AnaConDa

Anaesthetic Conserving Device

ON OFF

SEDANAMEDICAL

FACILITATES INHALED SEDATION FOR ICU PATIENTS

ON OFF

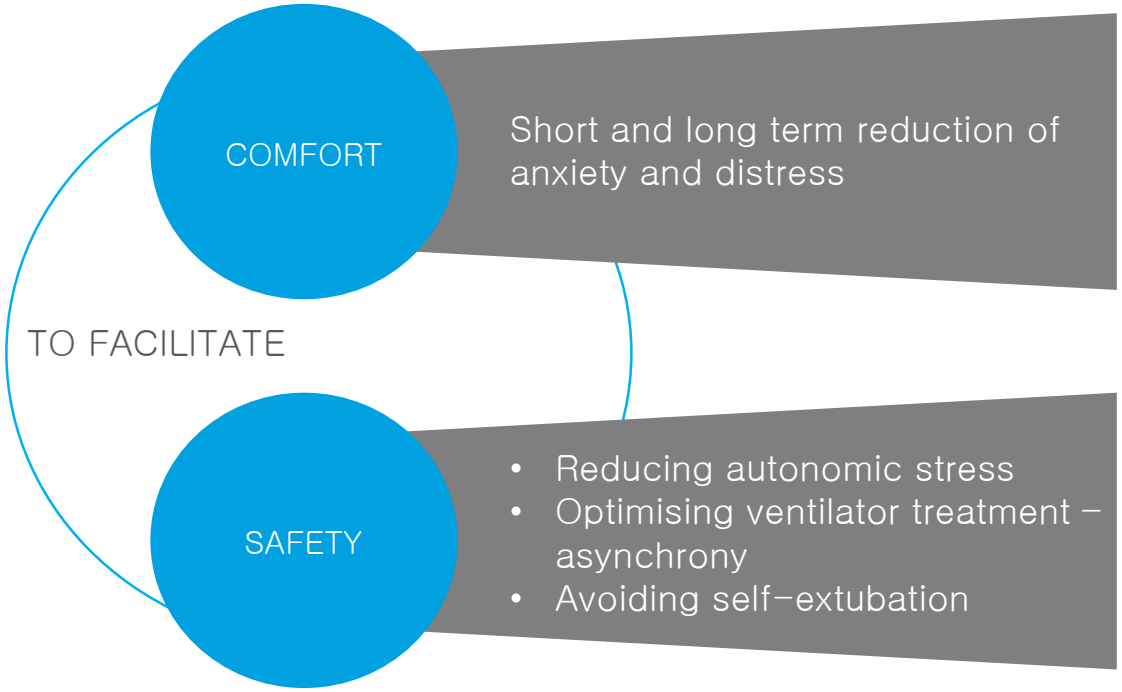
SEDANAMEDICAL

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

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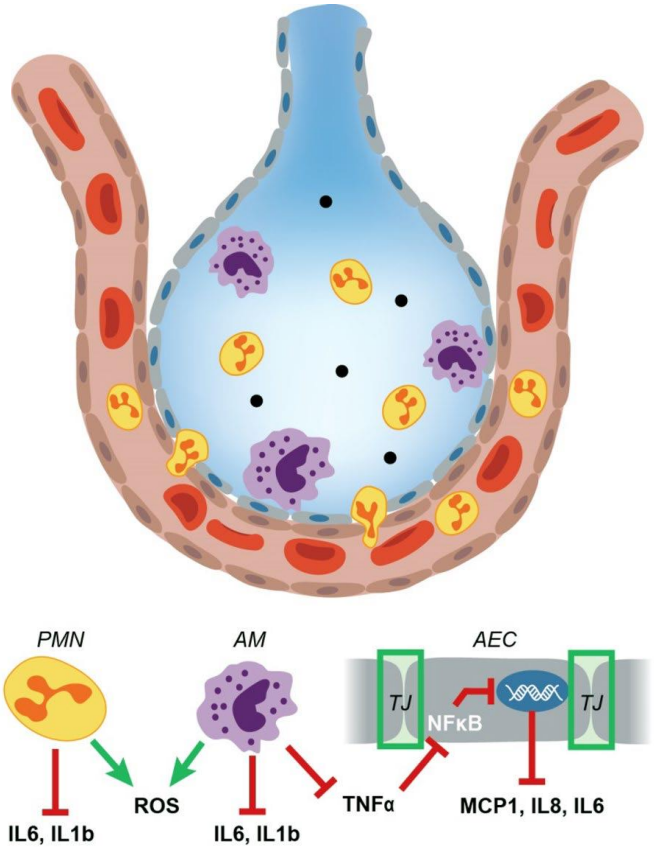
LUNG PROTECTIVE PROPERTIES OF INHALED SEDATION ARE WELL CHARACTERISED

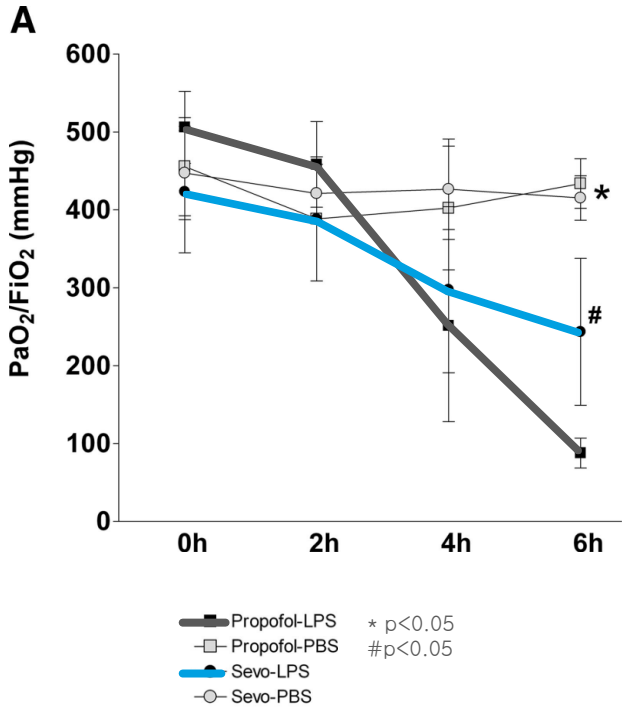


REFERENCES

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

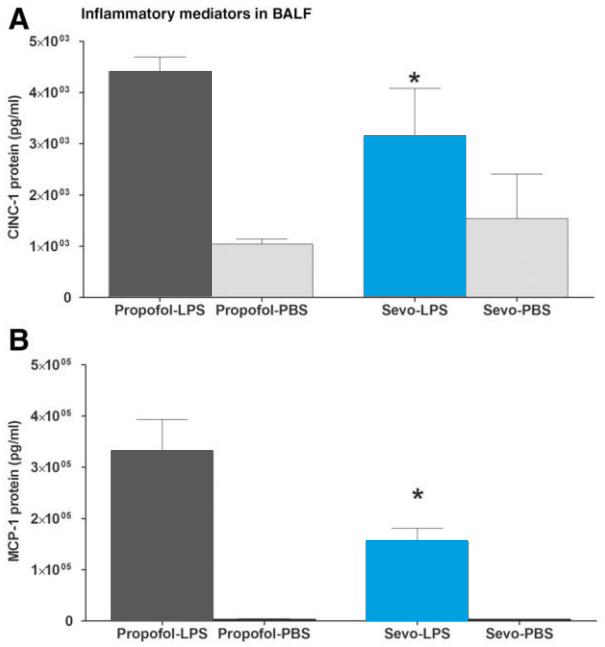
IMPROVED OXYGENATION AND REDUCED PULMONARY INFLAMMATORY RESPONSE IN ARDS

PaO_2/FiO_2 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)



* p<0.05

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. $p<0.05$

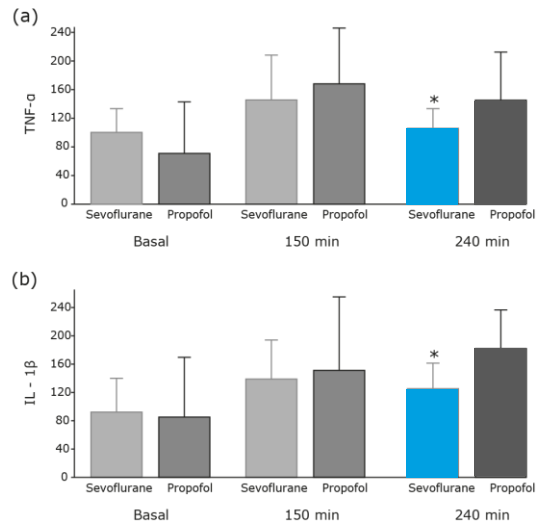
REFERENCES

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)

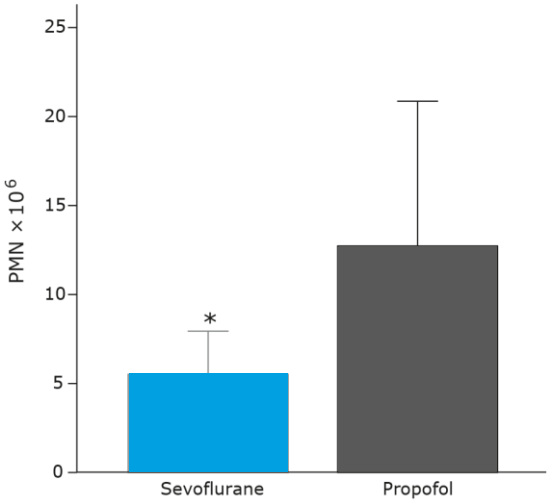
Fig. 3



*p<0.05

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

Fig. 2

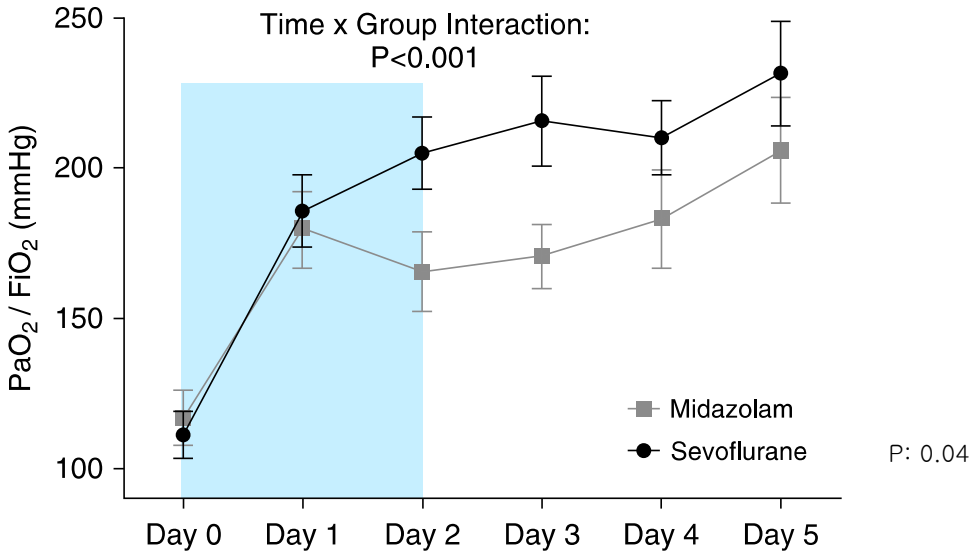


*p<0.007

REFERENCES

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

IMPROVED OXYGENATION AND REDUCED PULMONARY INFLAMMATORY RESPONSE IN ARDS

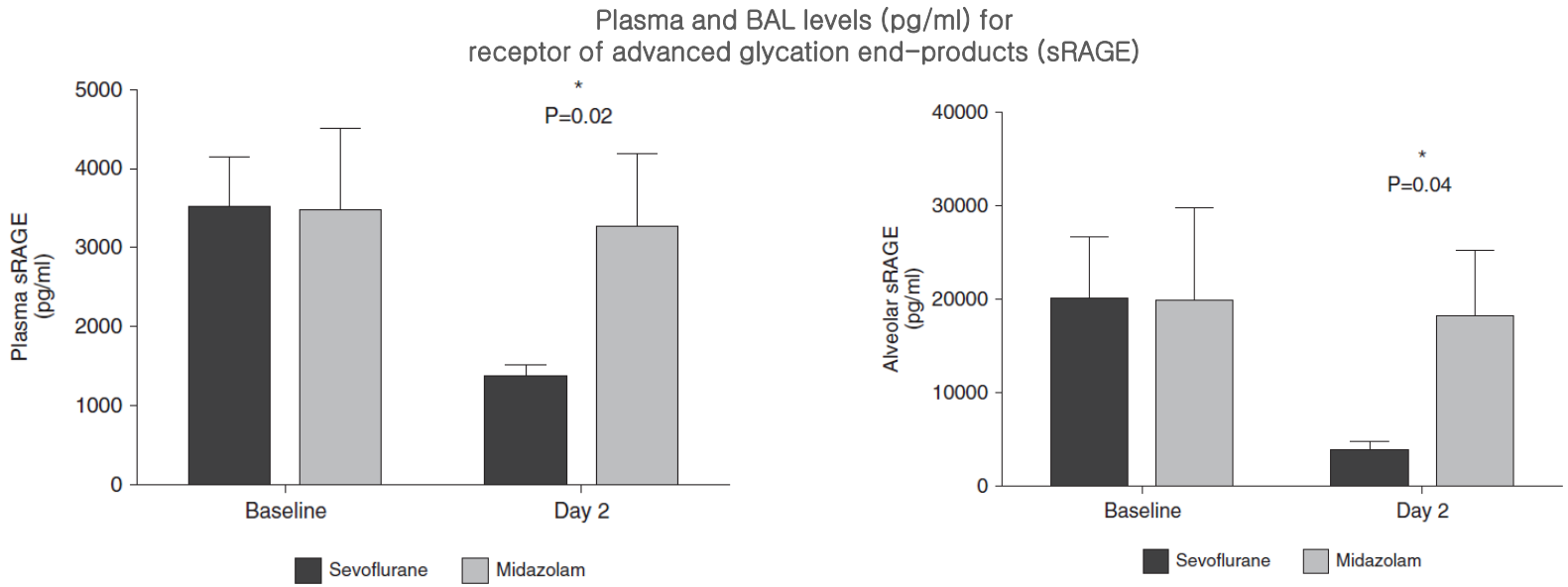


In patients with ARDS sevoflurane improved oxygenation

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

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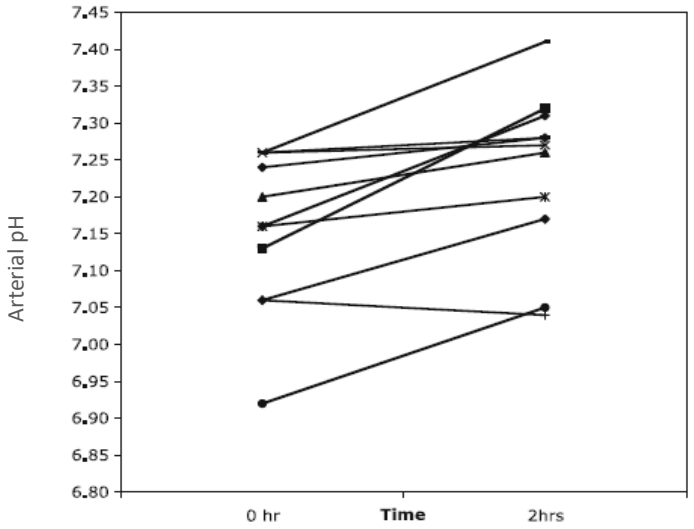
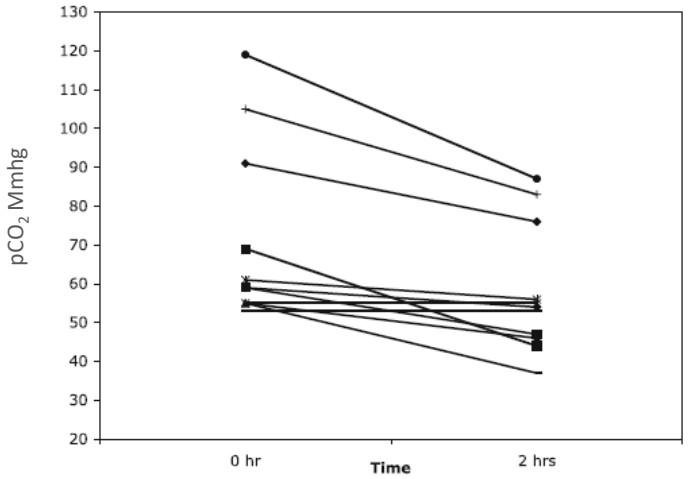
ISOFLURANE IS BRONCHODILATORY IN ASTHMA

Reversed acidosis



Reversed hypercarbia

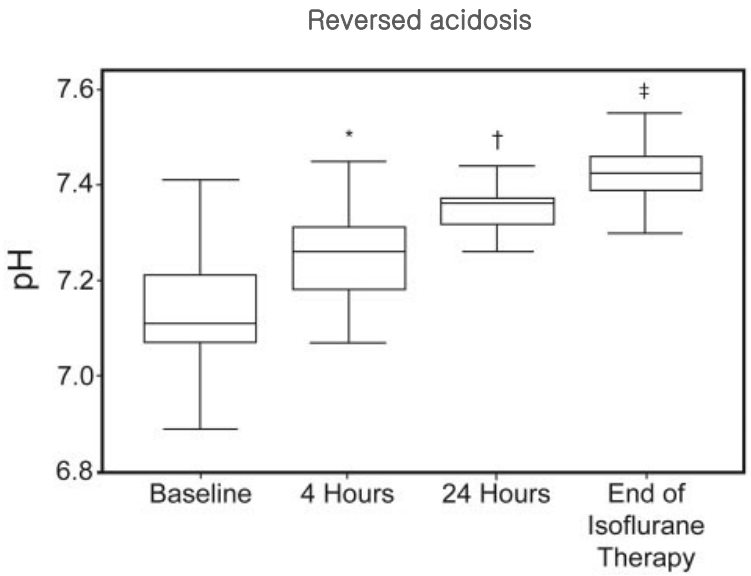


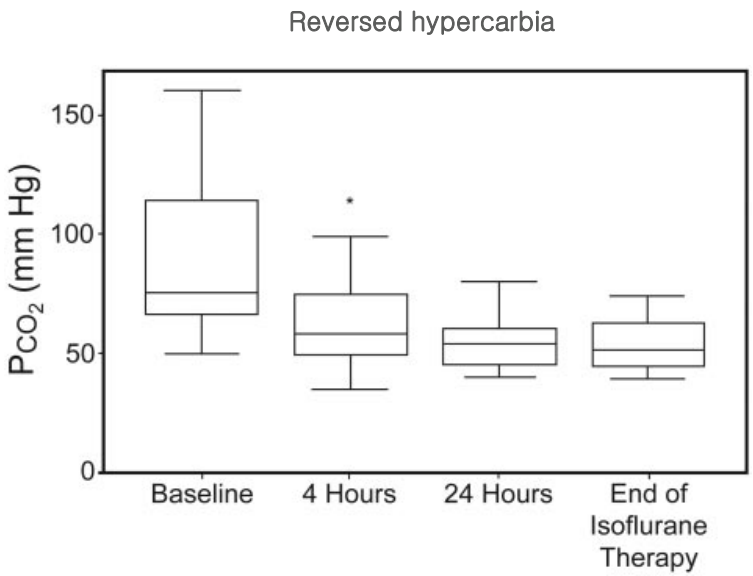
Isoflurane led to improvement in arterial pH and a reduction in partial pressure of pCO_2

REFERENCES

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

ISOFLURANE IS BRONCHODILATORY IN ASTHMA





Isoflurane led to improvement in pH and pCO_2 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

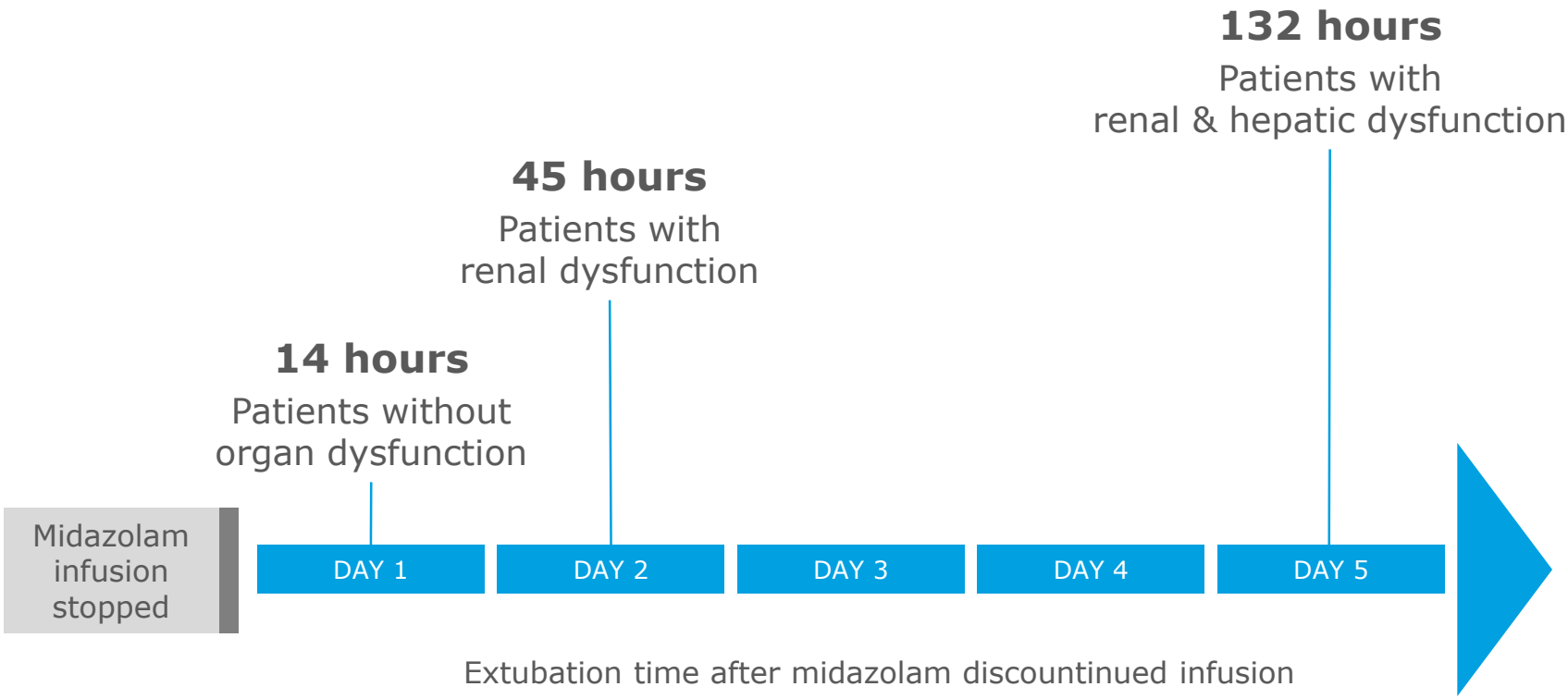
ON  OFF

RAPID ELIMINATION

Need for reliable wake-up

- Low GCS
- Post cardiac arrest
- Stroke

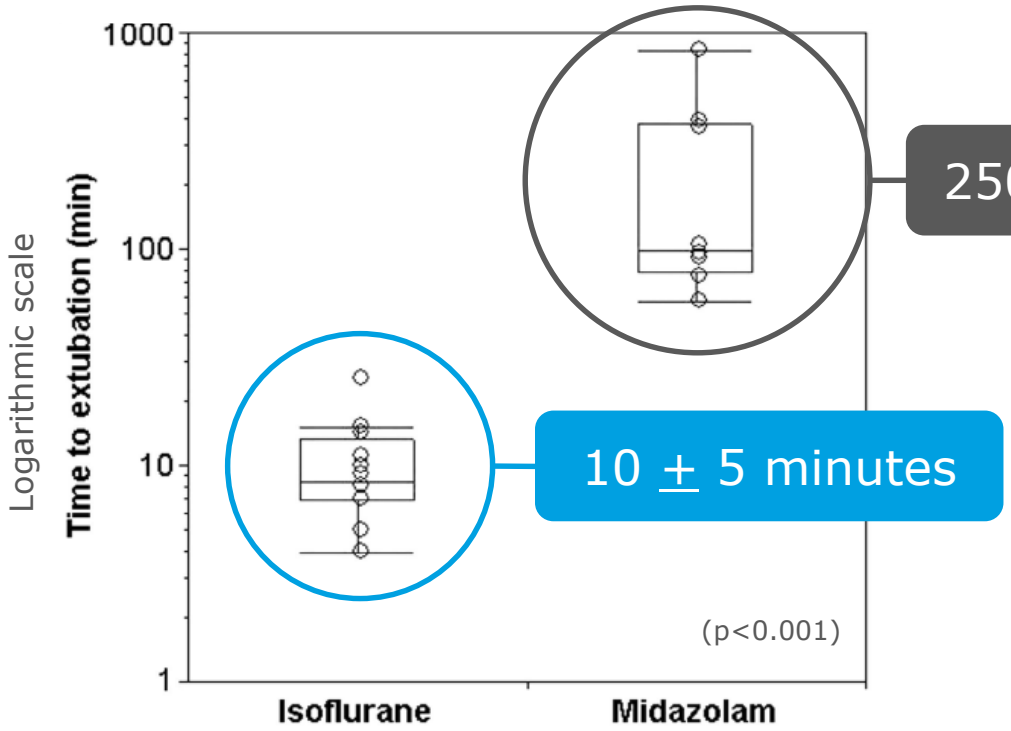
BENZODIAZEPINES TIME TO WAKE-UP



REFERENCES

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

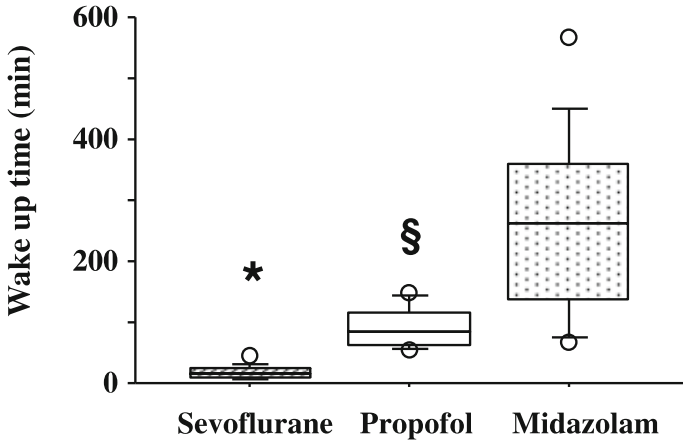
SHORT EXTUBATION TIME WITH ISOFLURANE

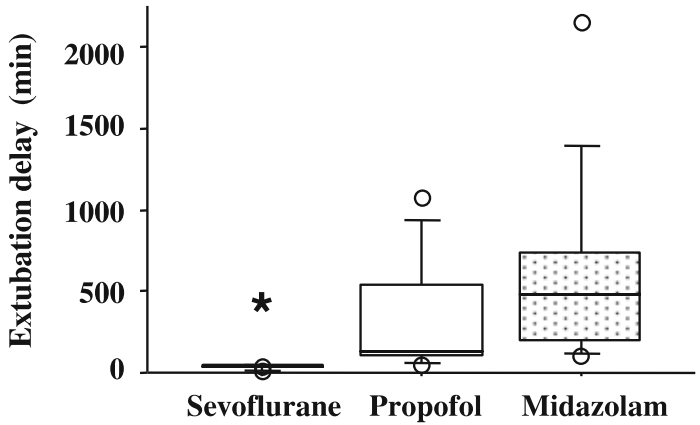


REFERENCES

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

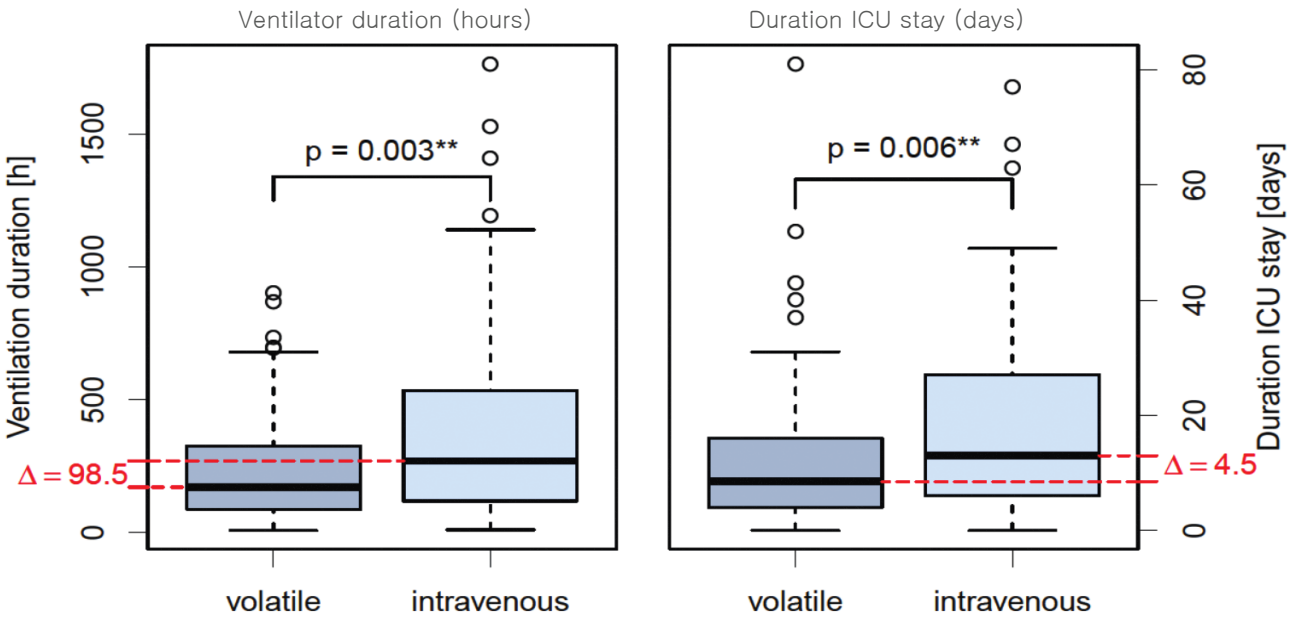
REFERENCES

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

SHORTER VENTILATOR TIME AND ICU STAY WITH ISOFLURANE IN CARDIC 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

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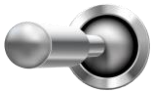
ON  OFF

RELIABLE EFFECT

The distressed patient

- IV tolerant
- Delirium prone
- Hallucinations/delusions

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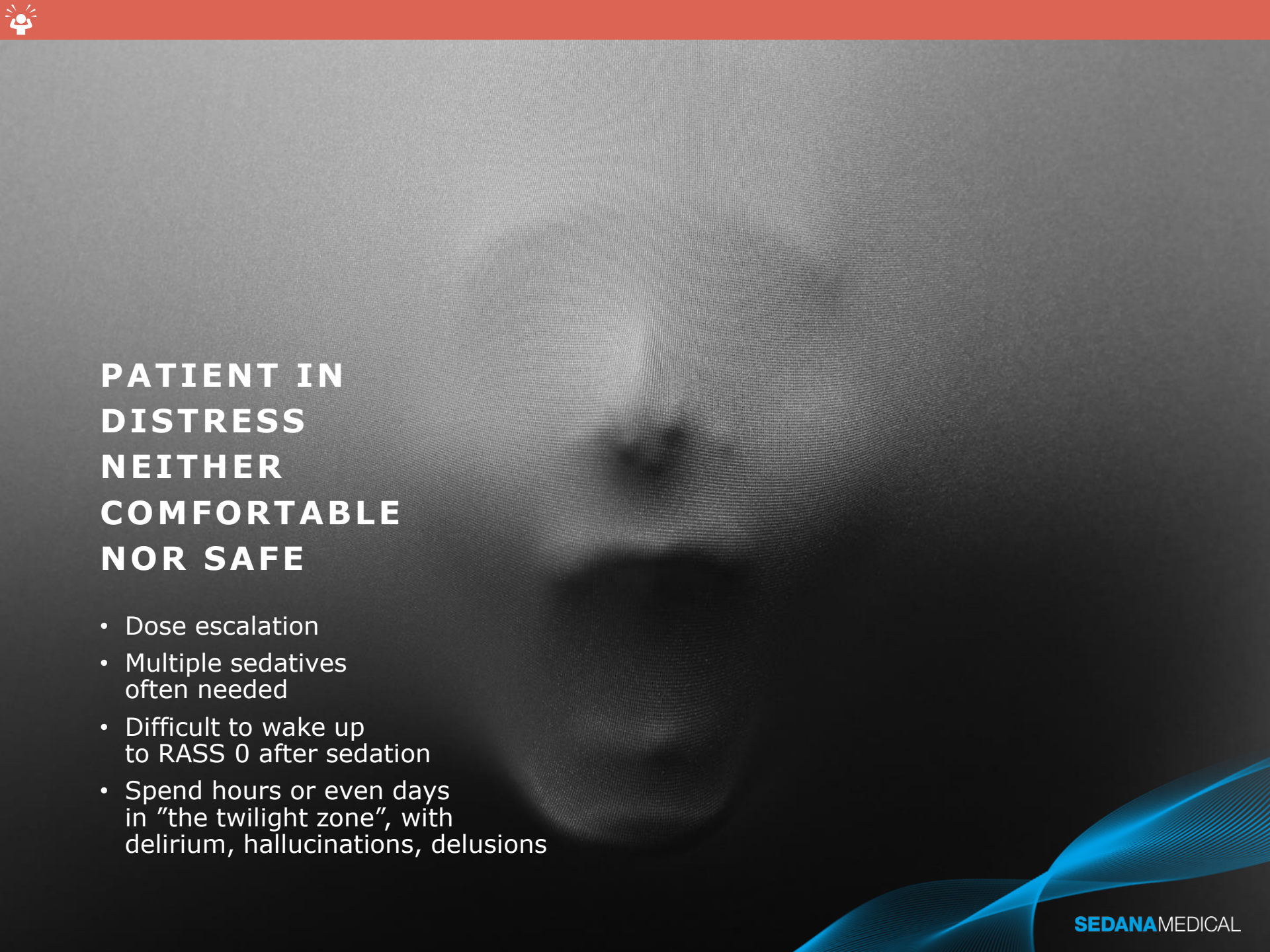

PATIENT IN DISTRESS NEITHER COMFORTABLE NOR SAFE

- 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

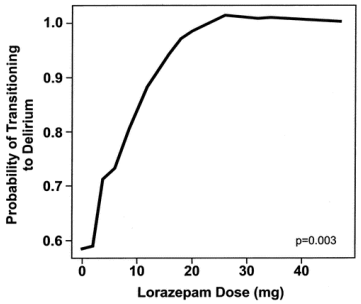

Table 2. Multivariable Analysis of Sedative and Analgesic Medications as Risk Factors for Transitioning to Delirium/Coma or Delirium Only*

Medication	Transitioning to Delirium Only Odds Ratio (95% CI)	*P* Valuel
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, arrythmias
  - 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

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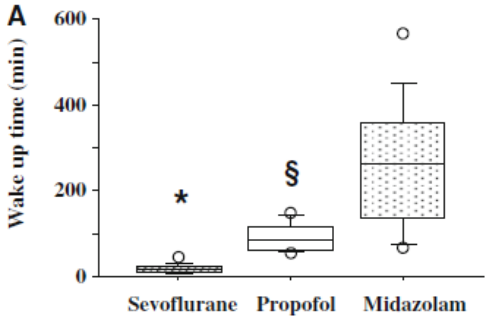
PATIENTS ARE LUCID WITH MINIMAL RESIDUAL SEDATION AFTER INHALED SEDATION

Sevoflurane vs IV

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

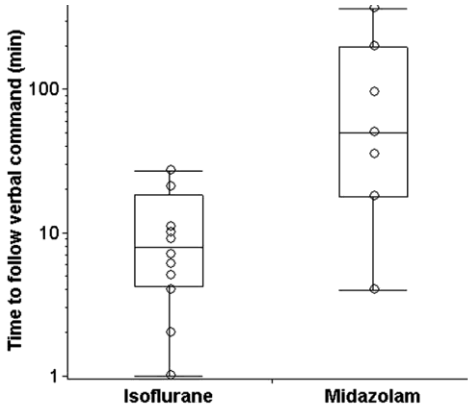
Awakening quality was better in patients treated with sevoflurane compared to IV (p<0.001)



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

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REPORTED HALLUCINATIONS OR DELUSIONS AFTER SEDATION IN ICU

Midazolam
5 out of 7

p<0.06

Solely Isoflurane
No cases

0

REFERENCES

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

REPORTED HALLUCINATIONS OR DELUSIONS AFTER SEDATION IN ICU

Midazolam
36%

Propofol
29%

p<0.04

Sevoflurane
No cases

0

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

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AnaConDa

Anaesthetic Conserving Device

A DEVICE CUSTOMIZED FOR ICU-USE

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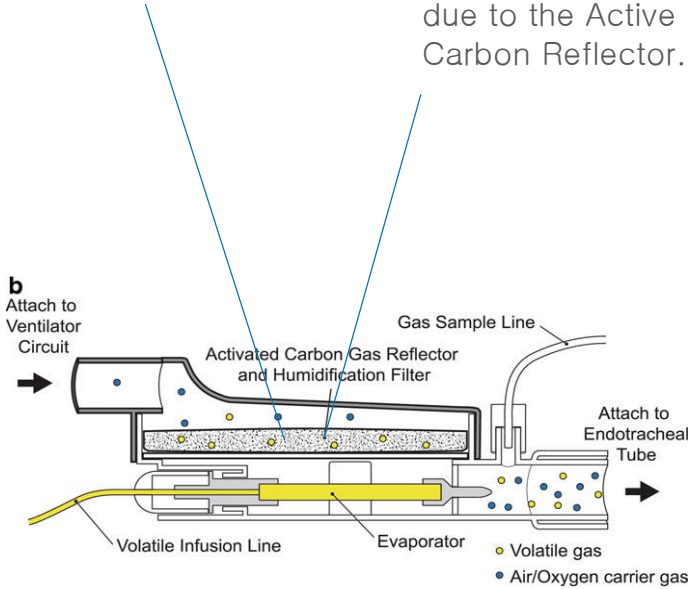
THE ANACONDA – CUSTOMIZED FOR ICU-USE

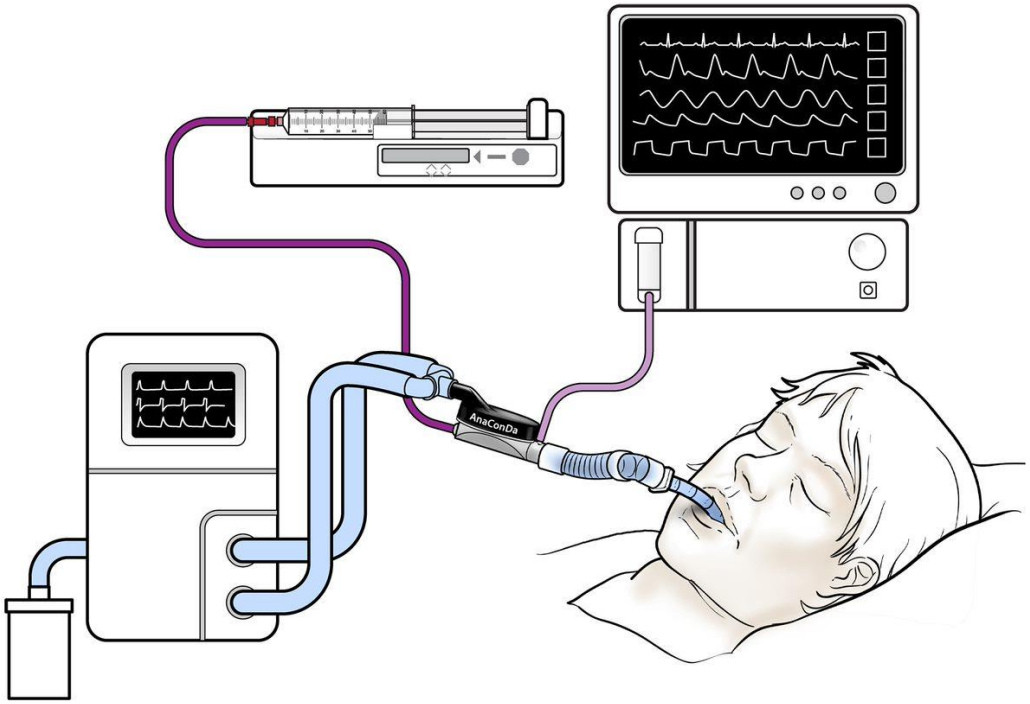
AnaConDa–S – 50 ml >200 ml Tidal volume
AnaConDa – 100 ml >350 ml Tidal volume

HME
Humidification 89%

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



THE ANACONDA SET-UP CUSTOMIZED FOR ICU-USE



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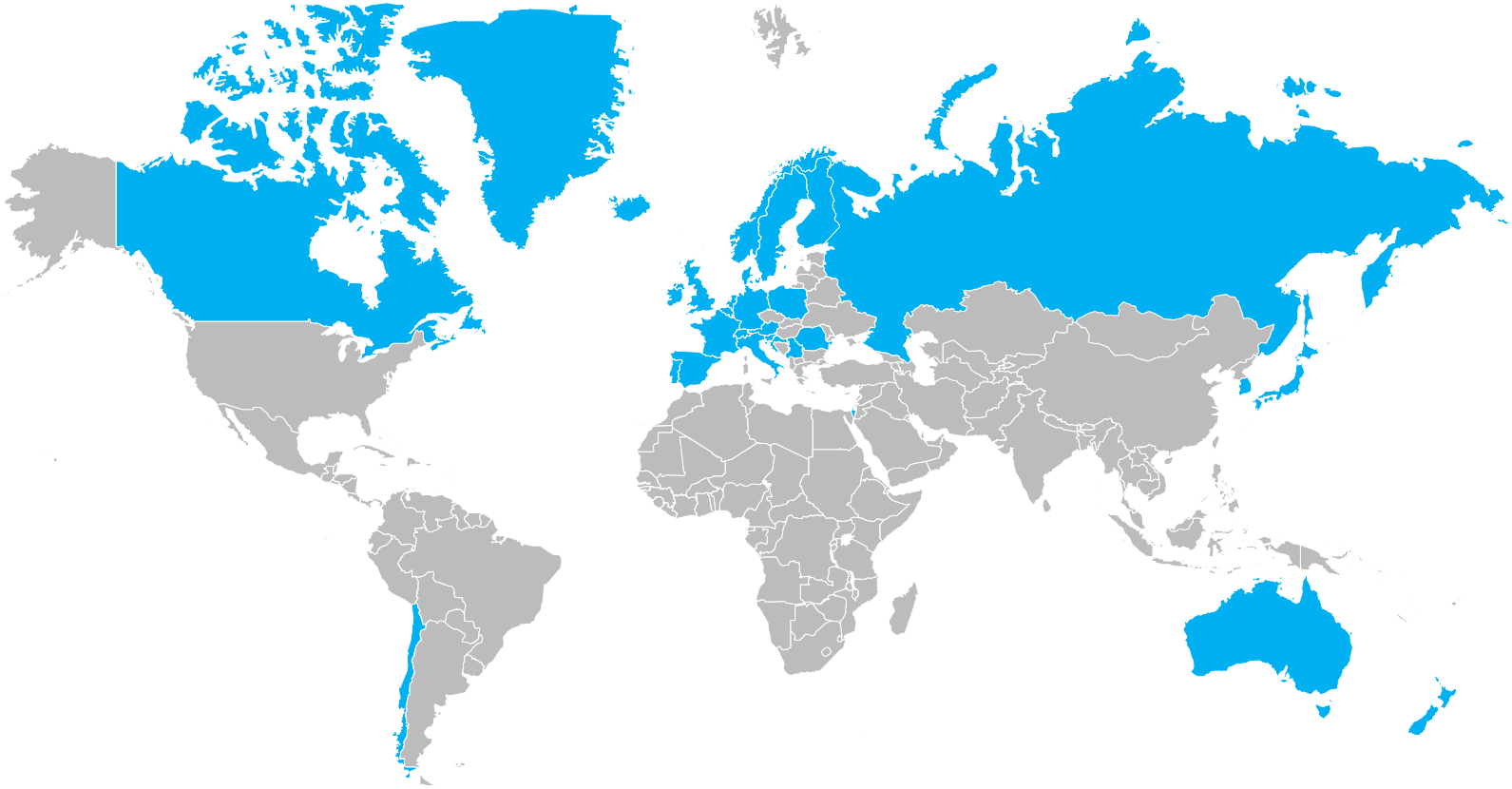
PIONEERING VOLATILE ANAESTHETIC DELIVERY

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

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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 predictabel 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

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AnaConDa

SAFE | EFFECTIVE | CONTROLLABLE

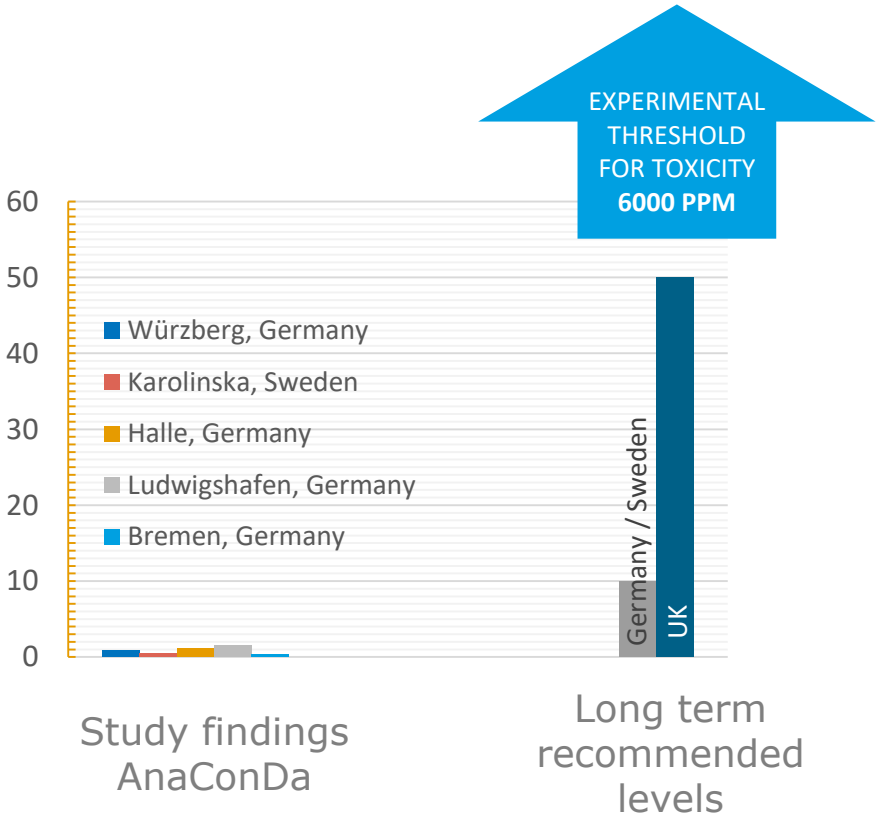
ON OFF

SEDANAMEDICAL

BACK-UP

GAS POLLUTION LIMITED WITH THE ANACONDA

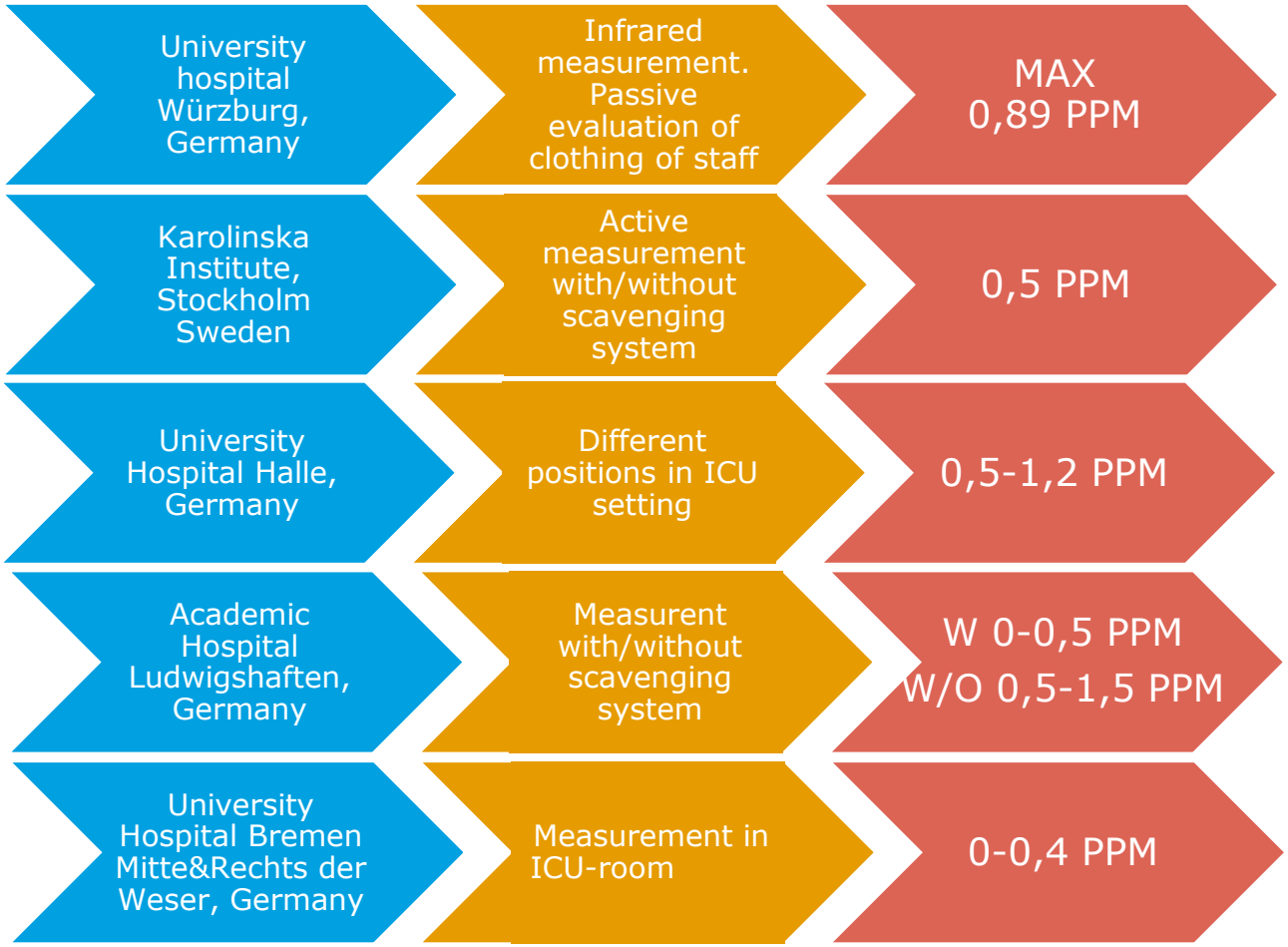
EXTENSIVE DATA IS AVAILABLE



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



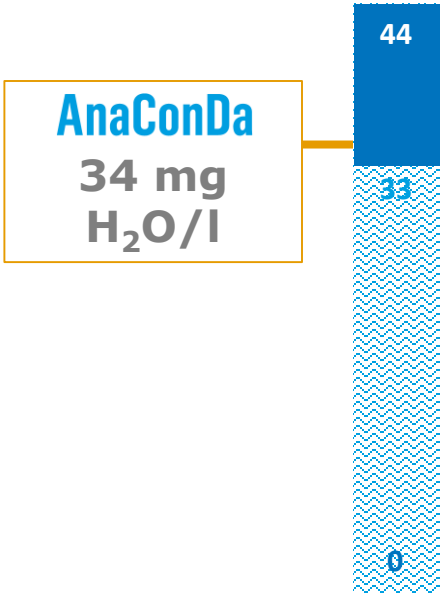
REFERENCES

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 H_2O/l



Active humidification;
recommended range
= 33-44 mg H_2O/l

REFERENCES

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