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Opioid Free Anaesthesia

Mulier ESPCOP Brugge 2015
Patient 2 h post surgery on Ward

No nausea
No pain
No cold
Comfortable
Sufficient awake
Overview

1. Who is giving OFA today? survey
   - Worldwide, more positive than negative responses
2. Protocols used to achieve OFA today
3. What is the outcome effect of OFA vs OA?
   1. Advantages and disadvantages of OFA from survey
   2. 50 pat Randomised bariatric surgery
      • It is possible, equal hemodyn stable, less post op analgetics, no cortisol rise, better VAS score
   3. 500 pat Prospective Qo40 quality of recovery bariatric surgery
      • ERAS and improvement patient satisfaction
   4. 5000 pat Retrospective lap gastric bypass
      • Less major complications
Do you give general anaesthesia without opioids (OFA) (in the absence of regional anaesthesia) today?

- Yes for most patients except when contra indications: 28%
- Yes for a selected group of patients: 18%
- No but reduce opioids (LOA) for some or all patients: 6%
- No but willing to learn more about it: 9%
- No and don’t see the possible advantages: 39%

623 Answers on survey with 21 questions
Anaesthesiologist who visited Bruges since the OFA introduction in 2011 (307 sent, 89 answers), Most Belgian anaesthesiologists (2350 sent, 392 answers), Some anaesthesiologists worldwide (823 sent, 117 answers), Web based link on ESPCOP site (25 answers)
Response from 623 anaesthesiologists

Where do you work?

- Public or private hospital with no academic activity or research: 37%
- Public or private hospital with academic activity or research: 34%
- University hospital: 29%

Your work experience.

- I am in training: 12%
- Specialist Anaesthesiologist for 0 - 5 years: 61%
- Specialist Anaesthesiologist for 6 - 10 years: 15%
- Specialist Anaesthesiologist for more than 10 years: 12%

I am in training

Specialist Anaesthesiologist for 0 - 5 years

Specialist Anaesthesiologist for 6 - 10 years

Specialist Anaesthesiologist for more than 10 years
OFA is used in 26 countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Usage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium Dutch speaking</td>
<td>56</td>
</tr>
<tr>
<td>Belgium French speaking</td>
<td>40</td>
</tr>
<tr>
<td>Mexico</td>
<td>4</td>
</tr>
<tr>
<td>Nigeria</td>
<td>4</td>
</tr>
<tr>
<td>Switzerland</td>
<td>4</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>4</td>
</tr>
<tr>
<td>Brasil</td>
<td>3</td>
</tr>
<tr>
<td>Russia</td>
<td>3</td>
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<tr>
<td>South Africa</td>
<td>3</td>
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<tr>
<td>USA</td>
<td>3</td>
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<tr>
<td>Austria</td>
<td>2</td>
</tr>
<tr>
<td>Netherlands</td>
<td>2</td>
</tr>
<tr>
<td>Poland</td>
<td>2</td>
</tr>
<tr>
<td>Algeria</td>
<td>1</td>
</tr>
<tr>
<td>Argentina</td>
<td>1</td>
</tr>
<tr>
<td>Canada</td>
<td>1</td>
</tr>
<tr>
<td>China</td>
<td>1</td>
</tr>
<tr>
<td>Denmark</td>
<td>1</td>
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<tr>
<td>Egypt</td>
<td>1</td>
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<tr>
<td>France</td>
<td>1</td>
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<tr>
<td>Greece</td>
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<tr>
<td>Israel</td>
<td>1</td>
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<tr>
<td>Malaysia</td>
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<td>New Zealand</td>
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</tr>
<tr>
<td>Saudi Arabia</td>
<td>1</td>
</tr>
<tr>
<td>Turky</td>
<td>1</td>
</tr>
<tr>
<td>Missing country</td>
<td>6</td>
</tr>
</tbody>
</table>

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How long have you been giving OFA?

For how long have you performed this opioid free (OFA) method?
- Started this year: 23%
- More than 1 year: 25%
- More than 2 years: 20%
- More than 5 years: 32%

Workplace of OFA users:
- Public or private hospital with academic activity or research: 30%
- Public or private hospital with no academic activity or research: 33%
- University hospital: 37%

Work experience of OFA users:
- I am in training: 12%
- Specialist Anaesthesiologist for 0 – 5 years: 7%
- Specialist Anaesthesiologist for 6 – 10 years: 17%
- Specialist Anaesthesiologist for more than 10 years: 64%
Patients selected for OFA. (all that apply)

Indicate which patients you select for OFA and LOA

Respiratory concerns is the reason today to avoid opioids

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Main reasons why you reduce or avoid opioids peri-operatively.
What methods do you use to reduce (LOA) or avoid (OFA) opioids peri-operatively?

- Add additives: 80%
- Combine with regional: 80%
- Combine with local infiltration: 60%
- Monitor BIS or analgesia: 40%
- Increase Propofol or Inhalation: 20%
- Titrate opioids before induction: 10%
- Other (please specify): 0%
When you use additives for general anaesthesia what do you add (all that apply)
Ketamine dose (59 answers)

- At induction 0.1 to 2 mg/kg (59 answers)
  - Mean 0.4 to 0.6 mg/kg
  - Median 0.5 mg/kg
- Maintenance 0.15 to 2 mg/kg/h (10 answers)
  - Mean 0.3 mg/kg/h
  - Median 0.25 mg/kg/h
- Large variation: Why? (1-20)
  - Preventing tolerance (0.2 mg/kg) (hyperalgesia) to analgesia (0.5 mg/kg) or anesthesia (2 mg/kg). (hallucinations)
Lidocaine dose (34 answers)

- At induction 0.6 to 2 mg/kg (59 answers)
  - Mean 1.2 - 1.6 mg/kg/h
  - Median 1 - 1.5 mg/kg/h
- Maintenance 1 to 5 mg/kg/h (10 answers)
  - Mean 1.25 - 2 mg/kg/h
  - Median 1 - 1.5 mg/kg/h
- Variation: Why? (1-4)
  - Minimum 1 mg/kg required
  - > 1.5 mg/kg or infusion for long procedures
Clonidine dose (50 answers)

- At induction 0,5 to 4 mkg/kg (50 answers)
  - Mean 1,6 – 2,5 mkg/kg
  - Mediaan 2 mkg/kg
- Maintenance 0,3 to 0,6 mkg/kg/h (10 answers)
  - Mean 0,3 mkg/kg/h
- Post operative?
  - Bolus 2 x 1 – 2 mkg/kg
- Large variation: Why? (1-8)
  - From additive (0,5) to strong sympathetic blocker (4)
  - Bradycardia, hypotension does not increase with dose
  - Prolonged sedation if > 2 used for short procedure
Dexmedetomidine dose (11 answers)

• At induction 0,1 to 1,4 mkg/kg
  – Mean 0,7 – 0,9 mkg/kg/h
  – Median 0,7 mkg/kg/h

• Maintenance 0,2 to 1 mkg/kg/h
  – Mean 0,3 mkg/kg/h

• Post operative?
  – 0,1 – 0,2 mkg/kg/h

• Larger variation than clonidine: Why? (1-14)
  – From additive (0,1) to strong sympathetic blocker (1)
  – Bradycardia, hypotension does not increase with dose
  – Prolonged sedation if > 1 used for short procedure
Problems with OFA

What do you do when a hypertensive/tachycardia reaction happens during OFA?

- Not until now: 87%
- Yes but probably not related to LOA/OFA: 6%
- Yes and probably related to LOA/OFA: 7%

What do you do when a hypotension/bradycardia reaction happens during OFA? (all that apply)

- Give ephedrine: 100%
- Lower the: 100%
- Give fluids: 100%
- Give atropine: 100%
- Other: 0%

Have you had any serious adverse events when reducing opioids (LOA) or working opioid free (OFA)?

- Not until now: 7%
- Yes but probably not related to LOA/OFA: 20%
- Yes and probably related to LOA/OFA: 83%

What do you do when patient has immediately post operative pain.

- Titrate an opioid: 0.2
- Give extra non-opioid: 0.4
- Start a PCA with: 0.6
- Give a normal opioid: 0.8
- Other: 0
Pro & Contra OFA - LOA

Advantages of LOA OFA

Disadvantages of LOA OFA
Obstacles to adopt OFA?

- Insufficient guidelines.
- No training.
- Outcome not proven yet.
- Other.
- Limited data.
- Not aware of OFA.
- Expensive.
- Outside prescription label.
- More work.
Opioid free anaesthesia (OFA) in Bruges started in 2010 - 2011

- Randomized study, ready for publication on 50 lap gastric bypass patients getting OFA vs. OA. Comparing post operative morphine PCIA
- Prospective study on 500 lap gastric bypass patients getting OFA vs. OA. Thesis M Crivits 2014 Comparing ERAS evaluation using the Qo40 questionnaire
- Retrospective analysis 5000 lap gastric bypass patients getting OFA vs. OA Comparing complications and outcome.
Randomized study in 50 lap RNY patients
Patients got OFA or Opioids per-op only
Same post op drugs: paracetamol and diclofenac
Morphine pump PCIA: VAS score at PACU and at ward first day

2013 R. Wouters; J. P. Mulier

• No demographic differences between the two groups with regard to age, weight, length, BMI, gender, the incidence of pre operative OSAS.
• No difference in Kalkman score (1. prediction of severe postoperative pain) and in the Amsterdam Preoperative Anxiety and Information Scale (2. APAIS).
• No differences in hemodynamic problems per operative, like bradycardia, hypotension, tachycardia or hypertension defined as a change of 20 % with or without a treatment requirement.
• Kalkman score and APAIS score did not predict morphine use or pain score.

VAS scores are better with a lower morphine consumption post operative
Randomized study on 50 pt

**Table 1:** Postoperative at PACU (Nr of pat)

<table>
<thead>
<tr>
<th>Condition</th>
<th>OA (21)</th>
<th>OFA (23)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>low saturation with O2 mask</td>
<td>8</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>obstructive breathing</td>
<td>3</td>
<td>0</td>
<td>0.06</td>
</tr>
<tr>
<td>PONV</td>
<td>7</td>
<td>3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>shivering or having cold</td>
<td>5</td>
<td>0</td>
<td>0.013</td>
</tr>
<tr>
<td>VAS score (mean)</td>
<td>4.88</td>
<td>1.66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Morphine need (mean in mg)</td>
<td>15.3</td>
<td>4.91</td>
<td>0.004</td>
</tr>
</tbody>
</table>

**Table 2:** Postoperative at Ward

<table>
<thead>
<tr>
<th>Condition</th>
<th>OA (21)</th>
<th>OFA (23)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>emotional state (9)</td>
<td>7.22</td>
<td>8.11</td>
<td>0.051</td>
</tr>
<tr>
<td>physical comfort (12)</td>
<td>7.94</td>
<td>10.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>psyche support (7)</td>
<td>6.60</td>
<td>6.73</td>
<td>0.62</td>
</tr>
<tr>
<td>physical independence (5)</td>
<td>3.80</td>
<td>4.71</td>
<td>0.007</td>
</tr>
<tr>
<td>pain score (7)</td>
<td>4.50</td>
<td>6.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>sleep score (4)</td>
<td>2.11</td>
<td>3.30</td>
<td>0.040</td>
</tr>
<tr>
<td>total Qo40 score (40)</td>
<td>29.60</td>
<td>35.81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cortisol change mg</td>
<td>10.55</td>
<td>3.57</td>
<td>0.029</td>
</tr>
<tr>
<td>VAS score (mean)</td>
<td>3.29</td>
<td>2.04</td>
<td>0.016</td>
</tr>
<tr>
<td>Morphine need (mean in mg)</td>
<td>18.18</td>
<td>14.73</td>
<td>0.330</td>
</tr>
</tbody>
</table>
500 patients questioned
day 1 post lap RNY  OFA vs. OA

Qo40 Questions that are significant different OFA versus OA

* Chi square p < 0.05
A prospectively kept database of all the patients undergoing fully stapled laparoscopic Roux-en-Y gastric bypass (FS-LRYGB) in a standardized fashion by a single surgeon or under his direct supervision since May 2004 contains today more than 10 000 consecutive procedures.

Low Opioid anesthesia (LOA) by using clonidine started in 2010. In 2011 total opioid free anesthesia (OFA) was given, first by using clonidine and from 2012 by using dexmedetomidine. Around half of the patients were selected for opioid free anesthesia (OFA) from the beginning, based on the attending supervising anesthesiologist and his assumed risk of using opioids.

A small group of patients were still given a low opioid anesthesia (LOA) by adding only a limited amount of additives in an effort to learn how to handle the switch to total opioid free anesthesia.

Patients given OA: 2451  OFA: 2337  LOA: 264 missing info: 9
All one month follow-up complications after lap RNY are recorded.

Risk for complications

- decreases by OFA
- increases by age, male gender, re intervention
- BMI no effect, OSAS increases risk in OA
OFA has more surgery related complications
OA has more respiratory, infectious and bleeding related complications
LOA has more complications on average but group is small
Are the groups comparable?

- Not randomized prospective database.
  - Variable OA       OFA       LOA  p
    - Male            28,21%    28,07%    24,62%  0,51
    - BMI             40,89     41,18     41,66  0,41
    - Age             41,09     42,19 *   41,27  0,009
    - OSAS            37%       39% *     31% *  0,024
    - Redo            15%       19% *     16%    0,001

- Not comparable: OFA has more patients with OSAS and redo surgery.
- OSAS if STOPbang > 3, probably underscored by missing data
Are other outcome variables different?

Not randomized prospective database.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OA</th>
<th>OFA</th>
<th>LOA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unplanned ICU</td>
<td>0.56% (14)</td>
<td>0.3% (4)</td>
<td>0.38% (1)</td>
<td>0.38</td>
</tr>
<tr>
<td>No of hospital days</td>
<td>2.73</td>
<td>2.53 *</td>
<td>2.86</td>
<td>0.001</td>
</tr>
<tr>
<td>1 week revisions</td>
<td>0.36% (9)</td>
<td>0.13 (3)</td>
<td>0.38 (1)</td>
<td>0.10</td>
</tr>
<tr>
<td>Hospital readmission</td>
<td>0.88% (22)</td>
<td>1.03% (24)</td>
<td>1.89% (5)</td>
<td>0.29</td>
</tr>
<tr>
<td>Morphine day 0 (SD)</td>
<td>21 mg (0.99)</td>
<td>6 mg (0.48)*</td>
<td>15 mg (1.9)*</td>
<td>0.001</td>
</tr>
<tr>
<td>No no-opioids postop</td>
<td>1.36% (34)</td>
<td>8.7% (205)</td>
<td>5.6% (15)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

OFA patients have a shorter hospitalization and need less or no opioids on the first day.
Perioperative opioids aggravate obstructive breathing in sleep apnea syndrome: mechanisms and alternative anesthesia strategies

Jan P. Mulier

Purpose of review
Opioids induce and increase the severity of most sleep-disordered breathing in all patients, but especially in morbidly obese patients. Discussed herein are the direct impact and mechanisms of opioids on inducing and exacerbating obstructive sleep apnea syndrome in normal and morbidly obese patients.

Recent findings
Respiratory depression is a larger problem than obstructive sleep apnea syndrome during the first night after an opioid anesthesia because of the reduced amount of deep sleep and rapid-eye-movement sleep. Acute tolerance to the analgesic effects of opioids can be observed after one anesthetic opioid dose, although tolerance to the side-effects of opioids develops more slowly. Therefore, it makes sense to avoid all opioids intraoperatively. A recently developed multimodal nonopioid anesthesia method may prevent development of acute tolerance and facilitate postoperative pain management with less opioids and sleep-disordered breathing.

Summary
A multimodal nonopioid anesthesia method avoids the necessity for intraoperative opioids, reduces the need for postoperative opioid use, and improves analgesia with less narcotic.

Keywords
analgesia, anesthesia, obstructive sleep apnea syndrome, opioids
Acute morphine tolerance was known for a long time but forgotten?


**ACUTE TOLERANCE TO NARCOTIC ANALGESIC DRUGS IN RATS**

BY

B. M. COX, M. GINSBURG AND O. H. OSMAN

From the Department of Pharmacology, Chelsea College of Science and Technology, London, S.W.3

(Received November 2, 1967)

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Morphine Tolerance starts after 2 hours
No analgesic effect after 8 hours
**Rapid Development of Tolerance to Analgesia During Remifentanil Infusion in Humans**

H. Ronald Vinik, MD*, and Igor Kissin, MD, PhD†

*Department of Anesthesiology, University of Alabama at Birmingham, Birm Anesthesia, Harvard Medical School, Brigham and Women’s Hospital, Boston

Anesth Analg 1998;86:1307

Reason why after TIVA:

- Crying of pain if no opioid is continued even when minor or not painfull surgery
- Shivering and need for bair hugger
- Vomiting requiring propofol and ondansetron

![Graph showing time course of analgesic effect of remifentanil](image)

**Figure 1.** Time course of the analgesic effect of remifentanil (constant-rate infusion of 0.1 mg · kg⁻¹ · min⁻¹) as determined by cold water pain tolerance test. aP < 0.0001 versus Time 0; bP < 0.05 versus 90 min; cP < 0.0001 versus 90 min.
Have OSAS patients more complications after OA vs. OFA?

- Not randomized prospective database.
  - Variable  No OSAS  OSAS  p
  - OA  2.02% (31)  5.05% (44)*  0.001
    - OFA  1.95% (27)  2.49% (22)  0.39
    - LOA  4.62% (8)  5.19% (4)  0.67

- Under standard OA, OSAS patients have a significant higher complication rate.
- Under OFA, OSAS patients have not a higher complications rate compared to non OSAS patients.
- LOA has a larger complication rate, the group is smaller and shows a learning curve!
- OFA is difficult in the beginning and requires an effort to learn.
OFA induction

- Sympathetic block: 10 min before induction
  - Dexmedetomidine: 0.3 ug/kg IBW (20 - 30 ug) further loading to 0.5 after intubation
- Local anesthetics iv: 1 min before induction (hypnotic and rapid stress block)
  - Lidocaine: 1.5 mg/kg IBW (100 mg)
- Hypnotics iv: induction (hypnotic)
  - Propofol 2.5 mg/kg IBW (200 mg)
- Hemodynamic stabilization (cave preload reduction)
  - Mg Sulfate 40 mg/kg IBW (2.5 gr)
- NMB if needed for anesthesia or surgery
- Anti-inflammatory agents before surgery (lap) corticoiden, NSAID
  - Dexamethasone 10 mg, Diclofenac 75 - 150 mg
- NMDA block (analgesic and blocking hyperalgesia by opioids)
  - Ketamine 10 - 25 mg bolus or slow infusion or at end operation
- Have B blocker, Ca antagonist, ephedrine and phenylephrine ready
  - Metoprolaat 1-5 mg, Nicardipine 1-5 mg, Ephedrine 3-9 mg, Phenylephrine 10-30 ug
OFA maintenance

• Sympathetic block
  – **Dexmedetomidine:** 0.5 ug/kg/h. (long half life) stop when 1 ug/kg is reached
  – Or Clonidine 150–300 ug loading up (very long half life)

• Local anesthetics
  – **Procaine** 0.1% 2 mg/kg/h short half life and safer except allergic reactions
  – (or **Lidocaine** 1% 1–3 mg/kg/h high dose has prolonged hypnotic effects)
  – Toxic dose lidocaine is probably very high > 10 mg/kg

• Mg Sulfate 2.5 mg/kg IBW/h

• Inhalation anesthesia
  – **Sevoflurane, Desflurane** 0.8 – 1 MAC with BIS around 40%.
  – **Propofol** infusion higher dose than TIVA required, difficult and BIS needed.

• NMDA block (if opioids might get used post op)
  – Ketamine 50 mg over 12 h

• Paracetamol 4 gr/24h post op
Opioids are not generally accepted anymore!

Balanced anesthesia:
Inhalation, opioids, NMB

TIVA:
propofol, opioids, NMB

1. hypnosis
2. Sympathetic block
3. relaxation

Unconsciousness
Hemodynamic stability
Immobility (relative)

We don’t need analgetics to achieve hemodynamic stability
Direct sympathetic block is possible.

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Conclusion

Patients love OFA as ERAS improves, nurses see the difference on the ward

Every change is difficult, requires more work and increases risks.

You will never see the difference if you do follow your patient post-operative.
Following the advice in using less peri-operative opioids in morbidly obese patients, it has now become time to discuss “from low-opioid to opioid free” anaesthesia (OFA).

Why, how and when do we use low-opioid or opioid free anaesthesia combined with post-operative multimodal analgesia in morbidly obese patients?
Monitoring in the morbidly obese patient

Ghent – Belgium
Het Pand Onderbergen 1
Registration 8 am
program 9 am - 6pm