

AnaConDa

Anaesthetic Conserving Device



FACILITATES INHALED SEDATION FOR ICU PATIENTS



AGENDA

1

WHAT DO WE EXPECT FROM
A MODERN SEDATIVE FOR
THE CRITICALLY ILL PATIENT?

2

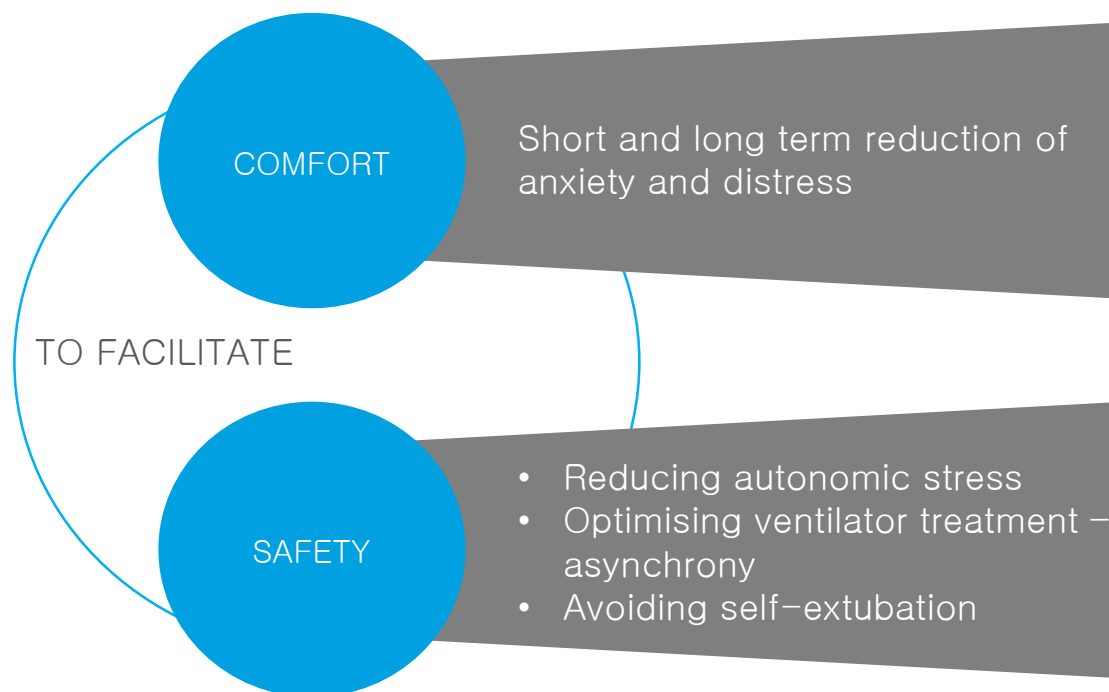
WHEN IS
INHALED SEDATION
A SUITABLE CHOICE?

3

ANACONDA –
A DEVICE CUSTOMIZED
FOR ICU-USE

SEDATION IN MECHANICALLY VENTILATED PATIENTS

IMPORTANT FEATURES IN SEDATION OF MECHANICALLY VENTILATED PATIENTS



REFERENCES

1. Jacobi et al. SCCM Guidelines 2002

WHAT DO WE EXPECT FROM A MODERN ICU SEDATIVE

- 1 Controllable sedation depth
- 2 Rapid on- and offset
- 3 Minimal accumulation
- 4 Minimal metabolism and no active metabolites
- 5 Few adverse effects

Volatile anaesthetics have been proposed as ideal ICU sedatives.¹⁻³

REFERENCES

1. Spencer et al. Intensive Care Medicine 1992;18(7):415-21
2. Kong et al. BMJ 1989 13;298(6683):1277-80
3. Hendrickx et al. J of Clin Monit Comput 2018;32(4)

WHEN IS INHALED SEDATION A SUITABLE CHOICE?

WHEN IS INHALED SEDATION A SUITABLE CHOICE?



Impaired
gas
exchange

- ARDS and AHRF
- COPD
- Asthma



Need for
reliable
wake-up

- Low GCS
- Post cardiac arrest
- Stroke



The
distressed
patient

- IV tolerant
- Delirium prone
- Hallucinations/delusions



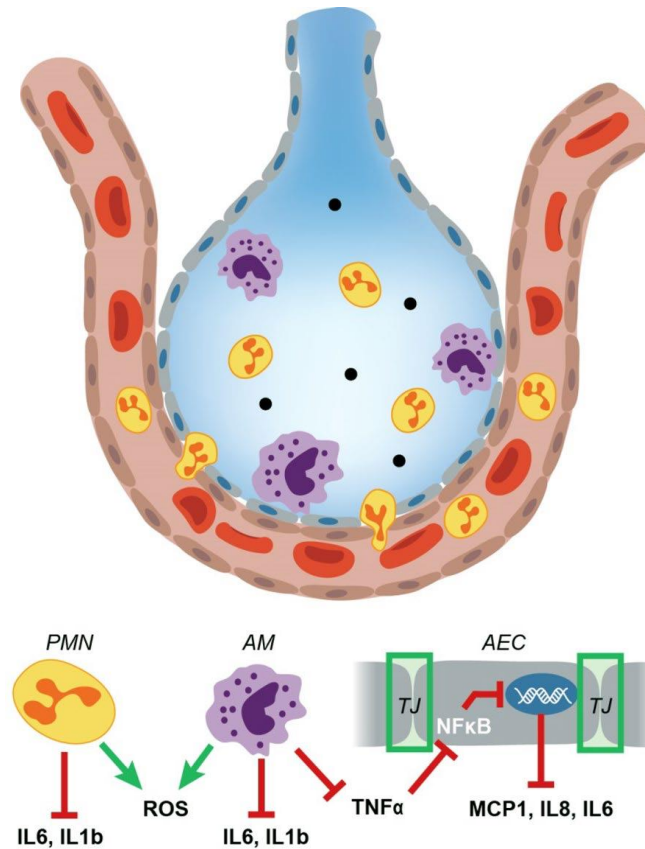
PULMONARY THERAPEUTIC EFFECTS

Impaired gas exchange

- ARDS and AHRF
- COPD
- Asthma



LUNG PROTECTIVE PROPERTIES OF INHALED SEDATION ARE WELL CHARACTERISED



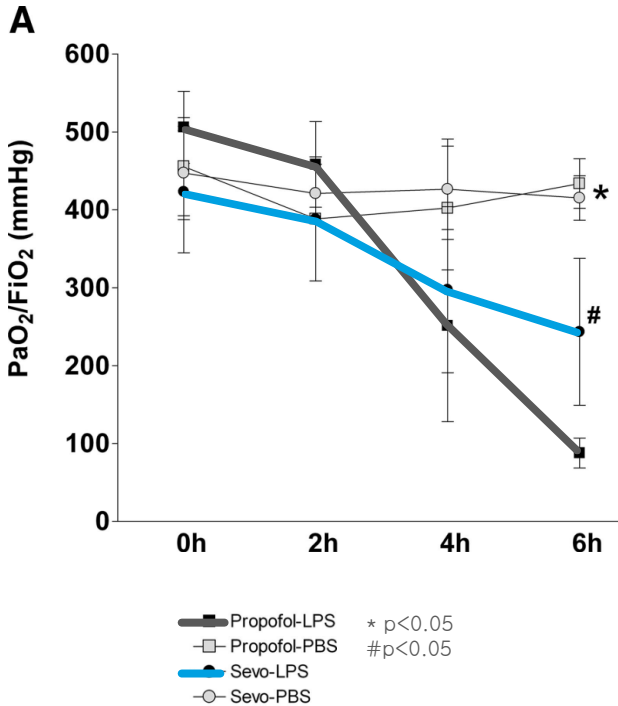
REFERENCES

1. O'Gara et al. Intensive Care Med 2016;42:1487-9.



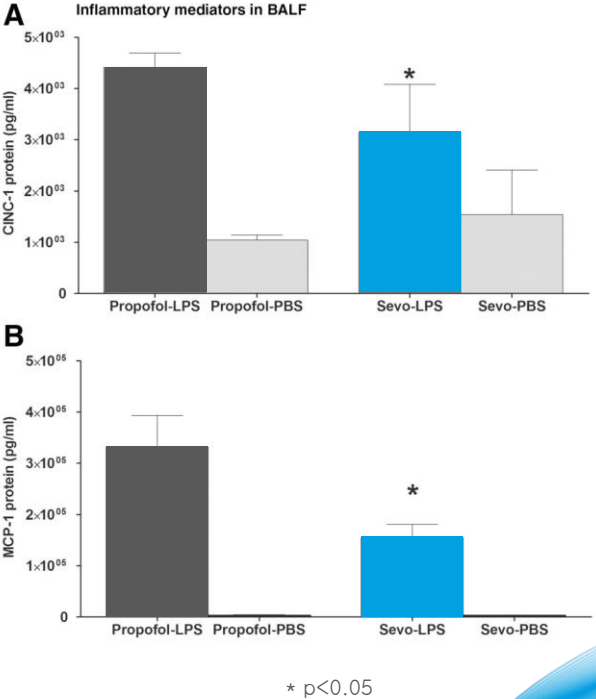
IMPROVED OXYGENATION AND REDUCED PULMONARY INFLAMMATORY RESPONSE IN ARDS

PaO₂/FiO₂ was less affected with sevoflurane than propofol (rat model)



Sevoflurane reduces inflammatory chemoattractants (CINC-1 and MCP-1) compared to propofol (rat model)

Bronchoalveolar lavage (BAL)



REFERENCES

1. Voigtsberger et al. Anesthesiology 2009;111:1238-48



IMPROVED OXYGENATION AND REDUCED PULMONARY INFLAMMATORY RESPONSE IN ARDS

Respiratory and blood gases parameters (pig model)

Parameter	Anaesthetic	T ₁ (10 min)	T ₂ (60 min)	T ₃ (150 min)	T ₄ (240 min)
PaO ₂ /FiO ₂ (kPa)	Sevoflurane	16.5±4.8	23.5±2.7	22.9±5.3	22.3±5.7
	Propofol	17.2±3.5	20.7±2.4	18.5±2.8	17.5±2.5 ^a
MV (l min ⁻¹)	Sevoflurane	5.5±0.5	6.3±1.2	6.3±1.2	6.3±1.2
	Propofol	5.2±0.8	5.2±0.7	5.2±0.9	5.2±0.9
RR (breaths per min)	Sevoflurane	15±1	17±3	17±4	17±4
	Propofol	14±1	14±1	14±1	14±1
EVLWI (ml kg ⁻¹)	Sevoflurane	14±2	13±1	14±1	16±3
	Propofol	16±2	17±3 ^a	19±5 ^a	22±7 ^a

^a Significant differences between the two groups. p<0.05

REFERENCES

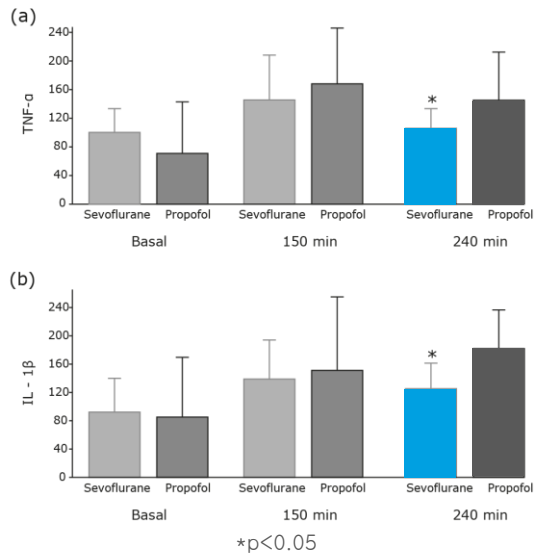
1. Ferrando et al. Eur J Anesthesiology 2013;30:455-63.



IMPROVED OXYGENATION AND REDUCED PULMONARY INFLAMMATORY RESPONSE IN ARDS

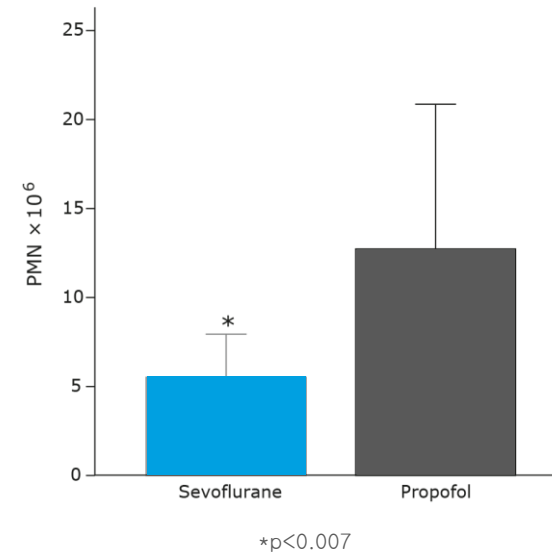
Significant reduction of inflammatory markers in bronchoalveolar lavage with sevoflurane compared to propofol after six hours (pig model)

Fig. 3



Polymorphonuclear neutrophils in bronchoalveolar lavage fluid. Six hours after induced ARDS (pig model)

Fig. 2

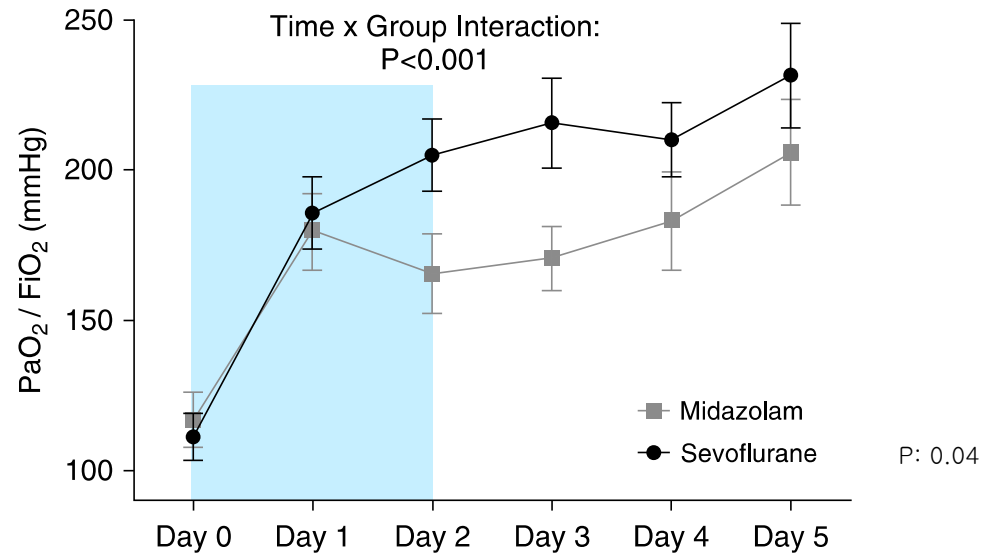


REFERENCES

1. Ferrando et al. Eur J Anesthesiology 2013;30:455-63



IMPROVED OXYGENATION AND REDUCED PULMONARY INFLAMMATORY RESPONSE IN ARDS



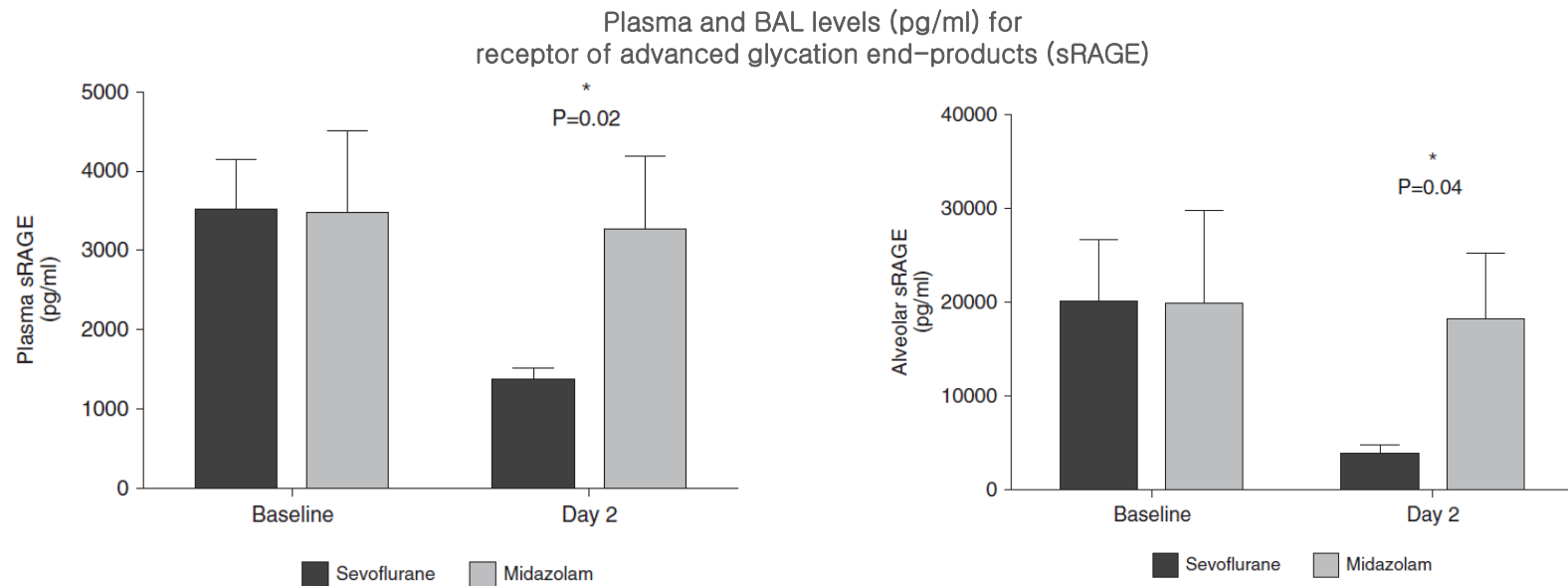
In patients with ARDS sevoflurane improved oxygenation

REFERENCES

1. Jabaudon et al. Am J of Resp Critic Care Med 2017;195(6),792-800



IMPROVED OXYGENATION AND REDUCED PULMONARY INFLAMMATORY RESPONSE IN ARDS



In patients with ARDS sevoflurane decreased markers of epithelial injury and inflammation

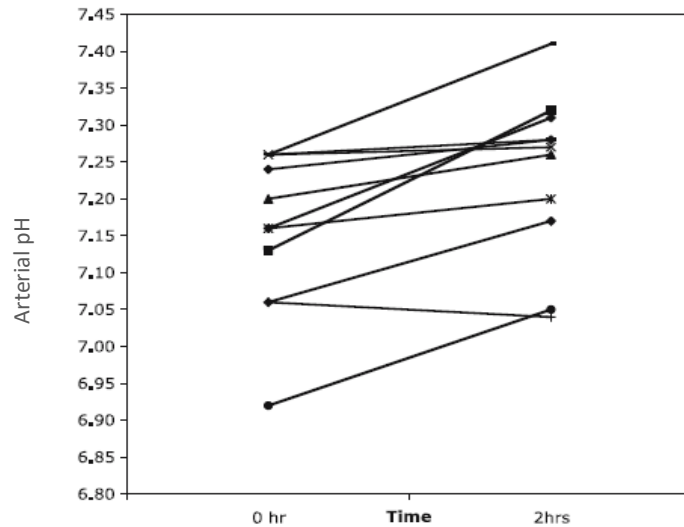
REFERENCES

1. Jabaudon et al. Am J of Resp Critic Care Med 2017;195(6),792-800

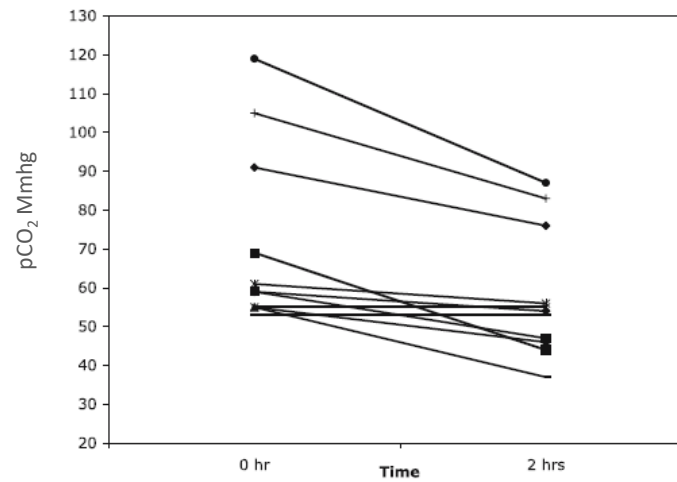


ISOFLURANE IS BRONCHODILATORY IN ASTHMA

Reversed acidosis



Reversed hypercarbia



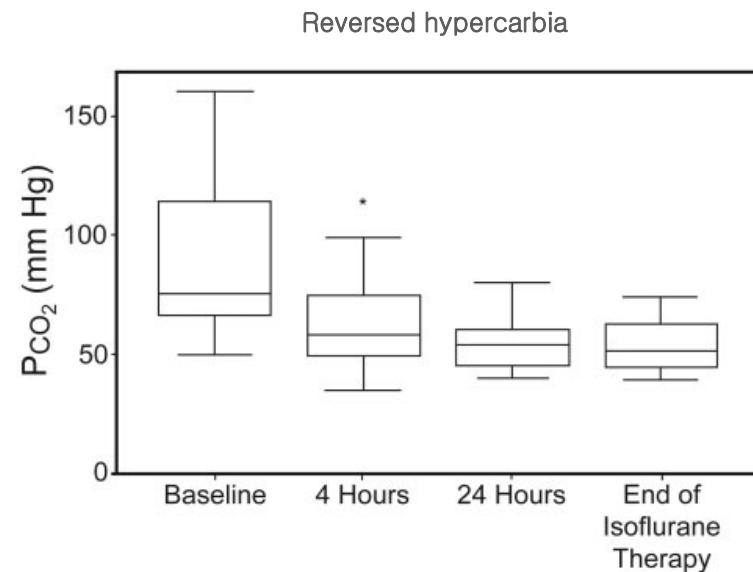
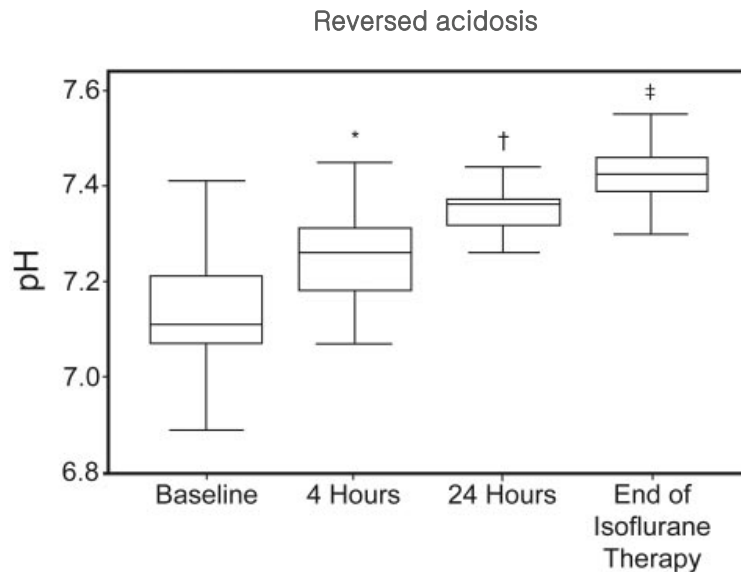
Isoflurane led to improvement in arterial pH and a reduction in partial pressure of pCO₂

REFERENCES

1. Shankar et al, Intensive Care Med 2006;32;927-933



ISOFLURANE IS BRONCHODILATORY IN ASTHMA



Isoflurane led to improvement in pH and pCO₂ in patients with life-threatening bronchospasm

REFERENCES

1. Turner et al, Respiratory Care 2012;57(11):1857-64



THERAPEUTICAL BENEFITS BY USING INHALED SEDATION

- ✓ Improved oxygenation
- ✓ Reduction of pulmonary inflammatory response
- ✓ Bronchodilatory effect

REFERENCES

1. Voigtsberger et al. Anesthesiology 2009;111:1238-48.
2. Ferrando et al. Eur J Anesthesiology 2013;30:455-63.
3. Jabaudon et al. Am J of Resp Critic Care Med 2017;195(6),792-800
4. Shankar et al, Intensive Care Med 2006;32:927-933
5. Turner et al, Respiratory Care 2012;57(11):1857-64



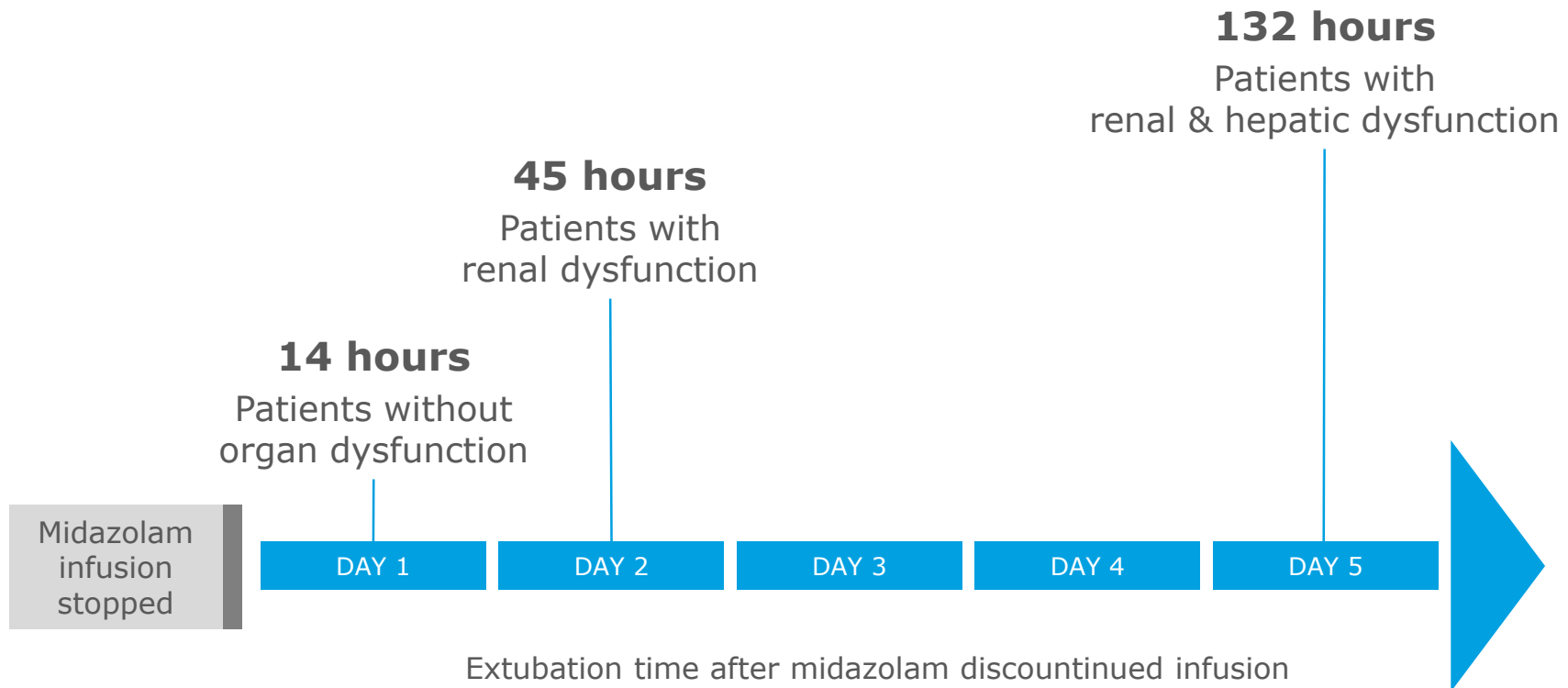
RAPID ELIMINATION

Need for reliable wake-up

- Low GCS
- Post cardiac arrest
- Stroke



BENZODIAZEPINES TIME TO WAKE-UP

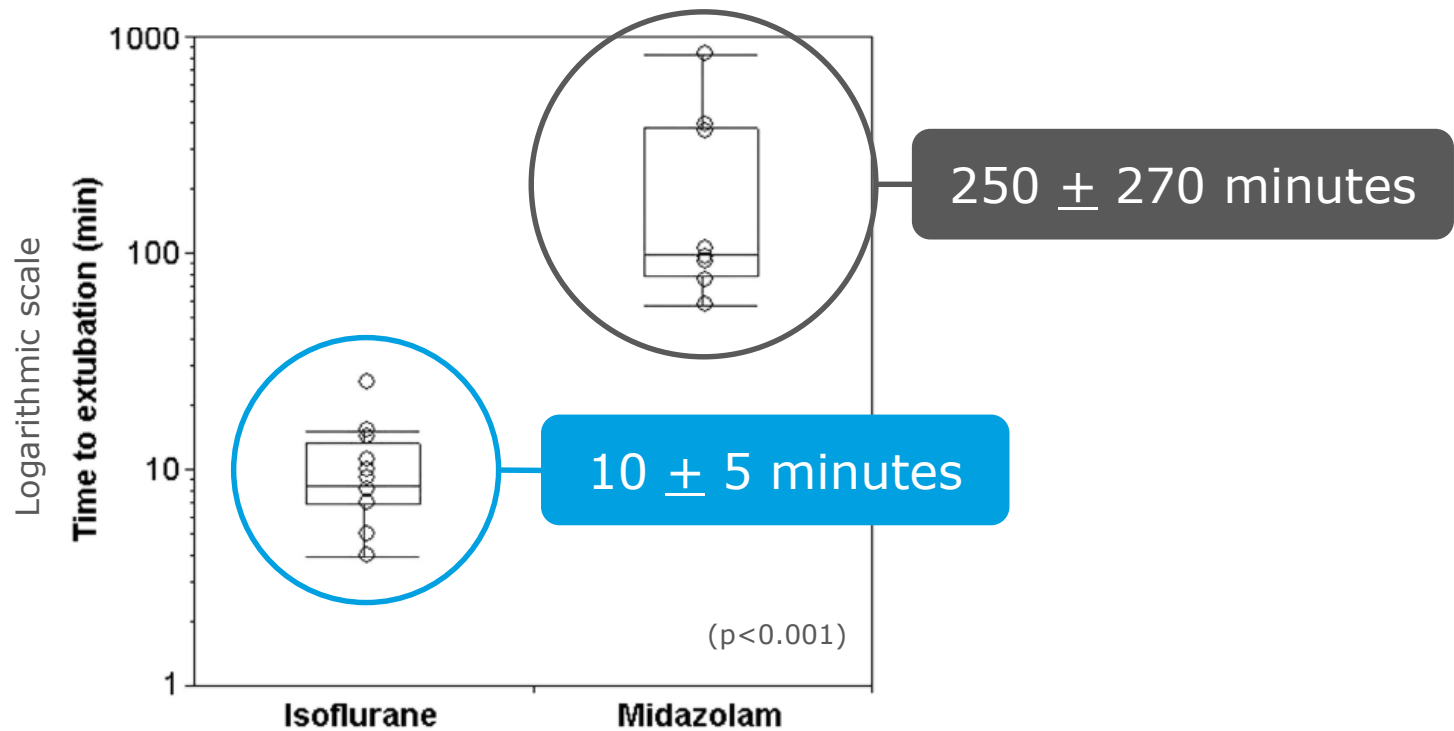


REFERENCES

1. Shelly MP et al, EJA 1991;8:21-27



SHORT EXTUBATION TIME WITH ISOFLURANE

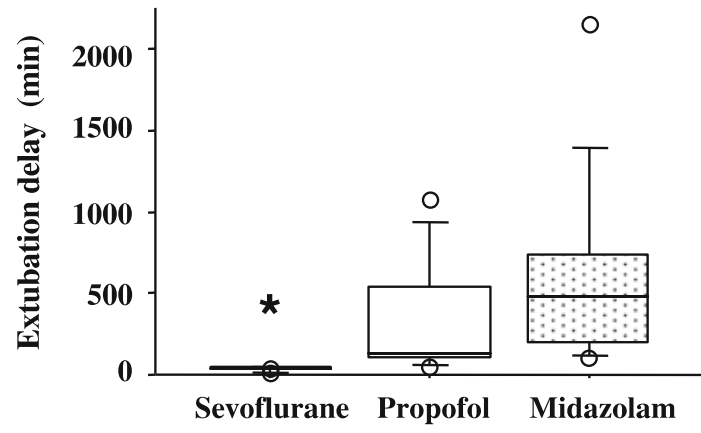
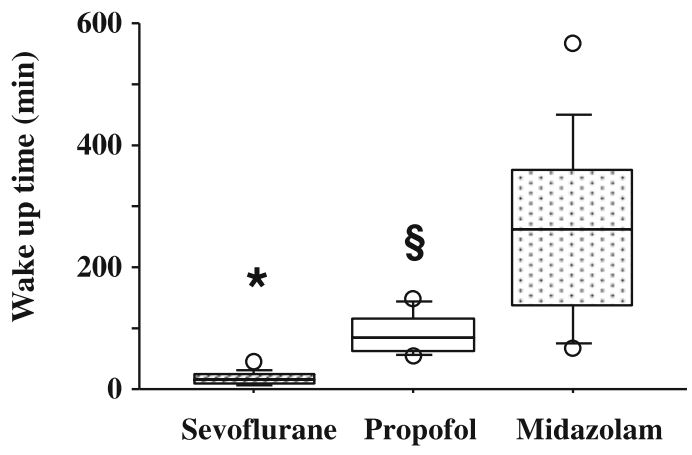


REFERENCES

1. Sackey et al, Crit Care Med 2004; 32(11):2241-6



SIGNIFICANTLY SHORTER TIME TO WAKE-UP AND EXTUBATION WITH INHALED SEDATION



*P<0.01

REFERENCES

1. Mesnil et al. Intensive Care Med 2011;37:933-41

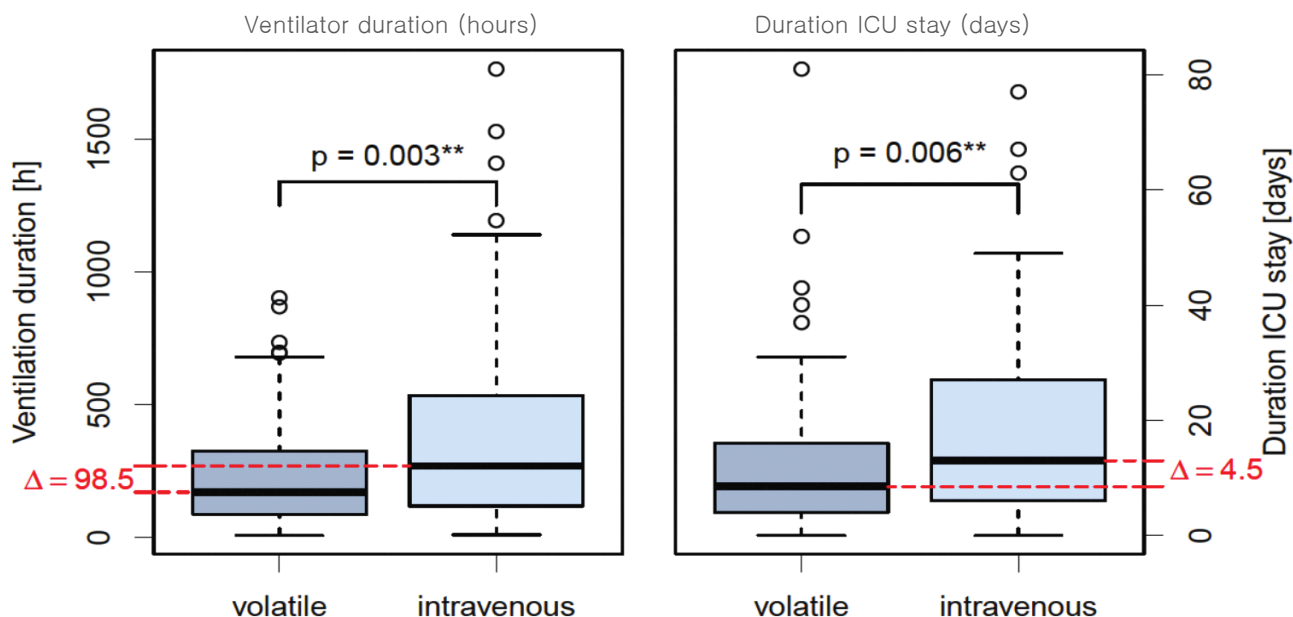


SHORTER VENTILATOR TIME AND ICU STAY WITH ISOFLURANE IN CARDIAC ARREST PATIENTS

Isoflurane sedation was associated with

- Shorter ventilator time ($p=0.003$)
- Shorter ICU stay ($p=0.006$)

Trend towards more tracheostomies in propofol/midazolam group



REFERENCES

1. Krannich et al, Critical Care Med 2017;45(4):e384-e390



RELIABLE WAKE-UP WITH INHALED SEDATION

- ✓ Shorter time to extubation...
- ✓ Shorter time to cooperation...
- ✓ Shorter ventilator time and ICU-stay...

compared with intravenous sedation

REFERENCES

1. Sackey et al, Crit Care Med 2004; 32(11):2241-6
2. Mesnil et al. Intensive Care Med 2011;37:933-41
3. Krannich et al, Critical Care Med 2017;45(4):e384-e390



RELIABLE EFFECT

The distressed patient

- IV tolerant
- Delirium prone
- Hallucinations/delusions



**PATIENT IN
DISTRESS
NEITHER
COMFORTABLE
NOR SAFE**

- Dose escalation
- Multiple sedatives often needed
- Difficult to wake up to RASS 0 after sedation
- Spend hours or even days in "the twilight zone", with delirium, hallucinations, delusions



RISK OF ESCALATING DOSES

Benzodiazepines

Dose-related transition to ICU delirium
Strong evidence for an association with delirium

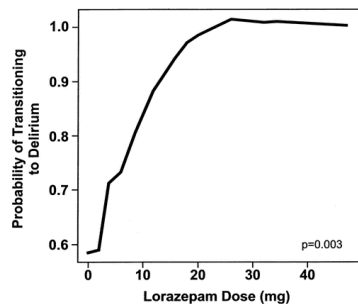


Table 2. Multivariable Analysis of Sedative and Analgesic Medications as Risk Factors for Transitioning to Delirium/Coma or Delirium Only*

Medication	Transitioning to Delirium Only Odds Ratio (95% CI)	P Value
Lorazepam	1.2 (1.1–1.4)	0.003
Midazolam	1.7 (0.9–3.2)	0.09
Fentanyl	1.2 (1.0–1.5)	0.09
Morphine	1.1 (0.9–1.2)	0.24
Propofol	1.2 (0.9–1.7)	0.18

Propofol Infusion syndrome

A potentially lethal side-effect

- 1/100 adults
- Prohibited for sedation of children
- Higher risk with >4 mg/kg/hour and >48 hours
- Inhibition of mitochondrial oxidative metabolism – mimics sepsis
 - Lactic acidosis
 - Renal failure
 - Cardiac dysfunction, arrhythmias
 - Sudden (cardiac) death
- Prevention of PRIS:
 - Limit the maximum dose and duration of propofol
 - Have a high index of suspicion: pay attention to the development of acute kidney injury, rhabdomyolysis, hyperkalemia, and bradycardia

With increasing doses of benzodiazepines the risk of delirium increases

Society of Critical Care Medicine: “...use with caution for long term sedation”

REFERENCES

1. Pandharipande et al Anesthesiology 2006;104(1):21-6
2. SCCM Guidelines 2018.
3. Robert et al. Criti Care 2009;13(5):R169

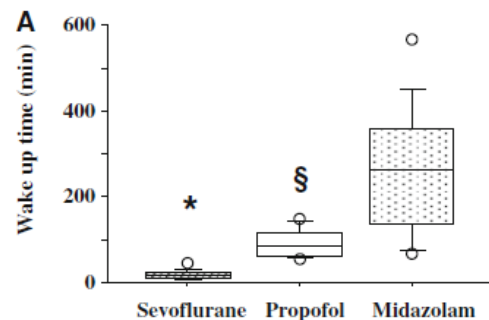


PATIENTS ARE LUCID WITH MINIMAL RESIDUAL SEDATION AFTER INHALED SEDATION

Sevoflurane vs IV

IV-sedated patients were more restless and aggressive, with more hallucinations (Sevoflurane no cases, $p=0.04$)

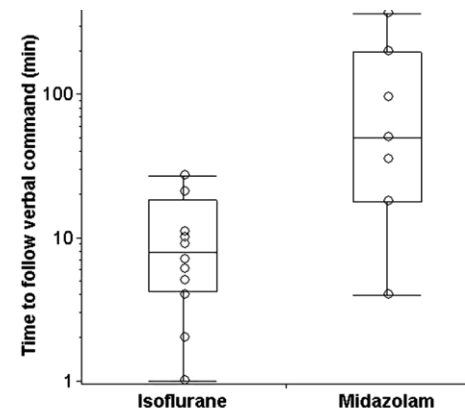
Awakening quality was better in patients treated with sevoflurane compared to IV ($p<0.001$)



Isoflurane vs IV

Patients sedated with isoflurane rapidly emerged from sedation compared to midazolam.

Time to follow verbal command
 10 ± 8 min vs 110 ± 130 min ($P=0.003$)



REFERENCES

1. Mesnil et al. Intensive Care Med 2011;37:933-41
2. Sackey et al, Crit Care Med 2004; 32(11):2241-6



REPORTED HALLUCINATIONS OR DELUSIONS AFTER SEDATION IN ICU

Midazolam
5 out of 7



$p < 0.06$

Solely Isoflurane
No cases

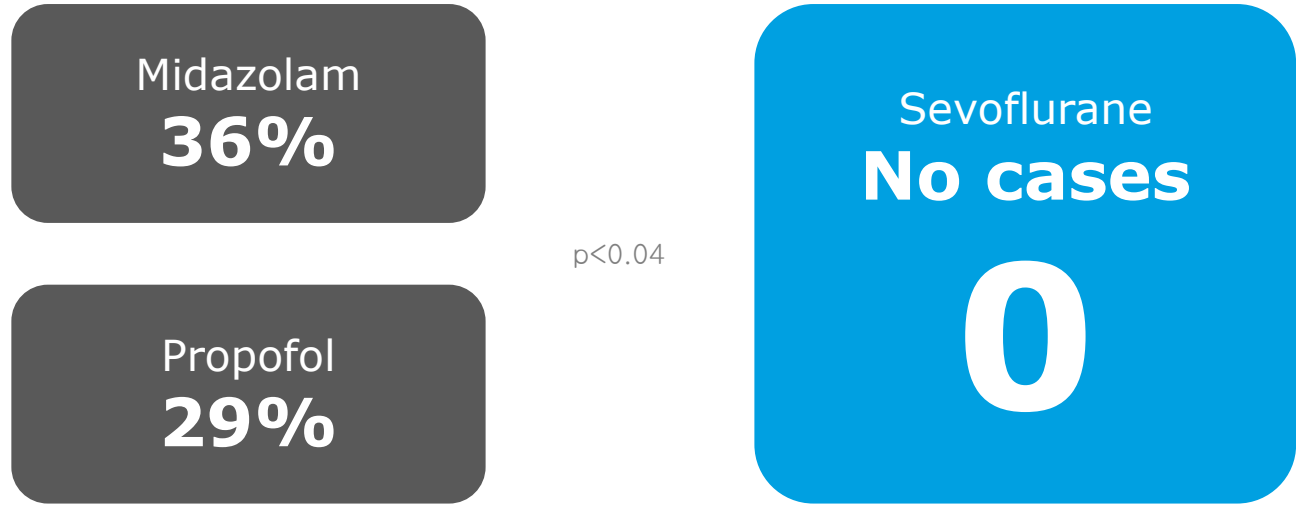
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REFERENCES

1. Sackey et al. Crit Care Med 2008, Vol 36(3):801-6



REPORTED HALLUCINATIONS OR DELUSIONS AFTER SEDATION IN ICU



REFERENCES

- 1. Mesnil et al. Intensive Care Med 2011;37:933-41



RELIABLE EFFECT WITH INHALED SEDATION

- ✓ Works in all patients
- ✓ No need for multiple sedatives
- ✓ Few problems after wake-up
- ✓ Patients are more lucid and calm with less hallucinations and delusions

REFERENCES

1. Mesnil et al. Intensive Care Med 2011;37:933-41
2. Sackey et al. Crit Care Med 2008, Vol 36(3):801-6

AnaConDa

Anaesthetic Conserving Device

**A DEVICE CUSTOMIZED
FOR ICU-USE**

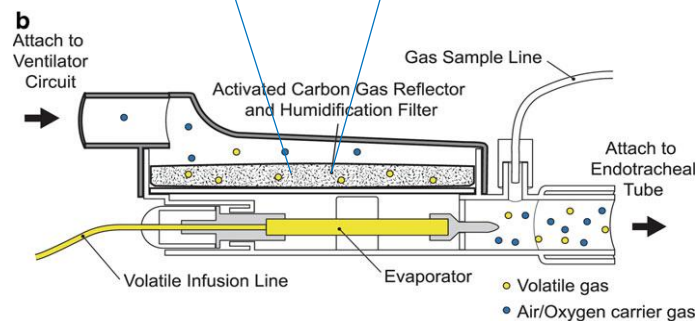
THE ANACONDA – CUSTOMIZED FOR ICU-USE

AnaConDa-S – 50 ml >200 ml Tidal volume
AnaConDa – 100 ml >350 ml Tidal volume

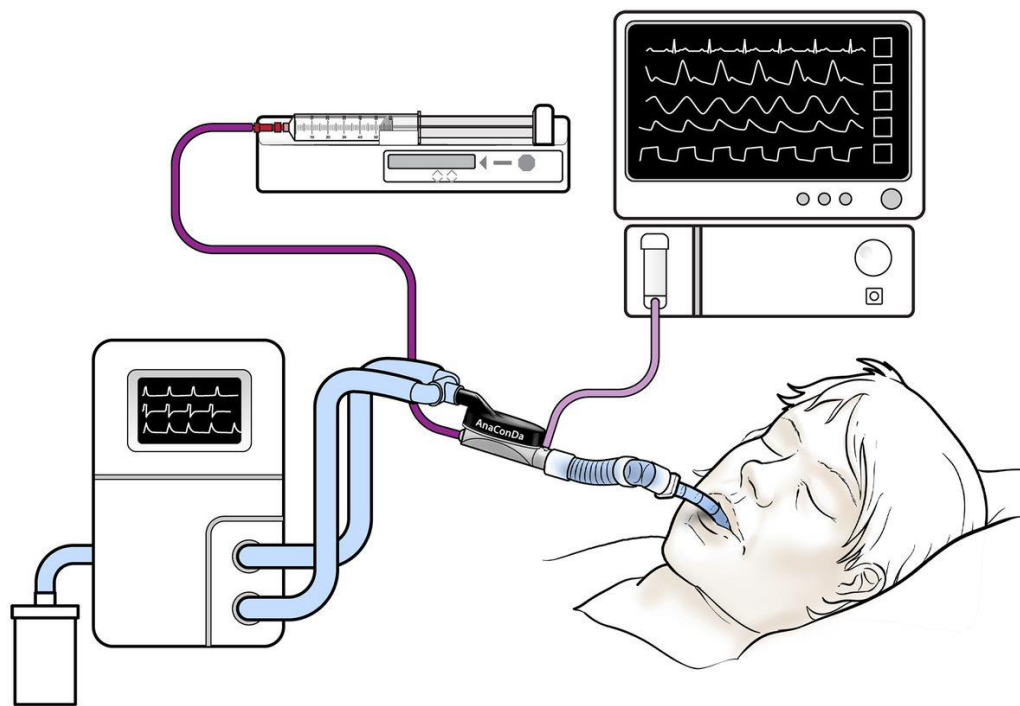


HME
Humidification 89%

90% of the Inhaled
Sedative is recycled,
due to the Active
Carbon Reflector.



THE ANACONDA SET-UP CUSTOMIZED FOR ICU-USE



SEDANAMEDICAL
**PIONEERING VOLATILE
ANAESTHETIC DELIVERY**

OVER A DECADE OF CLINICAL EXPERIENCE WITH MORE THAN 90 PEER-REVIEWED PUBLICATIONS

Prolonged isoflurane sedation of intensive care unit patients with

Isoflurane Sedation on the ICU in Cardiac
Intensive Care
DOI 10.1097/EJA.0000000000000133

AN ORIGINAL ARTICLE

EJA

Eur J Anaesthesiol 2016; **33**:6–13

ORIGINAL ARTICLE

Survival after long-term isoflurane sedation as opposed to intravenous sedation in critically ill surgical patients

Retrospective analysis

Martin Bellgardt, Hagen Bomberg, Jenny Herzog-Niescery, Burkhard Dasch, Heike Vogelsang, Thomas P. Weber, Claudia Steinfort, Waldemar Uhl, Stefan Wagenpfeil, Thomas Volk and Andreas Meiser

Distress Syndrome

René-Sébastien Faure¹,
Benoît Guérin¹, Sébastien Perbet¹,
Thomas Bazin¹, Emmanuel Futier^{1,2}, and

Department of Clinical
Biology, and ⁴Department of Clinical
Montpellier University, Université d'Auvergne

INCREASING USE GLOBALLY



Proven in clinical practice

- 100.000 sedated ICU-patients
- 300.000 AnaConDa used in 20 countries
- more than 500.000 treatment days

 Current use of AnaConDa

DEVELOPMENT TO MEET A GLOBAL NEED



EU:

Ongoing study:

IsoConDa study pivotal RCT >300 patients

Planning phase:

Pediatric IsoConDa study RCT 150 patients

2019/2020:

Filing for isoflurane sedation label in Europe

US:

Approval process initiated

WHEN INHALED SEDATION MAKES A DIFFERENCE



Impaired
gas
exchange

- ARDS and AHRF
- COPD
- Asthma

- Improved oxygenation
- Reduced inflammatory response
- Bronchodilatory



Need for
reliable
wake-up

- Low GCS
- Post cardiac arrest
- Stroke

- Short and predictable wake-up time
- Shorter time to extubation, and shorter time at the ICU
- Rapid recovery time
- Elimination independent of organ function



The
distressed
patient

- IV tolerant
- Delirium prone
- Hallucinations/delusions

- Full range sedative
- No/low risk of tolerance development, ceiling effect and withdrawal
- Reduction of opioid use

AnaConDa

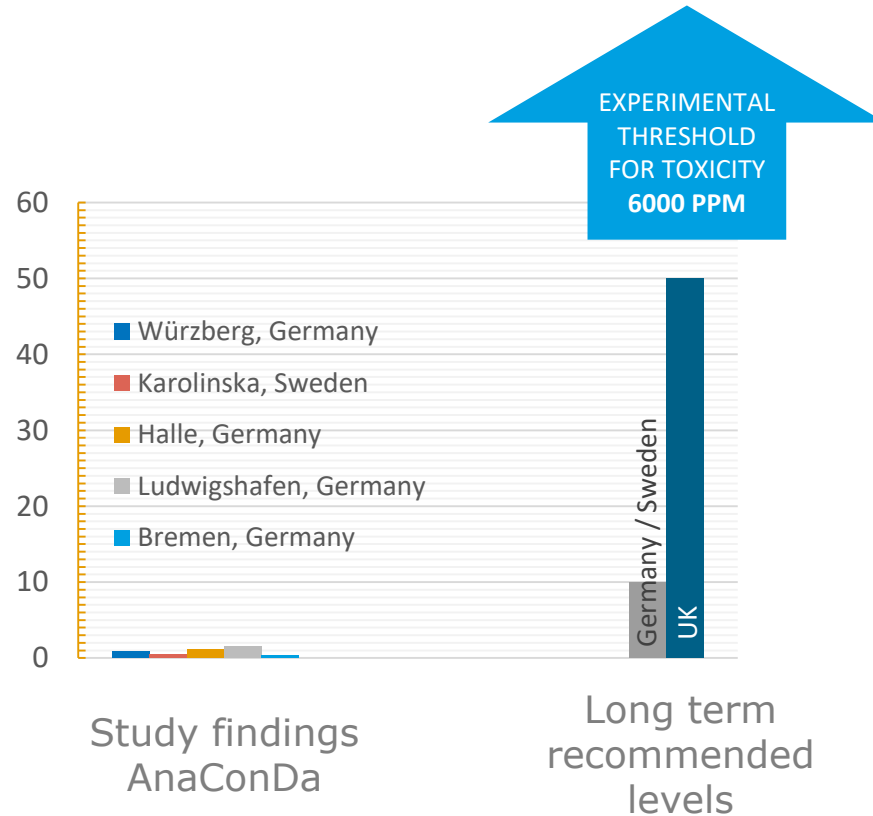
SAFE | EFFECTIVE | CONTROLLABLE



BACK-UP

GAS POLLUTION LIMITED WITH THE ANACONDA

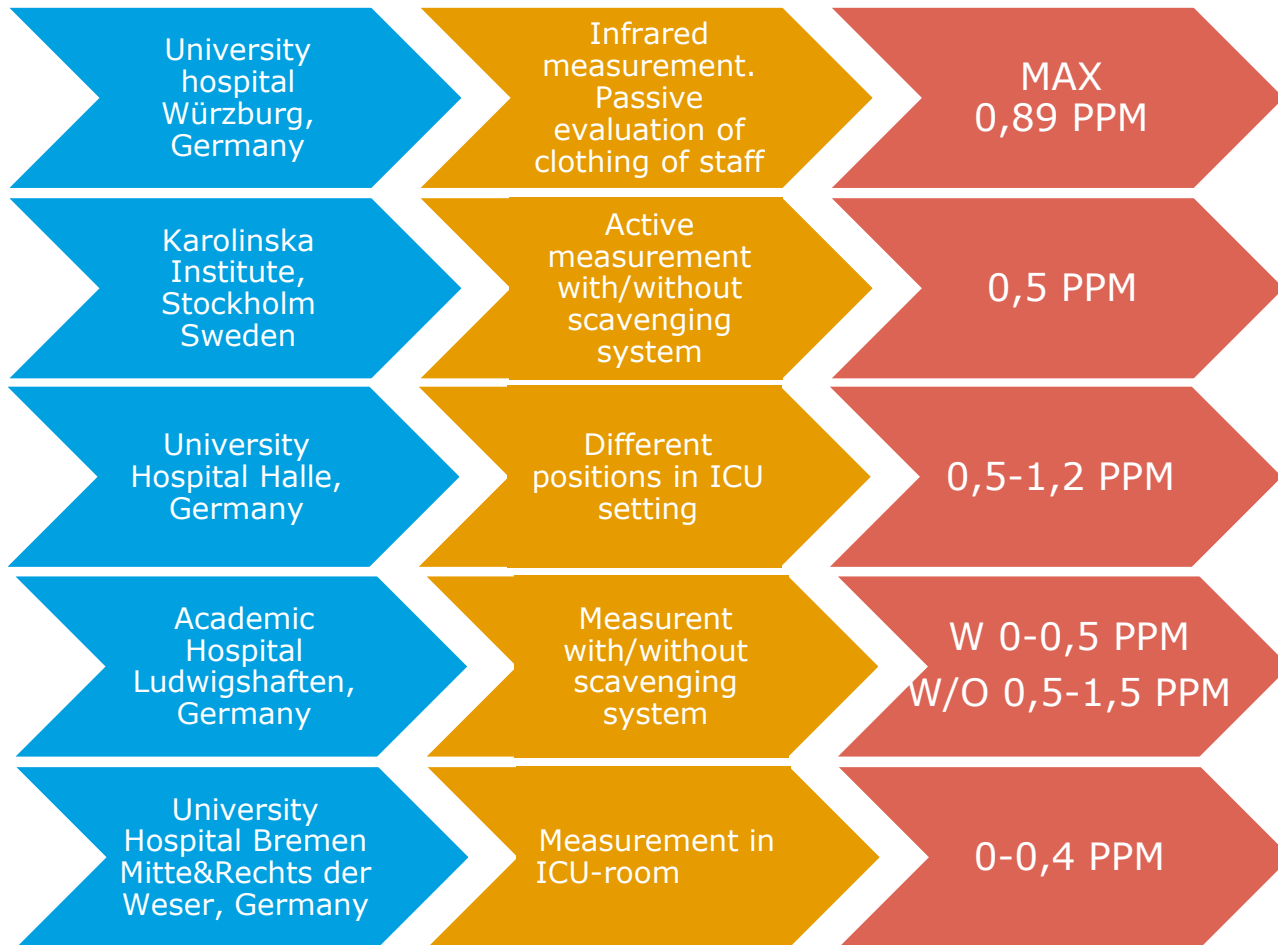
EXTENSIVE DATA IS AVAILABLE



REFERENCES

1. Herzog-Niescery et al, Minerva Anestesiol 2018;84(1):25-34
2. Mazze et al, Teratology 1985; 32:339-45
3. Sackey et al Crit Care Med 2005;33(5):1141-3
4. Data on file

SEVERAL MEASUREMENTS CONDUCTED IN ICU 's SHOWING A RANGE OF 0-1,5 PPM



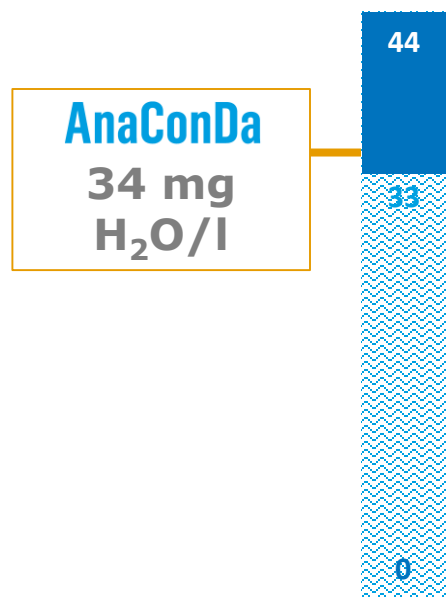
REFERENCES

1. Data on file
2. Sackey et al Crit Care Med 2005;33(5):1141-3

ANACONDA IS IN THE RANGE OF ACTIVE HUMIDIFICATION

HUMIDIFICATION IS IMPORTANT FOR LONG-TERM MECHANICAL VENTILATION

100% humidification
= 44 mg H₂O/l



Active humidification;
recommended range
= 33-44 mg H₂O/l

REFERENCES

1. ATS guidelines for Humidification, 2012
2. Data on file