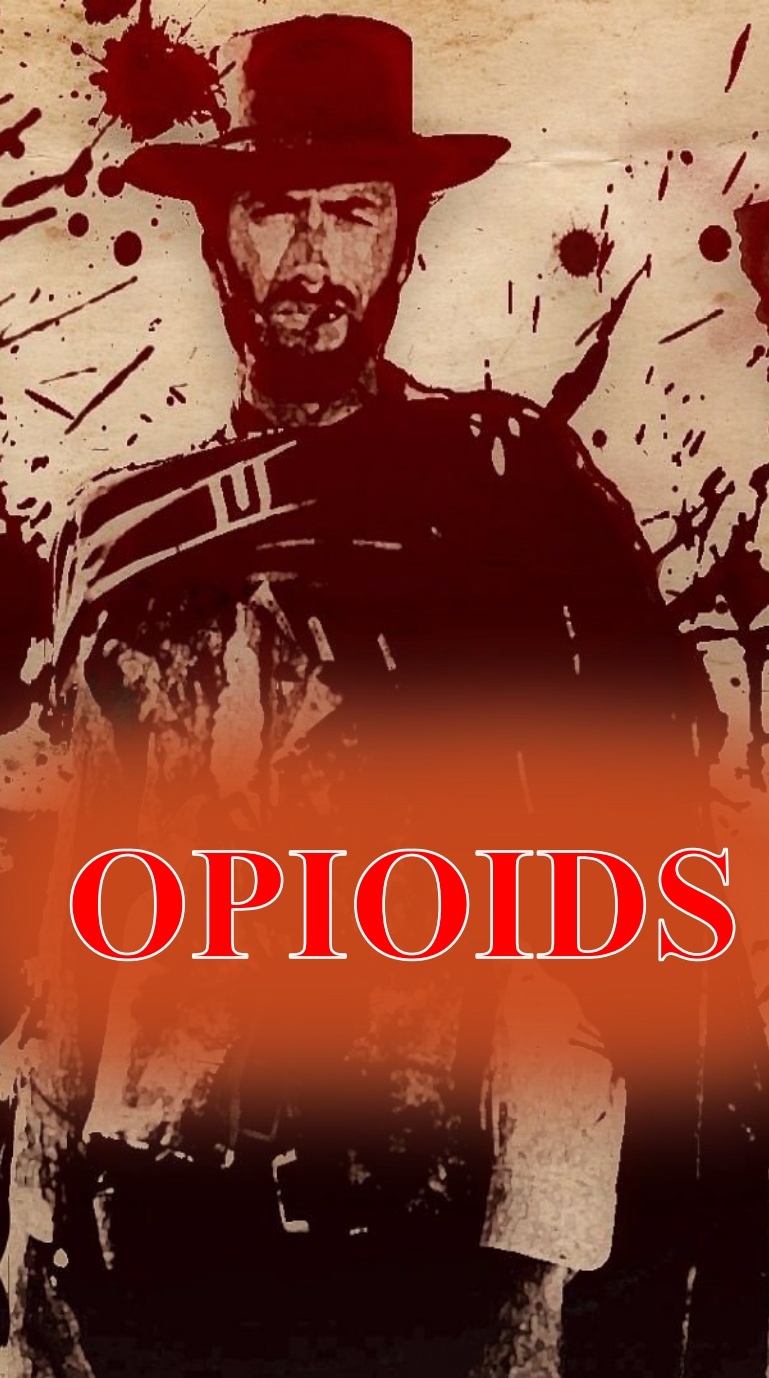
*Medical director day care hospital*

*Albert Schweitzer Hospital. Dordrecht – The Netherlands*

*President of the Dutch Society Ambulatory Care*



THE GOOD  
THE BAD  
AND THE UGLY



OBA?

OSA?

OFA?

OPIOIDS

# WHY SHOULD WE WORK WITHOUT OPIOIDS?

Because it's the latest craze in anesthesiology?

Because we need new development within anesthesiology?

Because it's fashionable?

OR

Because it's really justified and better for the patient?

Is it evidence based?



Articles & Issues ▼	CME	Subjects	Collections	中文翻译	Multimedia ▼	For Authors ▼	Journal Info ▼	
---------------------	-----	----------	-------------	------	--------------	---------------	----------------	--

[Home](#) > [October 2017 - Volume 125 - Issue 4](#) > **Opioid-Free Analgesia in the Era of Enhanced Recovery After...**

[< Previous Article](#) | [Next Article >](#)

## **Opioid-Free Analgesia in the Era of Enhanced Recovery After Surgery and the Surgical Home: Implications for Postoperative Outcomes and Population Health**

Kamdar, Nirav V., MD, MPP; Hoftman, Nir, MD; Rahman, Siamak, MD; Cannesson, Maxime, MD, PhD

Anesthesia & Analgesia: October 2017 - Volume 125 - Issue 4 - p 1089–1091

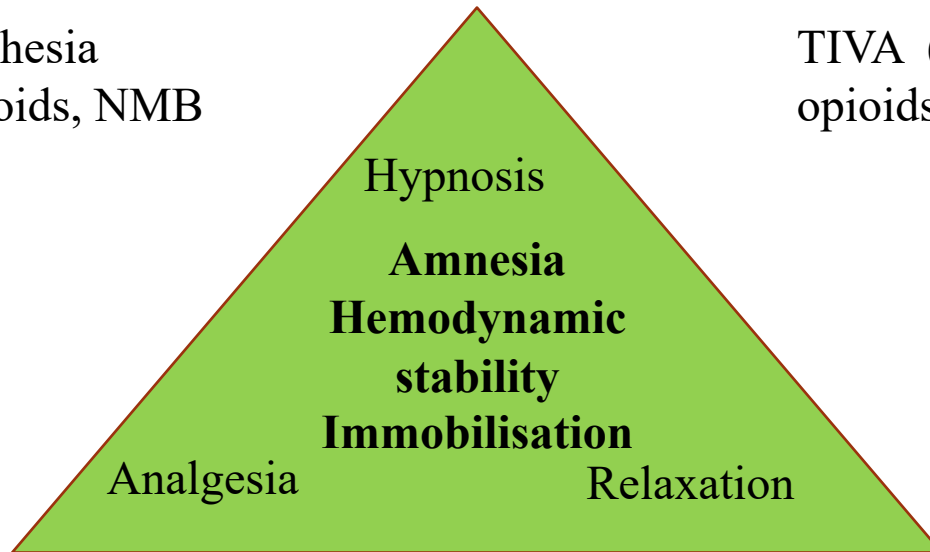




# WHAT HAVE WE LEARNED?

Balanced anesthesia  
Inhalation, opioids, NMB

TIVA (TCI): propofol,  
opioids, NMB



# BACK TO DEFINITIONS

- Analgesia: αναλγησία absence of pain
- Anesthesia: αναισθησία absence of sensations

In the practice of medicine, **anesthesia** is a state of temporary induced loss of sensation or awareness.

It may include:

- analgesia (relief from or prevention of pain),
- paralysis (muscle relaxation),
- amnesia (loss of memory), or unconsciousness.

A patient under the effects of anesthetic drugs is referred to as being **anesthetized**.



# FROM CLASSICAL GENERAL ANESTHESIA TO OFA

## ■ **The questions we may ask ourselves:**

- **If the patient is deep asleep, do we need opioid analgesia?**
- **Do we feel pain during anesthesia?**
- **Do we need opioids to achieve hemodynamic stability?**





# Opioid-free anesthesia: a different regard to anesthesia practice

Best Practice & Research Clinical Anaesthesiology 31 (2017) 445–467

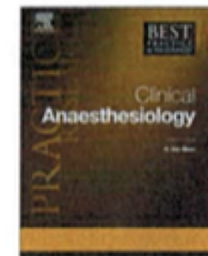


ELSEVIER

Contents lists available at [ScienceDirect](#)

Best Practice & Research Clinical  
Anaesthesiology

journal homepage: [www.elsevier.com/locate/bean](http://www.elsevier.com/locate/bean)



1

Do we feel pain during anesthesia? A critical review on surgery-evoked circulatory changes and pain perception





**NOCICEPTION  $\neq$  PAIN**



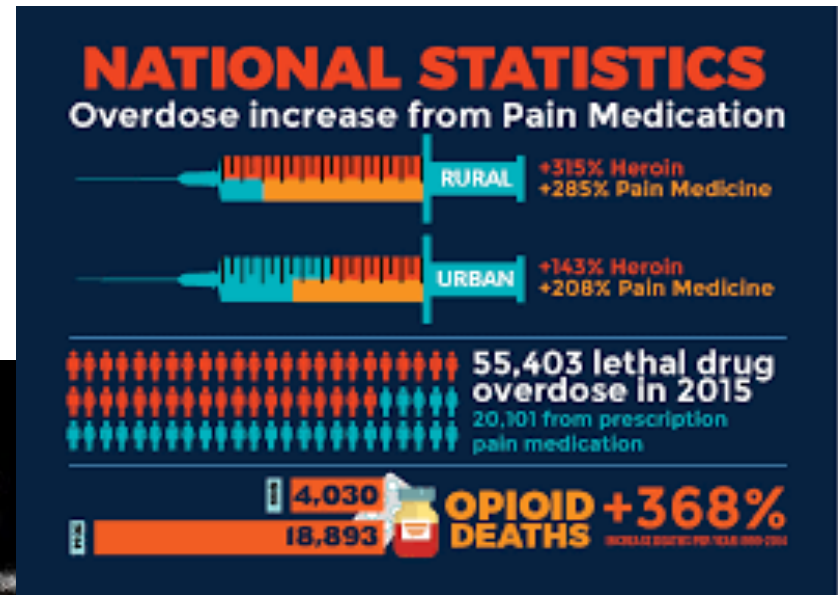
**WHY SHOULD WE AVOID OPIOIDS?**



# OPIOIDS ADDICTION



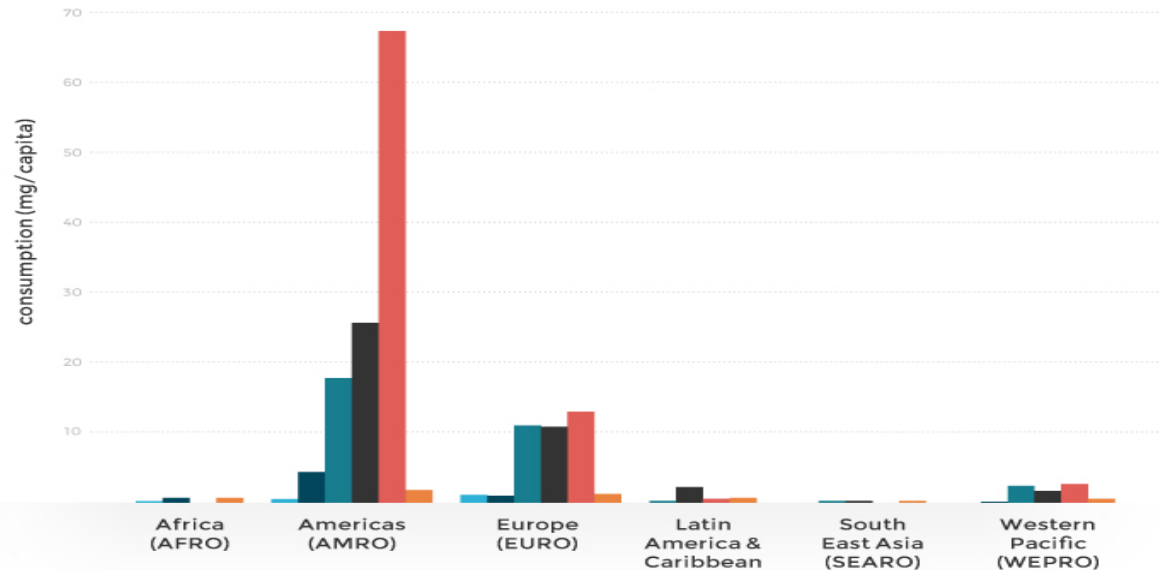
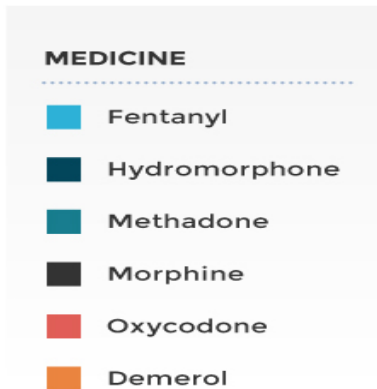
# OPIOIDS ADDICTION IN THE U.S.





# AND IN THE REST OF THE WORLD?

## OPIOID CONSUMPTION (mg/capita) 2015



Sources: International Narcotics Control Board; World Health Organization population data  
By: Pain & Policy Studies Group, University of Wisconsin/WHO Collaborating Center, 2017

 **ConsumerProtect**



REPORTAGE PIJNSTILLERS

## De dokter als dealer: 'In Nederland is allang sprake van een stille opioïde-epidemie'

Steeds vaker worden in Nederland zware pijnstillers voorgeschreven, hoewel uit de VS bekend is dat ze te vergelijken zijn met heroïne. De Volkskrant sprak met vier patiënten die verslaafd raakten. 'Als mijn vrouw de oxycodon niet had verstoppt, was ik zo weer begonnen.'

**Maud Effting** en **Anneke Stoffelen** 21 juli 2018, 2:00

# In The Netherlands



▲ Verpakkingen van het pijnstillend opiaat Oxycodon © ANP

## Alarm om gebruik verslavende pijnstillers

**OXYCODON** | Het kabinet grijpt in om het alarmerende gebruik van verslavende pijnstillers, zoals het beruchte oxycodon, in te tomen. Herhaalrecepten mogen niet langer doodnormaal zijn, gebruikers moeten een afbouwschema krijgen en alternatieve pijnbestrijding dient meer in beeld te komen.



# OPIOIDS, IMMUNE RESPONSE, CANCER AND SURGICAL SITE INFECTION

Immunosuppression by opioids? Doubts since 1979

What we know:

- Morphine decreases natural and acquired immunity, both directly and indirectly via the activation of central receptors.
- Opioid-induced changes in the immune system may affect the outcome of surgery, including bacterial and viral infections and cancer.
- The impact of the opioid-mediated immune effects could be particularly dangerous in selective vulnerable populations, such as the elderly or immunocompromised patients.



# OPIOIDS, IMMUNE RESPONSE, CANCER AND SURGICAL SITE INFECTION

Kim J *Transl Med* (2018) 16:8  
<https://doi.org/10.1186/s12967-018-1389-7>

Journal of  
Translational Medicine

REVIEW

Open Access



## Effects of surgery and anesthetic choice on immunosuppression and cancer recurrence

Ryungsa Kim\*

**Conclusion:** Local anesthetics such as lidocaine increase NK cell activity. Anesthetics such as propofol and locoregional anesthesia, which decrease surgery-induced neuroendocrine responses through HPA-axis and SNS suppression, may cause less immunosuppression and recurrence of certain types of cancer compared to volatile anesthetics and opioids.

It is also emerging that not all opioids induce the same immunosuppressive effects and evaluating each opioid profile is important for appropriate analgesic selection. The impact of the opioid-mediated immune effects could be particularly dangerous in selective vulnerable populations, such as the elderly or immunocompromised patients. Indeed, it is evident that the possibility of reaching adequate and equivalent pain control by choosing either immunosuppressive drugs or drugs without an effect on immune responses may be an important consideration in opioid therapy.

Due to their widespread and expanding use, the immunological effects of opioid are receiving considerable attention because of concerns that opioid-induced changes in the immune system may affect the outcome of surgery or of variety of disease processes, including bacterial and viral infections and cancer.

## Choosing anesthetic drugs without an effect on immune responses may be an important consideration in anesthesia.

Wybran J. Suggestive evidence for receptors for morphine and methionine-enkephalin on normal human blood T lymphocytes. *J Immunol*. 1979;123:1068-70  
Paola Sacerdote, Silvia Franchi and Alberto E. Panerai. Non-Analgesic Effects of Opioids: Mechanisms and Potential Clinical Relevance of Opioid-Induced Immunodepression. *Current Pharmaceutical Design*. 2012; 18: 6034  
Kim J Effects of surgery and anesthetic choice on immunosuppression and cancer recurrence *Transl Med* (2018) 16:8





# OPIOIDS AND CANCER

Dozens of articles: contradictory conclusions but all retrospective

WAITING?  
OR  
ACTION NOW?



# OPIOIDS AND HYPERALGESIA

- **1992:** Dr Paul Janssens invented remifentanyl but refused to market remifentanyl and sold it to Beecham afraid of unknown long-lasting effects of opioids...
- Opioids Induced Hyperalgesia:
  - Patients receiving opioids, also at low dose, become *more sensitive to pain*
  - Patients receiving opioids during surgery will need higher doses morphine postoperatively

**Hyperalgesia induced by low-dose opioid treatment before orthopaedic surgery: An observational case-control study**

Hina, Nabil; Fletcher, Dominique; Poindessous-Jazat, Frédérique; Martinez, Valéria European Journal of Anaesthesiology (EJA); [April 2015 - Volume 32 - Issue 4 - p 255-261](#)

**Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis** D. Fletcher and V. Martinez British Journal of Anaesthesia

112(6): 991-1004 (2014)



# OFA TOOLS



**How to avoid opioids  
in  
ambulatory setting?**

# BASIS ANESTHESIA

Hypnosis and immobilization:  
Classical TIVA / TCI, inhalational  
agents with or without muscle  
relaxants



- **Direct sympathetic block central - peripheral**
  - Clonidine, Dexmedetomidine, B blockers
- **Indirect block of sympathetic effects**
  - Nicardipine, lidocaine, Mg sulfate, inhalation vapor
- **Multimodal analgetics (non opioids) loading up per-operative to be active when waking up:**
  - low dose ketamine, clonidine, dexmedetomidine, lidocaine, dexamethason, NSAID's, paracetamol
- **Epidural, truncal blocks, plexus and local infiltration block**
- **Spinal anesthesia / analgesia with higher sympathic nerve block.**



# ALPHA 2-ADRENERGIC AGONISTS

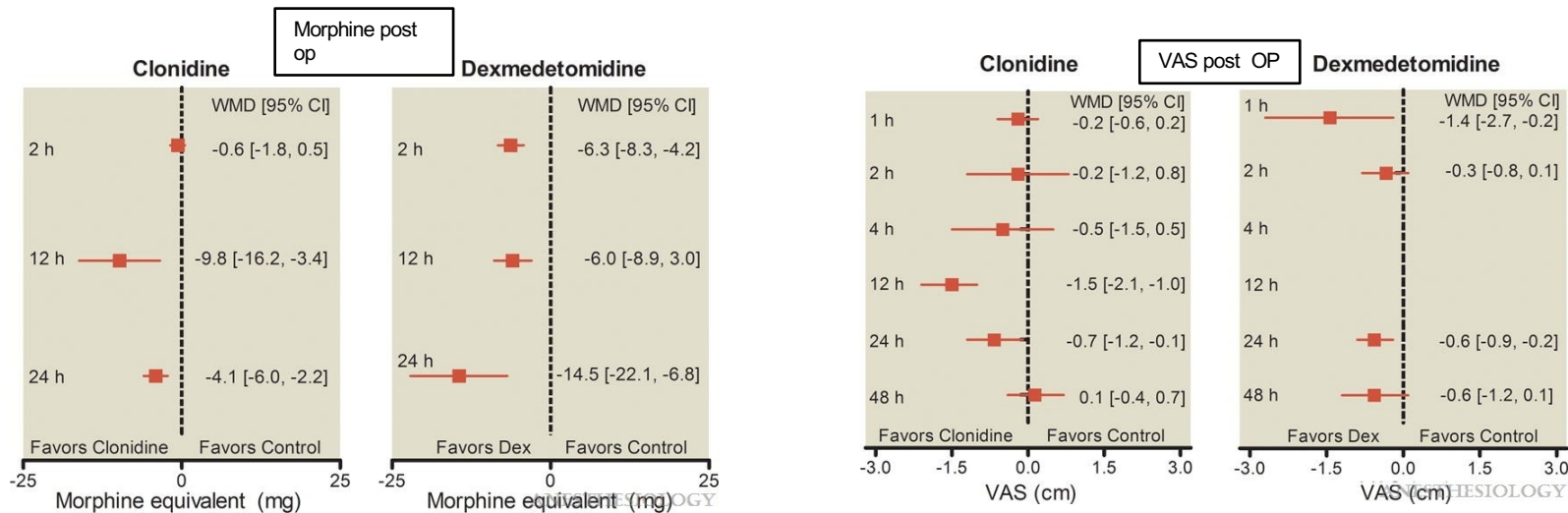
$\alpha_2$ -adrenergic agonists: lower significantly the hypnotic needs during operation and the postoperative opioid use.

Clonidine: 2 to 4 mcg/kg: less or not indicated in ambulatory setting

Dexmedetomidine:

- Dose 0,4 to max 1 mcg/kg/h. No bolus.
- Stop 30 minutes before end of surgery.

Both 15-30 min prior to surgery



# BETA-BLOCKERS

Reduce stress response. Very useful e.g. in laparoscopic surgery. Esmolol contributes to a significant decrease in postoperative pain and PONV and facilitates earlier discharge.

*British Journal of Anaesthesia* **93** (6): 799–805 (2004)  
doi:10.1093/bja/ae268 Advance Access publication September 17, 2004

BJA

---

## Role of $\beta$ -blockade in anaesthesia and postoperative pain management after hysterectomy

Y. Y. Chia\*, M. H. Chan, N. H. Ko and K. Liu

*Department of Anaesthesiology, Kaohsiung Veterans General Hospital, and School of Medicine, National Yang-Ming University, 386, Ta-Chung First Road, Kaohsiung 813, Taiwan*

*\*Corresponding author. E-mail: yychia@isca.vghks.gov.tw*

**Conclusion.** The results suggest that perioperative esmolol administration during anaesthesia reduces the intraoperative use of inhalation anaesthetic and fentanyl, decreases haemodynamic responses, and reduced morphine consumption for the first 3 postoperative days.





Glass, Peter S. A. Collard, Vincent MD\*; Mistraletti, Giovanni MD\*; Taqi, Ali MD†; Asenjo, Juan Francisco MD\*; Feldman, Liane S. MD†; Fried, Gerald M. MD†; Carli, Franco MD, MPhil\*

**Intraoperative Esmolol Infusion in the Absence of Opioids Spares Postoperative Fentanyl in Patients Undergoing Ambulatory Laparoscopic Cholecystectomy**  
Anesthesia & Analgesia: November 2007 - Volume 105 - Issue 5 - p 1255-1262

**CONCLUSIONS: Intraoperative IV infusion of esmolol contributes to a significant decrease in postoperative administration of fentanyl and ondansetron and facilitates earlier discharge.**



# Intraoperative Esmolol as an Adjunct for Perioperative Opioid and Postoperative Pain Reduction: A Systematic Review, Meta-analysis, and Meta-regression

Amanda M. Gelineau, MD,\* Michael R. King, MD,† Karim S. Ladha, MD, MSc,‡  
Sara M. Burns, MS,\* Timothy Houle, PhD,\* and T. Anthony Anderson, MD, PhD\*

**BACKGROUND:** Esmolol is an ultrashort  $\beta$ -1 receptor antagonist. Recent studies suggest a role for esmolol in pain response modulation. The authors performed a meta-analysis to determine if the intraoperative use of esmolol reduces opioid consumption or pain scores.

**METHODS:** PubMed, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, pubget, and Google Scholar were searched. Studies were included if they were randomized, placebo- or opioid-controlled trials written in English, and performed on patients 18 years of age or older. For comparison of opioid use, included studies tracked opioid consumption intraoperatively and/or in the postanesthesia care unit. Pain score comparisons were performed during the first hour after surgery.

**RESULTS:** Seventy-three studies were identified, 23 were included in the systematic review, and 19 were eligible for 1 or more comparisons. In 433 patients from 7 trials, intraoperative esmolol decreased intraoperative opioid consumption (Standard Mean Difference [SMD],  $-1.60$ ; 95% confidence interval [CI],  $-2.25$  to  $-0.96$ ;  $P \leq .001$ ). In 659 patients from 12 trials, intraoperative esmolol decreased postanesthesia care unit opioid consumption (SMD,  $-1.21$ ; 95% CI,  $-1.66$  to  $-0.77$ ;  $P \leq .001$ ). In 688 patients from 11 trials, there was insufficient evidence of change in postoperative 1 hour pain scores (SMD,  $-0.60$ ; 95% CI,  $-1.44$  to  $0.24$ ;  $P = .163$ ).

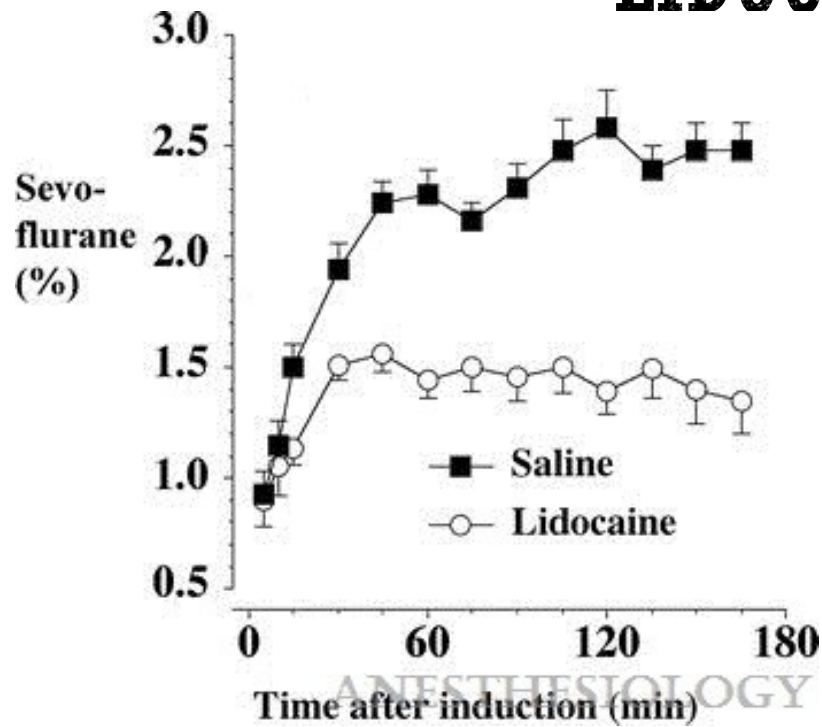
**CONCLUSIONS:** This meta-analysis demonstrates that intraoperative esmolol use reduces both intraoperative and postoperative opioid consumption, with no change in postoperative pain scores. (Anesth Analg 2018;126:1035–49)



# LIDOCAINE



# LIDOCAINE



Effect of lidocaine on per-op  
hypnotics



# LIDOCAINE

- 33% reduction vs placebo in opioid consumption postoperative when the lidocaine infusion was maintained for 1 hour
- Intravenous lidocaine did not result in toxicity or clinically adverse events.
- Positive oncolytic effect?

**Lidocaine: 1 to 1,5 mg/kg followed by  
infusion 1 to 1,5 mg/kg/h till discharge  
recovery**

McCarthy G. Impact of Intravenous Lidocaine Infusion on Postoperative Analgesia and Recovery from Surgery A Systematic Review of Randomized Controlled Trials. *Drugs*. 2010;70:1149-63

Kim J Effects of surgery and anesthetic choice on immunosuppression and cancer recurrence *Transl Med* (2018) 16:8



# (ES)KETAMINE AND POSTOP PAIN

**Pain Medicine**

Pain Medicine 2015; 16: 383–403  
Wiley Periodicals, Inc.



## ACUTE & PERIOPERATIVE PAIN SECTION

---

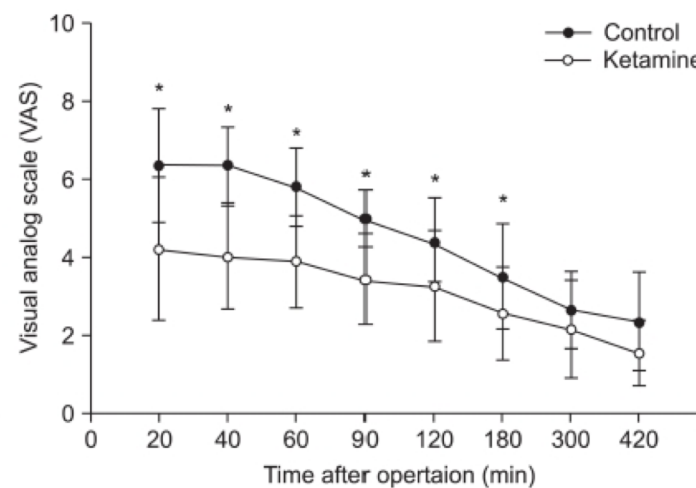
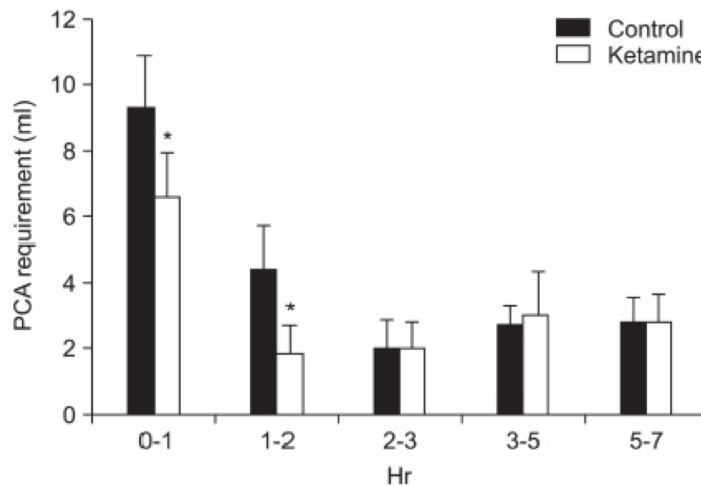
### *Original Research Article*

### **The Use of Intravenous Infusion or Single Dose of Low-Dose Ketamine for Postoperative Analgesia: A Review of the Current Literature**

**Results.** Low-dose IV ketamine reduces opioid consumption by 40%. It also lowers pain scores, but these findings are less clear. No major complications have been reported with low-dose IV infusion of ketamine when given up to 48 hours after surgery. While our review lends support to using low-dose IV infusion of ketamine in the management of perioperative pain, its optimal dose and regimen remain to be determined.



# (ES)KETAMINE REDUCES OPIOID INDUCED HYPERALGESIA



Boo Hwi Hong Effects of intraoperative low dose ketamine on remifentanyl-induced hyperalgesia in gynecologic surgery with sevoflurane anesthesia. Korean J Anesthesiol.2011; 61: 238.





# (ES)KETAMINE AND POD / POCD

## Pharmacological Delirium Prophylaxis: Ketamin

### Postoperative Delirium:

Incidence of Delirium during the first 3 postoperative days

- 19,82% in the Placebo group
- 17,65% in the 0.5 mg/kg Ketamin group
- 21,30% in the 1.0 mg/kg Ketamin group

### Primary Outcome of the PODCAST Study:

**No Difference** (19.45% vs 19.82% Placebo vs. Ketamin; absolute difference: 0.36%, 95% CI, -6.07 to 7.38, **p=0.92**).



# (ES)KETAMINE AND POD / POCD

*Acta Anaesthesiol Scand* 2009; 53: 864–872  
Printed in Singapore. All rights reserved

© 2009 The Authors  
Journal compilation © 2009 The Acta Anaesthesiologica Scandinavica Foundation

---

ACTA ANAESTHESIOLOGICA SCANDINAVICA  
doi: 10.1111/j.1399-6576.2009.01978.x

## **Ketamine attenuates post-operative cognitive dysfunction after cardiac surgery**

J. A. HUDETZ, Z. IQBAL, S. D. GANDHI, K. M. PATTERSON, A. J. BYRNE, A. G. HUDETZ, P. S. PAGEL and D. C. WARLTIER  
*Department of Anesthesiology, Clement J. Zablocki Veterans Administration Medical Center, Milwaukee, WI*



# (ES)KETAMINE AND POD / POCD

Anesth Pain Med. 2015 October; 5(5): e28844.

DOI: 10.5812/aapm.28844

Published online 2015 October 17.

Research Article

## Influence of Ketamine on Early Postoperative Cognitive Function After Orthopedic Surgery in Elderly Patients

Ki Hwa Lee,<sup>1</sup> Ji Yeon Kim,<sup>2</sup> Jeong Won Kim,<sup>2</sup> Jang Su Park,<sup>2,\*</sup> Kyu Won Lee,<sup>1</sup> and Sang Yoon Jeon<sup>3</sup>

<sup>1</sup>Department of Anesthesia and Pain Medicine, Haeundae Paik Hospital, Inje University, Busan, South Korea

<sup>2</sup>Department of Anesthesia and Pain Medicine, Ilsan Paik Hospital, Inje University, Goyang, South Korea

<sup>3</sup>Department of Anesthesia and Pain Medicine, Halla Hospital, Jeju, South Korea

\*Corresponding author: Jang Su Park, Department of Anesthesia and Pain Medicine, Ilsan Paik Hospital, Inje University, Goyang, South Korea. Tel: +81-319107114, Fax: +51-7970499, E-mail: jangpark@palk.ac.kr

**Conclusions:** There were no negative effects of ketamine on POCD



# DOSE (ES)KETAMINE

- Ideal dose is still not known. More studies are needed.
- One low-dose recommended schema could be;

**Ketamine. 0,2 mg/kg bolus, infusion 0,1 mg/kg. Possible to continue at recovery 0,05 mg/kg/h. Halve the dose with Esketamine.**



- Dexamethasone: positive effects in anesthesia known since 1959: Vey active on postop PONV and postoperative pain. 0,15 mg/kg (0,1 to 0,2 mg/kg).
  - No problem in DM patient if only single dose.
  - No problem in oncological surgery
- Non opioid analgesics: begin before incision.
  - Paracetamol: loading 40 mg/kg, max 2 g
  - NSAID's: loading diclofenac 2 mg/kg max 150 mg or ketorolac 40 mg
  - When available: metamizol up to 2 g loading
- Local infiltrations, analgesic blocks: use lower concentration, high volume. Before incision if possible. Calculate toxic dose.



**MAGNESIUM SULFATE IS NOT  
RECOMMENDED IN AMBULATORY SETTING**



# ANESTHESIA DEPTH MEASUREMENT

Is highly recommended when you  
are not experienced giving OFA

No risk for awareness if you keep  
BIS below 60%  
during OFA.





# OFA AND LOCAL / LOCO-REGIONAL ANESTHESIA. SOME EXAMPLES

- Use wound infiltration.
- Give blocks:
  - Breast surgery: PECS I + SAB / PVB / ESPB
  - Thorax: SAB / PVB / ESPB / Epidural
  - GI surgery: TAP / ESPB / Epidural
- in postoperative painful surgery, to make ambulatory possible, the use catheters for continuous infusion of LA with disposable infusion systems can be a good solution.



# GOOD OFA INDICATIONS

- Ambulatory and all ERAS
- Cancer
- Obese
- Osa
- Immunodeficient patients (inclusive elderly)
- Chronic pain patients and high risk of postop chronic pain
- Opioids / drugs addict patients
- As for CRPS: there are certainly some psychological profiles who are more at risk to develop opioids addiction.



# ARE THERE CONTRAINDICATIONS FOR OFA?

- All ischemic heart diseases, Low LVEF, ASA 4 bad condition patients, trauma, etc...
- Allergy to one of the drugs.
- Controlled hypotension with need for dry surgical field by a low cardiac output.



# CONCLUSION

Is OFA the future?

"Successive transition from one paradigm to another via revolution is the usual developmental pattern of mature science."

Thomas Kuhn, *The Structure of Scientific Revolutions*, 1962.

- More studies focused on quality of outcome are needed.
- Try to limit opioid use in anesthesia
  - from liberal policy to restrictive
  - from restrictive to OFA when possible

**Stress induced postoperative pain has a negative influence on outcome:  
use opioids if needed but titrate them.**

**Postoperative opioid free is also the new debate in the literature**



We need to inverse our way of thinking:

From opioid based anesthesia with non  
opioids medication as rescue

to

Non opioid based anesthesia with opioids  
as rescue



# CONCLUSION

***Opioid Free Anesthesia is one of the best indications of opioid-free anesthesia***



# THANK YOU

