

# Aktuální otázky sedace kriticky nemocných

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*ICU, Landesklinikum Baden bei Wien, Austria*

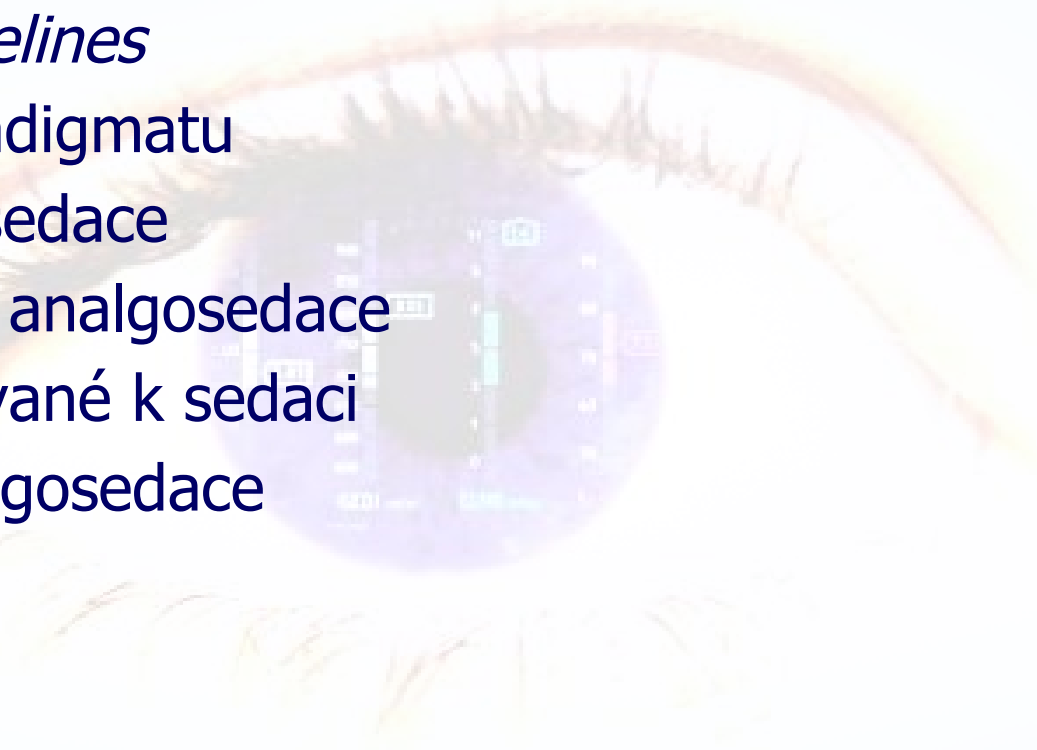
*no conflict of interest*

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# přehled

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  3. cíle analgosedace
  4. monitorace analgosedace
  5. látky používané k sedaci
  6. taktika analgosedace
  7. *Covid-19*
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***current  
guidelines***

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# Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

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# Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU

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***změna  
paradigmatu***

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# změna paradigmatu

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- ✓ koncept hluboké sedace (*deep level of sedation*) opuštěn
- ✓ analgetická terapie by měla předcházet sedaci
- ✓ je doporučována „*first-line*“ *analgesia* pomocí intravenózních opioidů
- ✓ nestačí-li analgésie k odstranění stresu, přidává se sedace (*sedation as needed*)



# změna paradigmatu

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- ✓ jsou doporučována **nebenzodiazepinová** sedativa (dexmedetomidin, propofol, clonidin)
- ✓ **nefarmakologické** postupy (mobilizace, redukce hluku a osvětlení, rytmus spánku – bdění ...) !!!
- ✓ nezbytným se jeví zavedení **skórovacích systémů** ke sledování výskytu agitovanosti, bolesti a deliria (RASS, CAM-ICU)

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***cíle***

***analgosedace***

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## 2. Cíle analgosedace u pacientů v intenzivní péči

Recentní práce definovaly správně prováděnou analgezii a sedaci jako takové farmakologické i nefarmakologické ovlivnění pacienta, který je orientován, zbaven bolesti a pocitů strachu či úzkosti, zároveň je však při vědomí či lehce probuditelný a dobře spolupracující. Současně je třeba minimalizovat riziko vědomého či bezděčného sebeohrožení pacienta, např. vytažením invazivních vstupů či endotracheální kanyly.





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***monitorace***  
***analgozedace***

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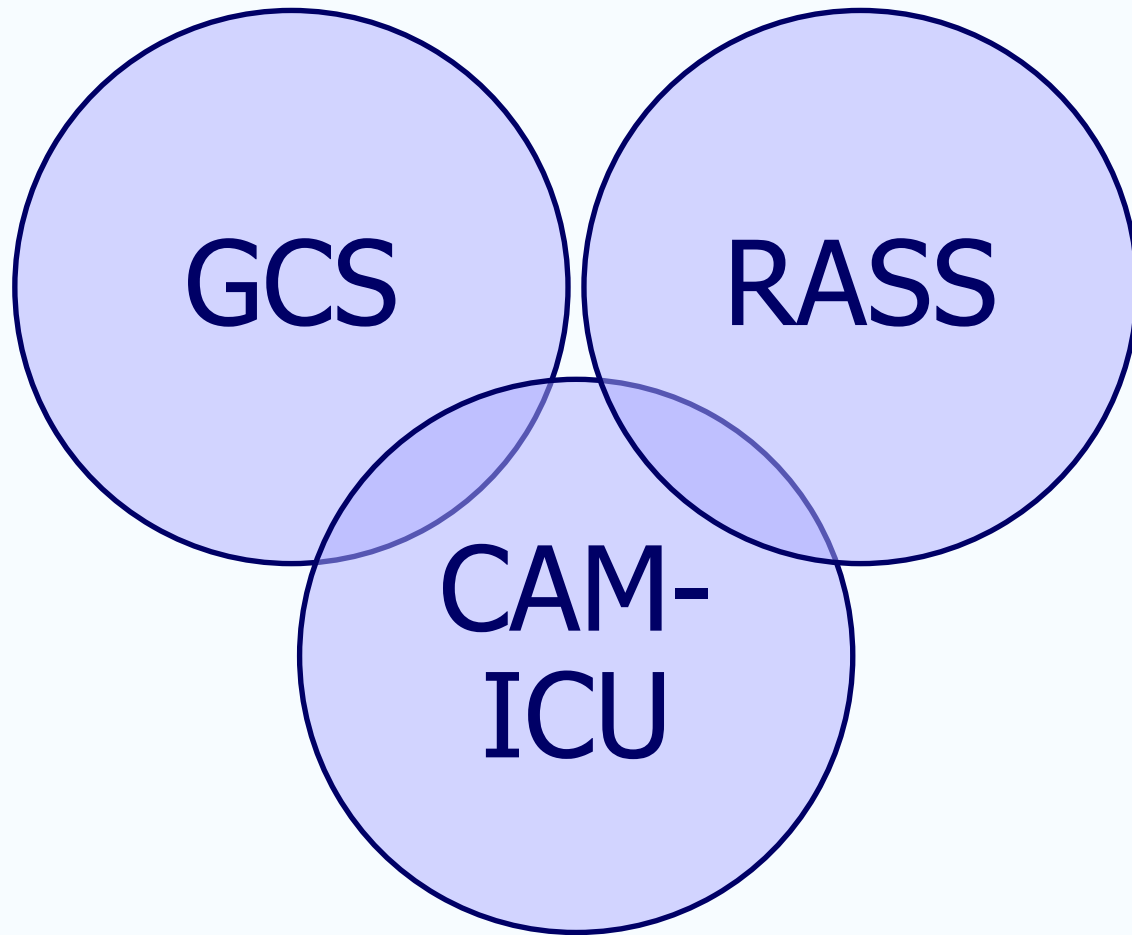
# monitorace analgosedace

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- ✓ laboratorní, přístrojové a zobrazovací možnosti jsou omezené
- ✓ důraz kladen na sledování klinického stavu
- ✓ systémy určeny pro pacienty komunikující i nekomunikující
- ✓ standard: *Richmond Agitation and Sedation Scale (RASS)*
- ✓ dle doporučení hodnotit každých 8 hodin

# monitorace analgosedace

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Tabulka 1. Richmond Agitation and Sedation Scale (RASS)

Skóre	Stav	Popis
+4	Bojovný	Očividně bojovný, násilný, bezprostředně ohrožuje personál
+3	Výrazně agitovaný	Tahá či vytahuje kanylu či katetry, agresivní
+2	Agitovaný	Časté bezcílné pohyby, zápasí s ventilátorem
+1	Neklidný	Úzkostný, ale pohyby bez známek živé agrese
0	Bdělý ale klidný	
-1	Somnolence	Není plně bdělý, ale reaguje při oslovení (otevření oči/oční kontakt >10 s)
-2	Lehká <u>sedace</u>	Krátké probuzení a oční kontakt na oslovení (<10 s)
-3	Střední <u>sedace</u>	Pohyb či otevření očí na oslovení (bez očního kontaktu)
-4	Hluboká <u>sedace</u>	Žádná odpověď na oslovení, pouze pohyb či otevření očí na fyzický podnět
-5	<u>Neprobuditelný</u>	Žádná odpověď na oslovení ani fyzický podnět

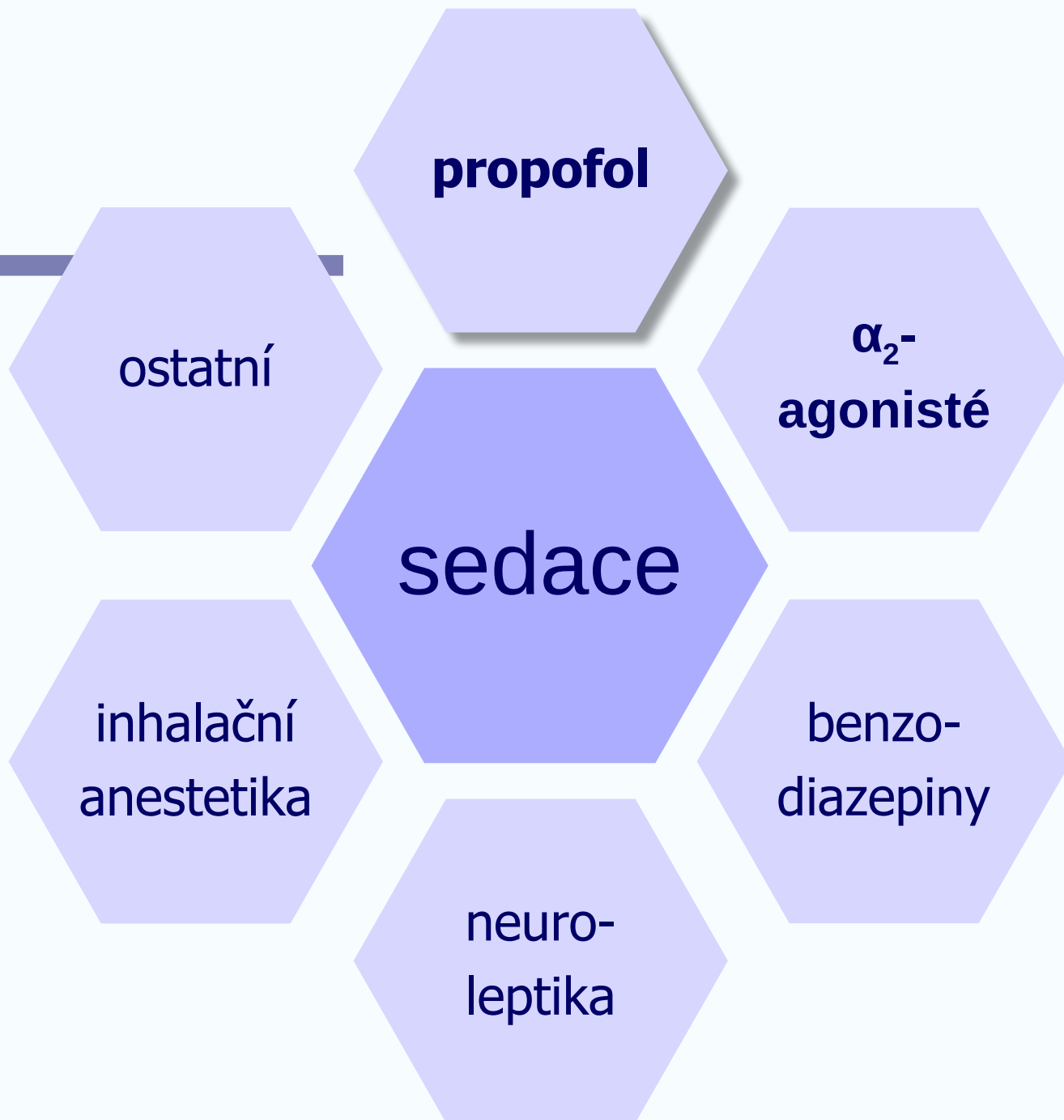




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***látky  
používané  
k sedaci***

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***propofol***



# propofol

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- ✓ nejčastěji používané sedativum
- ✓ Německo: povoleno použití od 17. roku věku, max. po dobu 7 dnů a v dávce  $\leq 4$  mg/kg/h
- ✓ být si vědom nežádoucích účinků!
- ✓ *propofol-related infusion syndrom*
- ✓ sterilita!
- ✓ energetický příjem (tuková emulze)

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***$\alpha_2$ -agonisté***

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# $\alpha_2$ - agonisté

- ✓ **sedativní** a mírně analgetický efekt bez dechové deprese
- ✓ clonidin, **dexmedetomidin**
- ✓ pacient snadno **probuditelný**, minimální amnézie a anxiolýza
- ✓ **cave: hypotenze a bradykardie**



# dexmedetomidin

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- ✓ jiný farmakokinetický i farmakodynamický profil (kratší poločas)
- ✓ nižší incidence deliria ve srovnání s midazolamem (clonidin pouze u odnětí alkoholu)
- ✓ lepší spolupráce pacientů ve srovnání s midazolamem und propofolem



## 2013 PAD *guidelines*

## 2018 PADIS *guidelines*

**nonbenzodiazepine** sedatives  
(either *propofol* or *dexmedetomidine*)

are **preferable**

to **benzodiazepine** sedatives  
(either *midazolam* or *lorazepam*) in critically ill patients

improved **short-term**  
outcomes

- ICU LOS
- duration of mechanical ventilation
- delirium

improved both **short-term**  
and **long-term** outcomes

- time to extubation, time to light sedation, delirium
- 90-day mortality, cognitive and physical functioning, institutionalization, and psychologic dysfunction

ORIGINAL ARTICLE

# Early Sedation with Dexmedetomidine in Critically Ill Patients

Y. Shehabi, B.D. Howe, R. Bellomo, Y.M. Arabi, M. Bailey, F.E. Bass, S. Bin Kadiman, C.J. McArthur, L. Murray, M.C. Reade, I.M. Seppelt, J. Takala, M.P. Wise, and S.A. Webb, for the ANZICS Clinical Trials Group and the SPICE III Investigators\*

## ABSTRACT

### **BACKGROUND**

Dexmedetomidine produces sedation while maintaining a degree of arousability and may reduce the duration of mechanical ventilation and delirium among patients in the intensive care unit (ICU). The use of dexmedetomidine as the sole or primary sedative agent in patients undergoing mechanical ventilation has not been extensively studied.

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***benzodiazepiny***

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# benzodiazepiny

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- ✓ nejsou doporučeny jako farmaka 1. volby k navození spánků u pacientů na ICU
- ✓ použití je rizikovým faktorem vzniku deliria
- ✓ léky 1. volby u syndromu z odnětí (alkohol, léky) a součást léčby epileptických stavů
- ✓ midazolam, lorazepam, lormetazepam, flunitrazepam ...

# lormetazepam

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- ✓ orální forma dostupná více jak 30 let
- ✓ od 2011 dostupný intravenózně (Sedalam®)
- ✓ sedativní, hypnotický, anxiolytický
- ✓ poruchy jaterních či ledvinných funkcí, vysoký věk nebo kombinace s jinými farmaky jeho farmakokinetiku neovlivňují

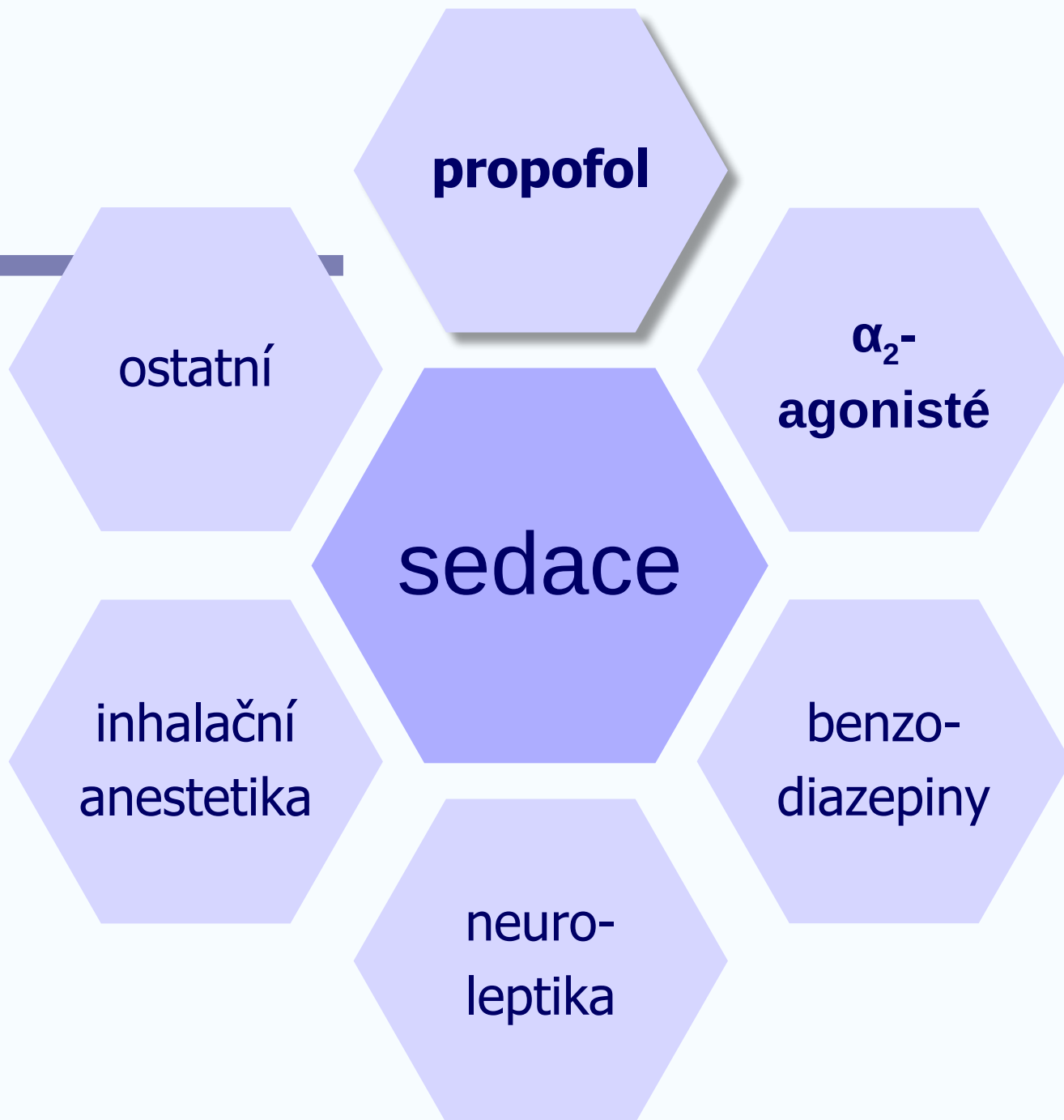
## S3-Leitlinie

# Analgesie, Sedierung und Delirmanagement in der Intensivmedizin (DAS-Leitlinie 2020)

AWMF-Registernummer: 001/012

Für Patient:innen mit Alkoholkrankheit und einem Delir (20-50% der ICU-Patient:innen) sind Benzodiazepine in Bezug auf Sicherheit und Effektivität vorteilhaft[386].

Ultrakurzwirksame Benzodiazepine (z.B. Remimazolam)[387] und Benzodiazepine mit alternativem Metabolisierungsweg und veränderter Pharmakodynamik (insbesondere einer stärkeren anxiolytischen Komponente (z.B. Lormetazepam[388]), können in Zukunft alternative Optionen darstellen und werden bereits erfolgreich eingesetzt.





***neuroleptika***





- blokují D receptory
- sedativní efekt u agitovanosti, agresivity, neklidu

neuro-  
leptika

- chlorpromazin
- levopromazin
- thioridazin
- promethazin

sedativní

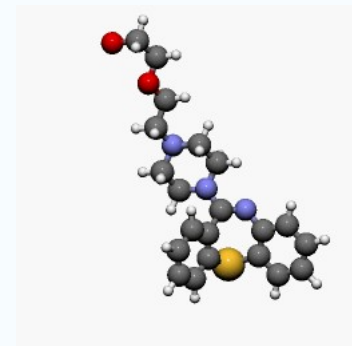
atypická

- tiaprid
- risperidon
- quetiapin
- clomethiazol

incizivní

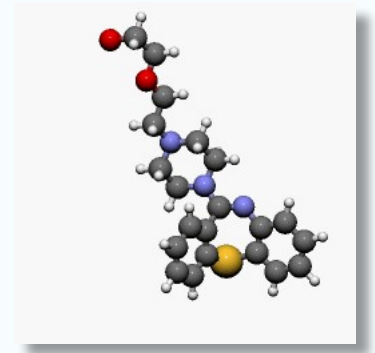
- haloperidol
- melperon
- prochlorperazin

# quetiapin



- ✓ Seroquel<sup>®</sup>, Xeroquel<sup>®</sup>, Ketipinor<sup>®</sup>, Quetiapin Sandoz<sup>®</sup>, Quenan<sup>®</sup>, Quetin<sup>®</sup>, Ketilept<sup>®</sup> ...
- ✓ atypické neuroleptikum
- ✓ **původní indikace:** schizofrenie, bipolární poruchy, přídatná léčba depresivních epizod
- ✓ vedlejší efekt: sedace pacienta (5. z 15)

# quetiapin



- ✓ účinek zesílen některými léky – azoly, makrolidy, inhibitory HIV-proteázy
- ✓ nemá extrapyramidové účinky
- ✓ velmi mírně prodlužuje QT-interval
- ✓ **dávkování** pro perzistující agitaci:  
12,5 mg 1-0-1  
až 50 mg 1-0-1  
až 600 mg/d (těžké psychotické příznaky)

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***antidepressiva***

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- ↓reuptake NOR, SER
- antidepressivní, anxiolytický účinek

antide-  
presiva

I.  
generace

- amitriptylin
- dosulepin
- klomipramin

III.  
generace

II.  
generace

- fluoxetin
- sertralin
- citalopram
- paroxetin

- dibenzepin
- maprotilin

# antidepresiva III. generace

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- ✓ *fluoxetin, sertralin, citalopram, paroxetin*
- ✓ SSRI (selective serotonin reuptake inhibitors)
- ✓ **indikace:** deprese (i ve stáří), obsedantně-kompulzivní, fobické a panické stavy
- ✓ **kontraindikace:** užívání IMAO, poruchy jater
- ✓ **cave:** serotoninový sy (*pocení, průjem, horečka, třes, hyperreflexie*)

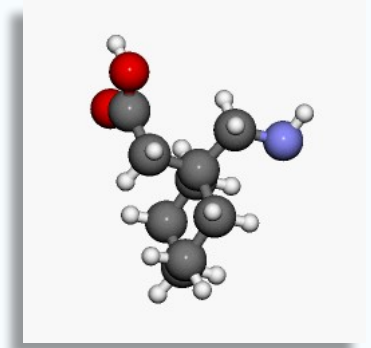
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***ostatní***

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# gabapentin

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- ✓ Neurontin<sup>®</sup>, Gabapentin-Teva<sup>®</sup>, Neurostil<sup>®</sup> ...
- ✓ antiepileptikum 3. generace
- ✓ **původní indikace:** léčba parciálních epilept. záchvatů a periferní neuropatické bolesti
- ✓ **cave:** delší nástup účinku (dny – týdny)
- ✓ nemetabolizuje se v játrech ani jiných tkáních, vylučován ledvinami (je dialyzovatelný)



# gabapentin

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- ✓ **ICU indikace:** hyperalgie (ztráta inhibiční kontroly centrální senzitivace) a alodynie (centrální reorganizace periferní senzitivace)
- ✓ doplňující analgetikum zvl. u myalgií a „celotělových“ bolestí
- ✓ snižuje spotřebu opioidních analgetik, zklidňuje pacienta
- ✓ **dávkování:** 300-1800 mg/d

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***inhalační  
anestetika***

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- “off-label use”

inhalační  
anestetika

sevofluran

- AnaConDa
- Mirus

xenon

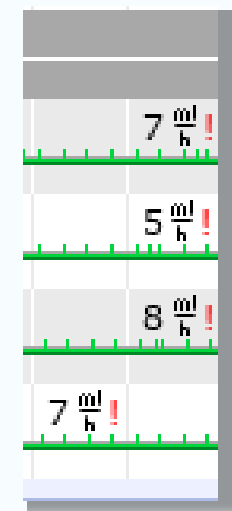
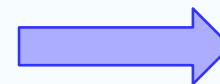
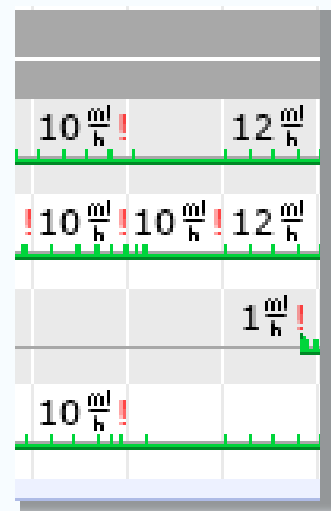
- experiment

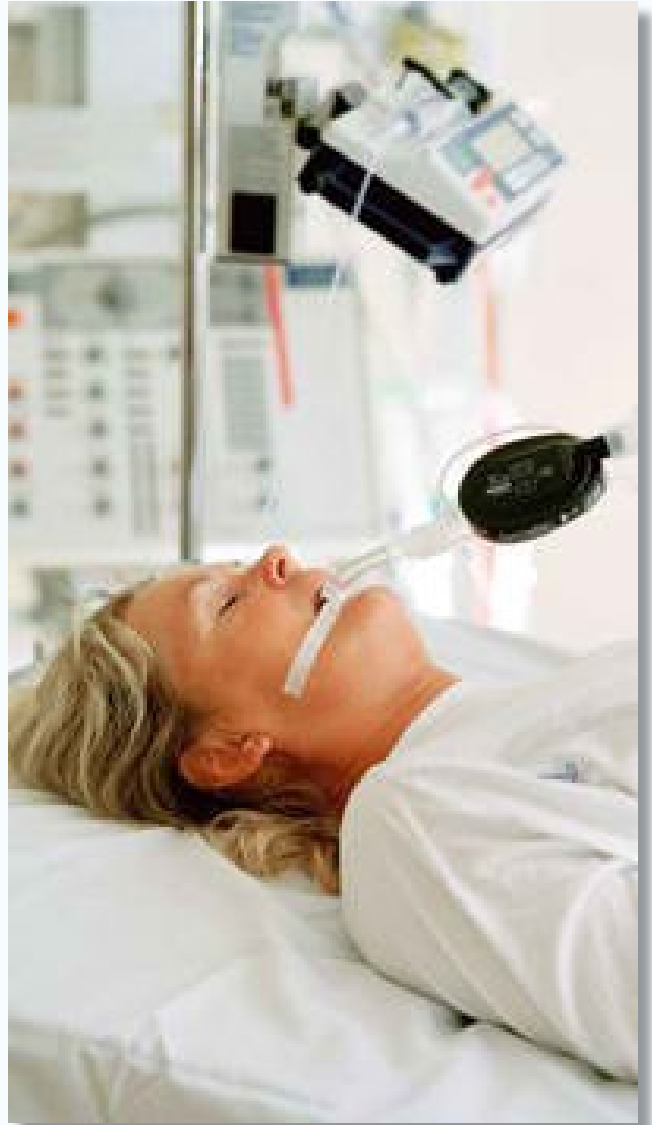
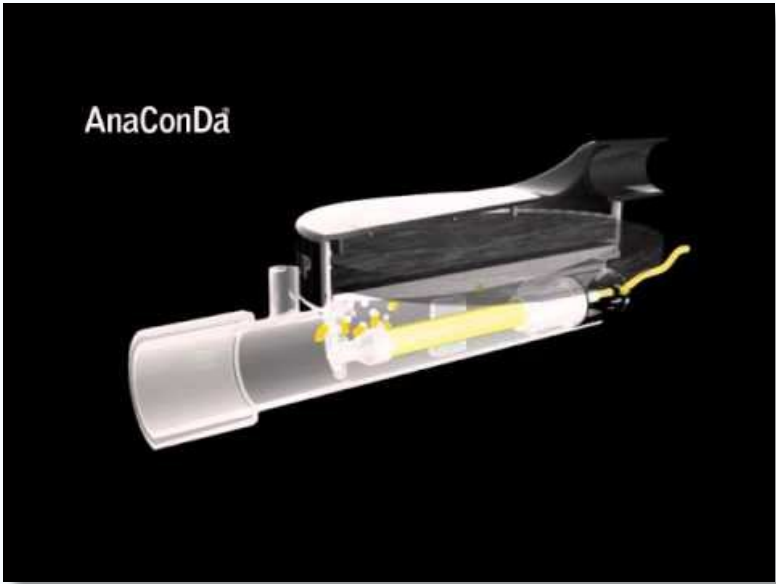
# advantages

- rapid onset and offset of action
- quick onset of sedation and awakening
- primarily act on the cerebral cortex
- leaves autonomic functions undisturbed
- volatile anaesthetics accumulate very little
- excreted by the lungs, independent of liver and kidney
- cardio and cerebroprotective properties
- bronchodilatation and anti-epileptic activity

13.09.2018 - 15.09.2018	18	20	22	00	02	04	06	08	10	12	14	16	18	20	22	00	02	04	06	08	10	12	14	16	Gesamt	
<b>Medikamente</b>																										
<b>Regelmässig</b>																										
Xylocain 2% Amp. 20 mg/ml		100 mg		100 mg		100 mg		100 mg		100 mg		100 mg		100 mg		100 mg		0 mg		0 mg						600 mg
<b>Einmalig Verabreichtes</b>																										
Dormicum 5mg / 5ml Ampullen 1 mg/ml								5 mg																		5 mg
Fentamed 0,05 mg/ml - Ampullen 0.05 mg/ml														0.1 mg												0.1 mg
Ketanest S 5mg/ml Ampullen 5 mg/ml														50 mg												50 mg
Esmeron 10mg / ml 10 mg/ml								100 mg																		100 mg
<b>Medikamenteninfusionen</b>																										
<b>Ziel</b>																										
Dexdor 1000µg-Bypass 20 µg/ml	10 $\frac{ml}{h}$ !		10 $\frac{ml}{h}$ !		10 $\frac{ml}{h}$ !		10 $\frac{ml}{h}$ !		12 $\frac{ml}{h}$ !	10 $\frac{ml}{h}$ !				10 $\frac{ml}{h}$ !	8 $\frac{ml}{h}$ !	8 $\frac{ml}{h}$ !			8 $\frac{ml}{h}$ !			8 $\frac{ml}{h}$ !			7 $\frac{ml}{h}$ !	8880 µg
Propofol 2% 50ml-Perfusor 20 mg/ml	10 $\frac{ml}{h}$ !		10 $\frac{ml}{h}$ !	10 $\frac{ml}{h}$ !			10 $\frac{ml}{h}$ !	10 $\frac{ml}{h}$ !	10 $\frac{ml}{h}$ !	12 $\frac{ml}{h}$ !	10 $\frac{ml}{h}$ !	10 $\frac{ml}{h}$ !	8 $\frac{ml}{h}$ !	10 $\frac{ml}{h}$ !	8 $\frac{ml}{h}$ !	8 $\frac{ml}{h}$ !			8 $\frac{ml}{h}$ !	8 $\frac{ml}{h}$ !		7 $\frac{ml}{h}$ !	6 $\frac{ml}{h}$ !		5 $\frac{ml}{h}$ !	8616 mg
Sevofluran Baxter 100% 1 ml/ml									1 $\frac{ml}{h}$ !	3 $\frac{ml}{h}$ !	4.5 $\frac{ml}{h}$ !		5 $\frac{ml}{h}$ !		5 $\frac{ml}{h}$ !				6 $\frac{ml}{h}$ !						8 $\frac{ml}{h}$ !	148 ml
Ultiva 5mg / 50 ml NaCl 0.1 mg/ml	10 $\frac{ml}{h}$ !		10 $\frac{ml}{h}$ !		10 $\frac{ml}{h}$ !		10 $\frac{ml}{h}$ !			8 $\frac{ml}{h}$ !	8 $\frac{ml}{h}$ !		10 $\frac{ml}{h}$ !	8 $\frac{ml}{h}$ !					8 $\frac{ml}{h}$ !			8 $\frac{ml}{h}$ !			7 $\frac{ml}{h}$ !	42.8 mg

<b>Medikamenteninfusionen</b>	
<b>Ziel</b>	
Dexdor 1000µg-Bypass 20 µg/ml	
Propofol 2% 50ml-Perfusor 20 mg/ml	
Sevofluran Baxter 100% 1 ml/ml	
Ultiva 5mg / 50 ml NaCl 0.1 mg/ml	

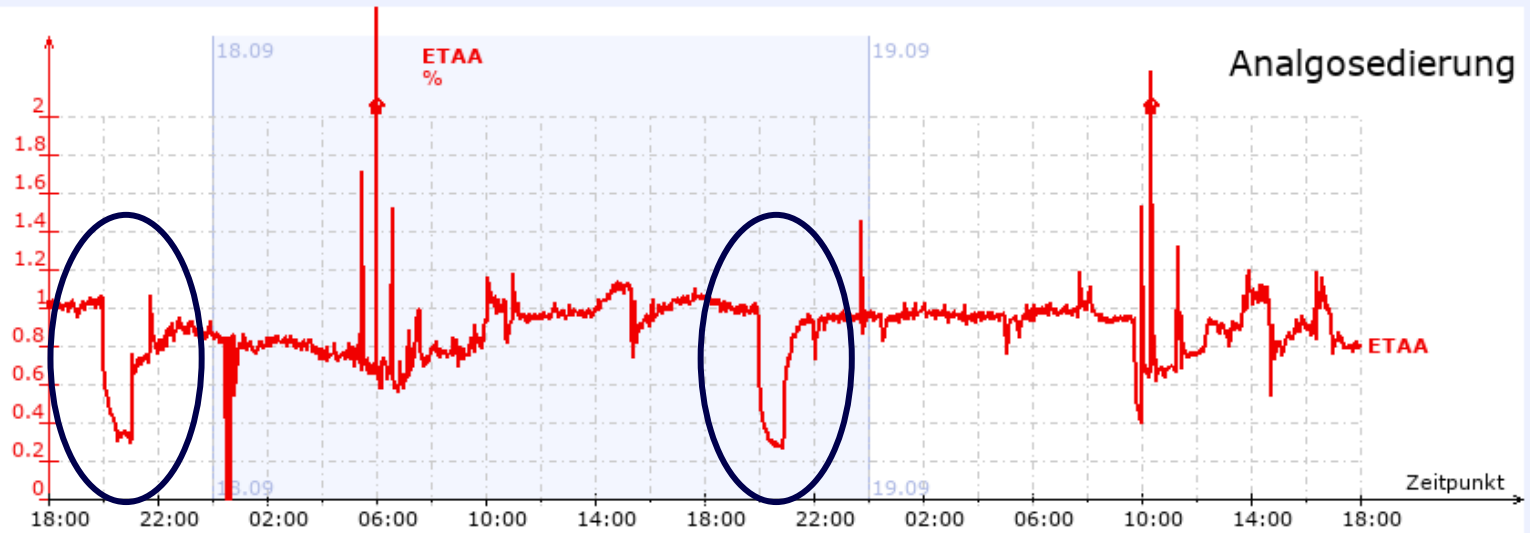




# disadvantages

- non-rebreathing high-flow ventilators in the ICU
- lack of dedicated vapourisers for the high-flow systems
- problems of workplace contamination with the gas
- unfamiliarity of the ICU staff
- increase in overall dead space
- closed loop tracheal suction system is advisable
- inadvertent intravenous injection is possible
- fluoride toxicity
- costs

Analgosedierung



17.09.2018 - 19.09.2018	18	20	22	00	02	04	06	08	10	12	14	16	18	20	22	00	02	04	06	08	10	12	14	16	Gesamt	
<b>Medikamenteninfusionen</b>																										
<b>Ziel</b>																										
Dexdor 1000µg-Bypass 20 µg/ml	6 ml			6 ml											6 ml											5497 µg
Propofol 2% 50ml-Perfusor 20 mg/ml	1 ml	1 ml				1 ml	5 ml	5 ml					5 ml						5 ml				5 ml	3 ml	2 ml	3540 mg
Ropinaest-Bypass 150mg + 0, 1mg Fenta 3 mg/ml																								2 ml		15.1 mg
Sevofluran Baxter 100% 1 ml/ml	8 ml	9 ml		9 ml			10 ml	10 ml	10 ml				0 ml	10 ml					10 ml	10 ml	10 ml	9 ml	9 ml	9 ml	9 ml	453 ml
Ulti																										





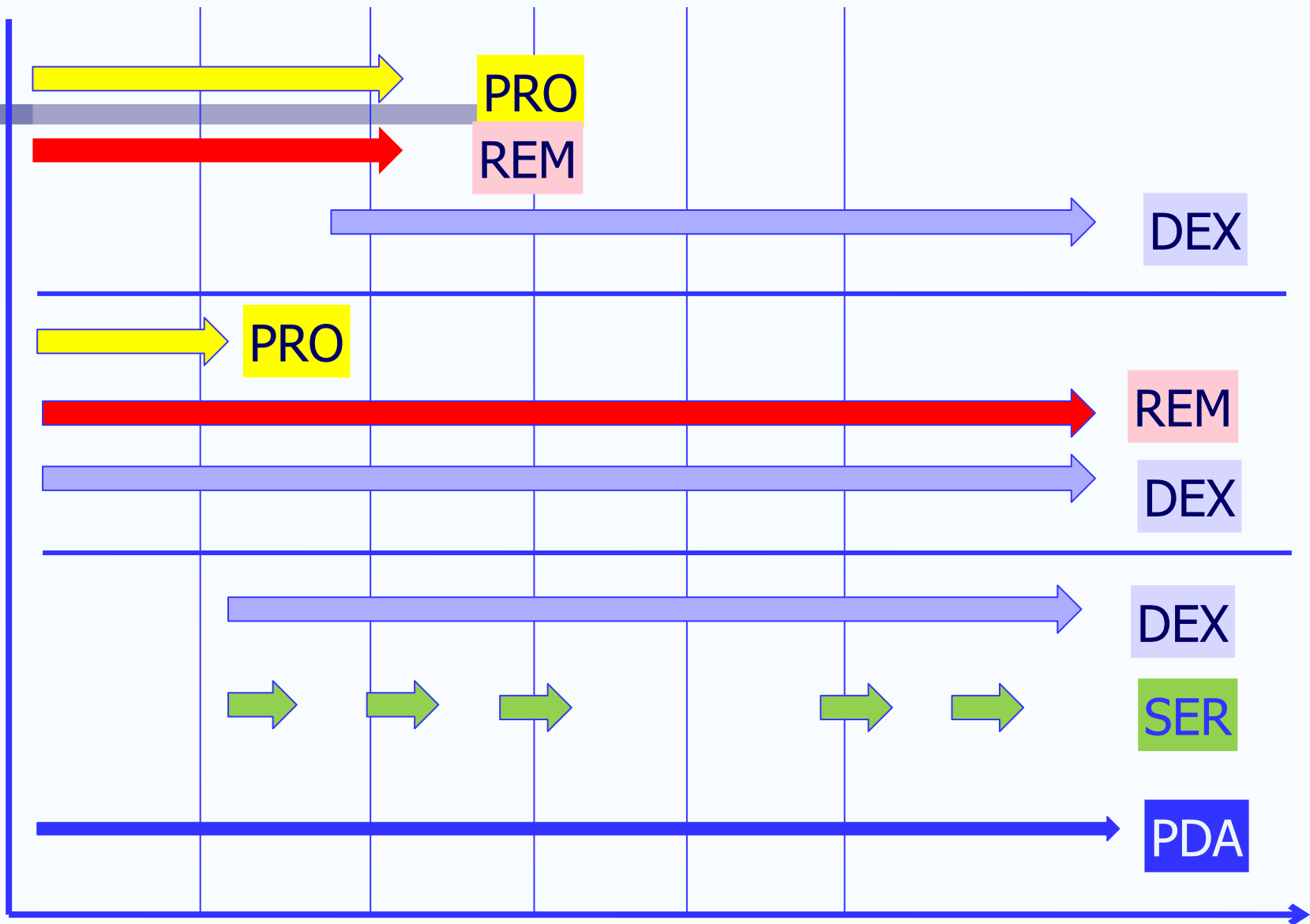
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***taktika***

***analgosedace***

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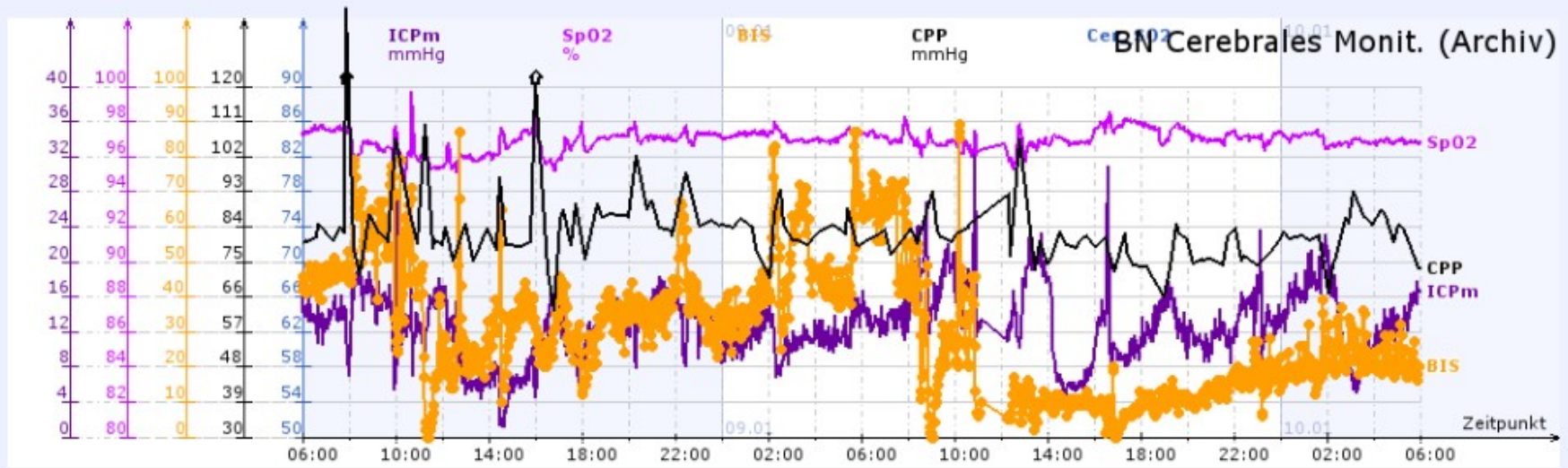
# taktika sedace





Cerebrales Monitoring (48h)

08.01.2017 06:00 - 10.01.2017 06:00



Analgosedierung

08.01.2017 - 10.01.2017

	06	08	10	12	14	16	18	20	22	00	02	04	06	08	10	12	14	16	18	20	22	00	02	04	Gesamt	
<b>Medikamente</b>																										
Bei Bedarf																										
Nimbex Injektionslö.. 2 mg/ml									10 mg		10 mg															20 mg
<b>Medikamenteninfusionen</b>																										
Ziel																										
Dexdor 400µg-Bypass 8 µg/ml	5 ml			6 ml					6 ml				6 ml		8 ml	6 ml			6 ml					6 ml		2247 µg
Propofol 2% 50ml-.. 20 mg/ml	10 ml		10 ml	12 ml	15 ml	12 ml			12 ml	12 ml	12 ml			12 ml	0 ml	14 ml		14 ml	14 ml			14 ml	14 ml		14 ml	11742 mg
Sedator 8mg Byp.. 0.08 mg/ml														1 ml		8 ml										9.95 mg
NaCl 0.9 % 0.5 ml/ml																										62.2 ml
Sufenta 1mg / 50.. 0.02 mg/ml	6 ml	6 ml	6 ml	6.5 ml	7 ml				7 ml					0 ml	9 ml		9 ml		9 ml			9 ml				7.12 mg

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***COVID-19***

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## ***pre COVID-19***

- substantial reduction in the use of benzodiazepine-based sedation
- in the past decade from about 80% to <10%
- reduction delirium prevalence in mechanically ventilated patients (from about 80% to 50%)
- delirium has also been shown to be a significant predictor of acquired dementia after critical illness

## ***COVID-19***

- deep sedation with widespread use of benzodiazepine infusions, immobilisation, and isolation from families
- significantly higher prevalence and duration of delirium
- delirium hyperactive

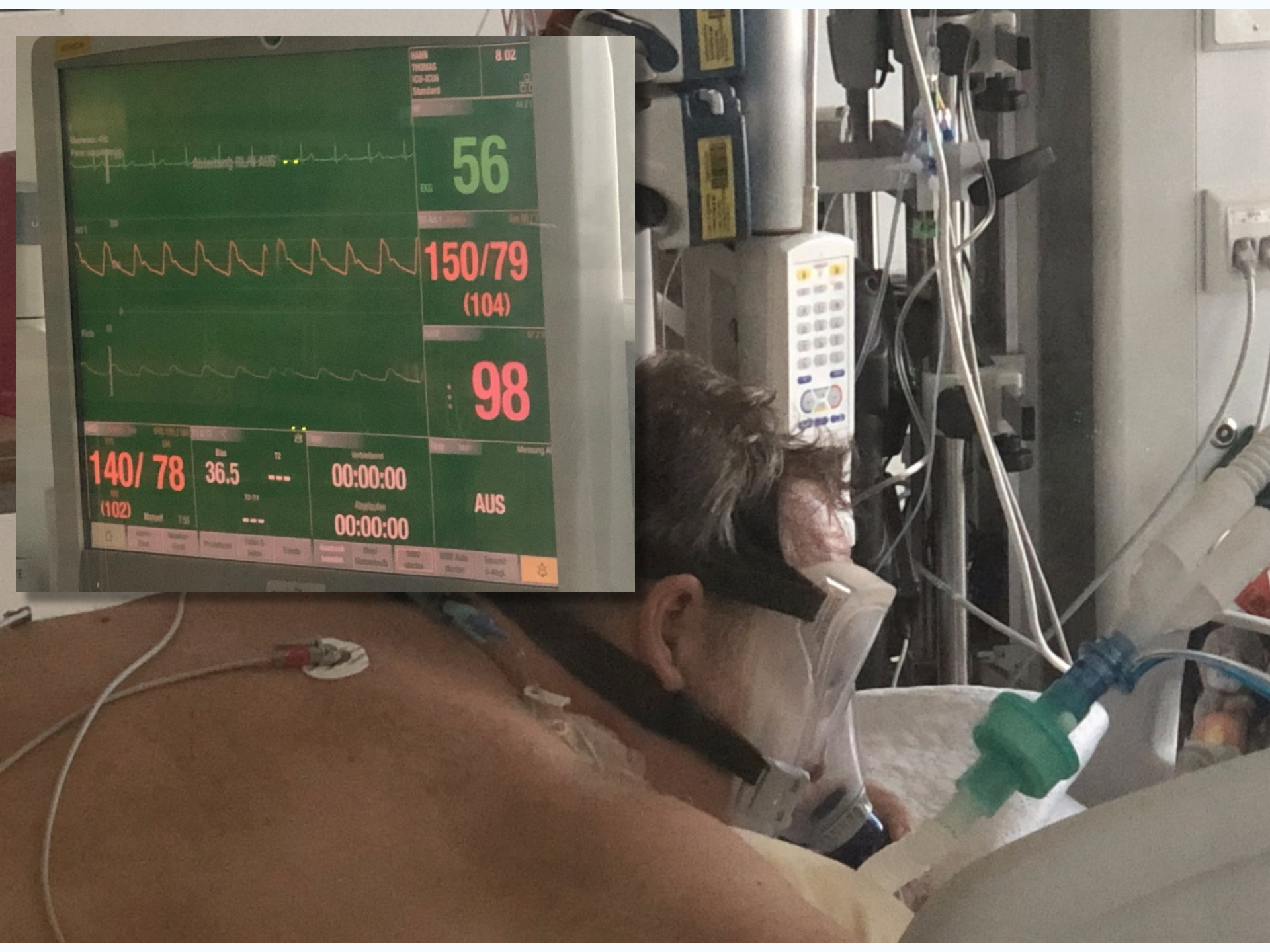
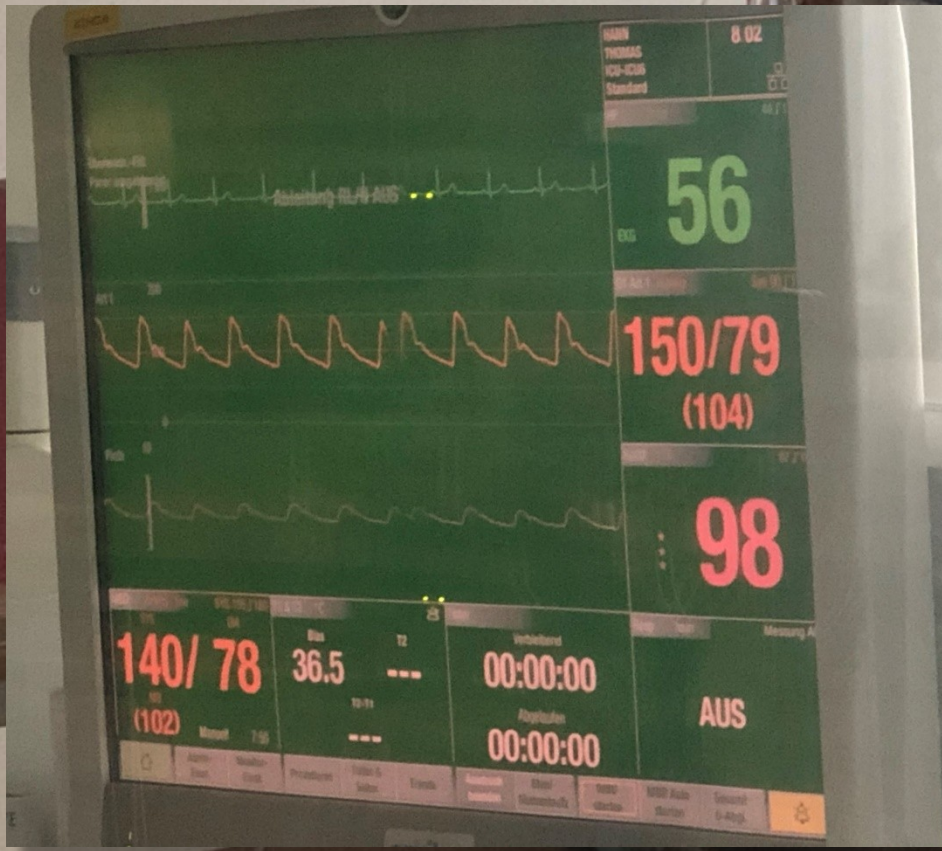
# COVID-19 a sedace

- pacient v izolaci
- zhoršený (opožděný) přístup k pacientovi i perfuzorům
- chybí vizuální kontrola pacienta
- sedace nezaintubovaných pacientů
- sedace pacientů v pronaci
- potřeba vyšších dávek sedace
- přechodný nedostatek léků
- méně zaškoleného personálu, *happy hypoxia*
- vyšší výskyt deliria (hyperaktivního?)











# High sedation needs of critically ill COVID-19 ARDS patients—A monocentric observational study

Armin Niklas Flinspach<sup>1\*</sup>, Hendrik Booke<sup>1</sup>, Kai Zacharowski<sup>1</sup>, Ümniye Balaban<sup>2</sup>, Eva Herrmann<sup>2</sup>, Elisabeth Hannah Adam<sup>1</sup>

## Background

Therapy of severely affected coronavirus patient, requiring intubation and sedation is still challenging. Recently, difficulties in sedating these patients have been discussed. This study aims to describe sedation practices in patients with 2019 coronavirus disease (COVID-19)-induced acute respiratory distress syndrome (ARDS).

## Methods

We performed a retrospective monocentric analysis of sedation regimens in critically ill intubated patients with respiratory failure who required sedation in our mixed 32-bed university intensive care unit. All mechanically ventilated adults with COVID-19-induced ARDS requiring continuously infused sedative therapy admitted between April 4, 2020, and June 30, 2020 were included. We recorded demographic data, sedative dosages, prone positioning, sedation levels and duration. Descriptive data analysis was performed; for additional analysis, a logistic regression with mixed effect was used.

## Results

In total, 56 patients (mean age 67 ( $\pm 14$ ) years) were included. The mean observed sedation period was 224 ( $\pm 139$ ) hours. To achieve the prescribed sedation level, we observed the need for two or three sedatives in 48.7% and 12.8% of the cases, respectively. In cases with a triple sedation regimen, the combination of clonidine, esketamine and midazolam was observed in most cases (75.7%). Analgesia was achieved using sufentanil in 98.6% of the cases. The analysis showed that the majority of COVID-19 patients required an unusually high sedation dose compared to those available in the literature.

## Conclusion

The global pandemic continues to affect patients severely requiring ventilation and sedation, but optimal sedation strategies are still lacking. The findings of our observation suggest unusual high dosages of sedatives in mechanically ventilated patients with COVID-19. Prescribed sedation levels appear to be achievable only with several combinations of sedatives in most critically ill patients suffering from COVID-19-induced ARDS and a potential association to the often required sophisticated critical care including prone positioning and ECMO treatment seems conceivable.

16.11.2021 - 18.11.2021	23	01	03	05	07	09	11	13	15	17	19	21	23	01	03	05	07	09	11	13	15	17	19	21	Gesamt	
<b>Medikamente</b>																										
<b>Regelmässig</b>																										
Ketanest S 5mg/ml Ampullen 5 mg/ml						250 <sub>mg</sub>	x																			250 mg
Praxiten 15 mg Tbl. 15 mg/Tabl																								15 <sub>mg</sub>	x	15 mg
Praxiten 15 mg Tbl. 15 mg/Tabl	15 <sub>mg</sub>				15 <sub>mg</sub>																					30 mg
Seropram 20 mg Filmtbl. 20 mg/Tabl					20 <sub>mg</sub>											20 <sub>mg</sub>										40 mg
Seroquel 200mg FTBL 200 mg/Tabl																					200 <sub>mg</sub>			400 <sub>mg</sub>	x	600 mg
Esmeron 10mg / ml 10 mg/ml						200 <sub>mg</sub>																				200 mg
<b>Einmalig Verabreichtes</b>																										
Novalgin Amp. 2,5g / 5ml 0.5 g/ml													2.5 <sub>g</sub>													2.5 g
<b>Medikamenteninfusionen</b>																										
<b>Ziel</b>																										
Dexdor 1000µg-Bypass 20 µg/ml	5 <sub>ml/h</sub>	5 <sub>ml/h</sub> !				5 <sub>ml/h</sub> !		3 <sub>ml/h</sub> !				1.2 <sub>ml/h</sub> !														2058 µg
Dexdor 1000µg-Bypass 20 µg/ml						1 <sub>ml/h</sub>						6 <sub>ml/h</sub>														2924 µg
Ketanest 1250mg Perfusor 25 mg/ml												5 <sub>ml/h</sub>														2808 mg
Propofol 2% 50ml-Perfusor 20 mg/ml												6 <sub>ml/h</sub> !	5.5 <sub>ml/h</sub> !	6 <sub>ml/h</sub> !		4.5 <sub>ml/h</sub> !				4.5 <sub>ml/h</sub> !					2576 mg	
Propofol 2% 50ml-Perfusor 20 mg/ml						0.1 <sub>ml/h</sub> !	12 <sub>ml/h</sub> !	12 <sub>ml/h</sub> !	12 <sub>ml/h</sub> !			6 <sub>ml/h</sub> !	6.5 <sub>ml/h</sub> !	6 <sub>ml/h</sub> !		4.5 <sub>ml/h</sub> !								8 <sub>ml/h</sub> !	5333 mg	
Propofol 2% 50ml-Perfusor 20 mg/ml						0.1 <sub>ml/h</sub> !	12 <sub>ml/h</sub> !	12 <sub>ml/h</sub> !	12 <sub>ml/h</sub> !			6 <sub>ml/h</sub> !	6.5 <sub>ml/h</sub> !	6 <sub>ml/h</sub> !		4.5 <sub>ml/h</sub> !									5278 mg	
Propofol 2% 50ml-Perfusor 20 mg/ml												6 <sub>ml/h</sub> !	5.5 <sub>ml/h</sub> !	6 <sub>ml/h</sub> !		4.5 <sub>ml/h</sub> !				4.5 <sub>ml/h</sub> !					2576 mg	
Sufenta 2mg / 50 NaCl 0.04 mg/ml																							3 <sub>ml/h</sub>			1.07 mg
Sufenta 2mg / 50 NaCl 0.04 mg/ml																							3 <sub>ml/h</sub> !		5 <sub>ml/h</sub> !	1.4 mg
Ultiva 5mg / 50 ml NaCl 0.1 mg/ml						0.1 <sub>ml/h</sub> !	10 <sub>ml/h</sub> !					3 <sub>ml/h</sub> !	6.7 <sub>ml/h</sub> !			6 <sub>ml/h</sub>								1 <sub>ml/h</sub>	0.01 mg	
Ultiva 5mg / 50 ml NaCl 0.1 mg/ml						0.1 <sub>ml/h</sub> !	10 <sub>ml/h</sub> !					3.5 <sub>ml/h</sub> !	6.7 <sub>ml/h</sub> !			6 <sub>ml/h</sub>								1 <sub>ml/h</sub>	0.01 mg	
Ultiva 5mg / 50 ml NaCl 0.1 mg/ml												3.5 <sub>ml/h</sub> !	6.7 <sub>ml/h</sub> !			6 <sub>ml/h</sub>								1 <sub>ml/h</sub>	15.3 mg	
<b>Bei Bedarf</b>																										
Novalgin 1g / 2ml 9.8 mg/ml NaCl 0.9 % 0.98 m/ml												100 <sub>ml/h</sub>														1000 mg 100 ml



# Prevalence and risk factors for delirium in critically ill patients with COVID-19 (COVID-D): a multicentre cohort study

**Interpretation** Acute brain dysfunction was highly prevalent and prolonged in critically ill patients with COVID-19. Benzodiazepine use and lack of family visitation were identified as modifiable risk factors for delirium, and thus these data present an opportunity to reduce acute brain dysfunction in patients with COVID-19.

for the COVID-19 Intensive Care International Study Group

## Summary

**Background** To date, 750 000 patients with COVID-19 worldwide have required mechanical ventilation and thus are at high risk of acute brain dysfunction (coma and delirium). We aimed to investigate the prevalence of delirium and coma, and risk factors for delirium in critically ill patients with COVID-19, to aid the development of strategies to mitigate delirium and associated sequelae.

**Methods** This multicentre cohort study included 69 adult intensive care units (ICUs), across 14 countries. We included all patients (aged  $\geq 18$  years) admitted to participating ICUs with severe acute respiratory syndrome coronavirus 2 infection before April 28, 2020. Patients who were moribund or had life-support measures withdrawn within 24 h of ICU admission, prisoners, patients with pre-existing mental illness, neurodegenerative disorders, congenital or acquired brain damage, hepatic coma, drug overdose, suicide attempt, or those who were blind or deaf were excluded. We collected de-identified data from electronic health records on patient demographics, delirium and coma assessments, and management strategies for a 21-day period. Additional data on ventilator support, ICU length of stay, and vital status was collected for a 28-day period. The primary outcome was to determine the prevalence of delirium and coma and to investigate any associated risk factors associated with development of delirium the next day. We also investigated predictors of number of days alive without delirium or coma. These outcomes were investigated using multivariable regression.

**Findings** Between Jan 20 and April 28, 2020, 4530 patients with COVID-19 were admitted to 69 ICUs, of whom 2088 patients were included in the study cohort. The median age of patients was 64 years (IQR 54 to 71) with a

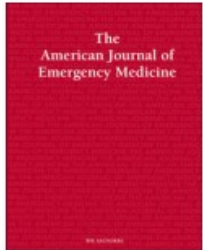




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## Sedation in mechanically ventilated covid-19 patients: A narrative review for emergency medicine providers

Sedatives play an integral role in patients with COVID-19 by acting as induction agents prior to neuromuscular blockade and reducing discomfort during periods of mechanical ventilation. During induction, sedatives facilitate amnesia and cause a blunted sympathetic response, creating favorable intubation conditions [1]. Post-intubation maintenance sedation improves pulmonary compliance, prevents asynchrony, and facilitates adaption to the ventilator; however, in severe cases, additional paralytics are required [2,3]. Although emergency medicine physicians are typically involved in the initial stabilization of patients that require prolonged sedation and mechanical ventilation, limited ICU capacity has created longer boarding times for patients in the ED. As such, ED physicians require a basic understanding regarding management of sedation for these critically ill patients, which will be summarized in this review.

Etomidate is a sedative hypnotic frequently used as an induction agent

ability to maintain hemodynamic stability make it an attractive option for sedation.

Propofol is a sedative hypnotic used for induction and maintenance of sedation in mechanically ventilated patients. It is a popular choice for sedation due to its highly predictable pharmacokinetic properties, including rapid onset and short duration of action [11]. The adverse effect profile of propofol makes it suboptimal for sedating critically ill COVID-19 patients. Diminished cardiac output and hypotension are known adverse effects of propofol and these effects are exacerbated in the setting of mechanical ventilation [11]. The use of propofol as an induction or maintenance agent in COVID-19 patients with shock could lead to profound hypotension. Propofol infusion syndrome is a rare, but potentially fatal adverse effect that can occur in the setting of prolonged use. It is characterized by bradycardia, metabolic acidosis, and rhabdomyolysis. Propofol should be discontinued, and sedation changed to another agent(s), such as dexmetomidine and midazolam, and supportive care for complications initiated [12]. It has been suggested the critical illness myopathy COVID-19 patients experience could be due in part to low-grade myotoxicity associated with prolonged propofol administration [13]. Although limited data exists

**Table 1**  
Sedatives considered in mechanically ventilated COVID-19 patients.

Sedatives	Current use	Potential benefits in COVID-19	Potential adverse effects	Any COVID-19 study	Findings related to COVID-19	Recommendation
Etomidate	Induction agent	<ul style="list-style-type: none"> <li>- Hemodynamic stability</li> <li>- Minimal respiratory depression</li> <li>- Reduced risk of histamine release</li> </ul>	<ul style="list-style-type: none"> <li>- Adrenocortical suppression</li> <li>- Hypercarbia</li> <li>- Cardiovascular instability in elderly patients with HTN</li> </ul>	No	N/A	May be used for induction in young patients
Ketamine	<ul style="list-style-type: none"> <li>- Induction agent</li> <li>- Maintenance at low doses</li> <li>- Analgesia in ICU</li> </ul>	<ul style="list-style-type: none"> <li>- Reduces inflammatory markers such as IL-6</li> <li>- Minimal respiratory depression</li> </ul>	<ul style="list-style-type: none"> <li>- Hallucinations</li> </ul>	Yes	<ul style="list-style-type: none"> <li>- Potential for immune modulation</li> <li>- Neuropsychiatric benefits</li> </ul>	Primary choice for induction of sedation of COVID patients, particularly those that are hemodynamically unstable
Propofol	<ul style="list-style-type: none"> <li>- Induction agent</li> <li>- Maintenance at low doses</li> </ul>	<ul style="list-style-type: none"> <li>- Rapid onset, rapid recovery</li> <li>- Anti-inflammatory/immunomodulatory effects</li> </ul>	<ul style="list-style-type: none"> <li>- Diminished cardiac output, hypotension</li> <li>- Propofol infusion syndrome</li> </ul>	Yes	<ul style="list-style-type: none"> <li>- Myotoxicity</li> <li>- Propofol infusion syndrome</li> </ul>	Should not be used for prolonged deep sedation
Dexmedetomidine	Light sedation in mechanically ventilated patients	<ul style="list-style-type: none"> <li>- Minimal risk of delirium</li> <li>- Hemodynamic stability</li> <li>- Reduced time requiring ventilation</li> <li>- Reduced peri-intubation agitation (lower risk of aerosolizing particles)</li> </ul>	<ul style="list-style-type: none"> <li>- Bradycardia and hypotension with initial bolus</li> <li>- Withdrawal when used in high doses &gt;24 h</li> </ul>	Yes	<ul style="list-style-type: none"> <li>- Combination of Dexmedetomidine and midazolam is effective dual therapy for long term sedation with limited side effects</li> </ul>	Primary choice for long-term sedation when used in conjunction with benzodiazepines
Benzodiazepines	Continuous sedation in the setting of anxiety and agitation	<ul style="list-style-type: none"> <li>- Treatment of acute agitation</li> <li>- Short-term breakthrough sedation</li> </ul>	<ul style="list-style-type: none"> <li>- Hypotension</li> <li>- Reduced respiratory drive</li> <li>- Longer ventilator times</li> <li>- delirium</li> </ul>	Yes		Should not be used as monotherapy for long term sedation due to increased risk of aspiration causing refractory hypoxemia and longer ventilation times
Inhalational Volatile Sedatives	<ul style="list-style-type: none"> <li>- Pediatric patients</li> <li>- Ambulatory surgeries</li> </ul>	<ul style="list-style-type: none"> <li>- Reduced need for hemodynamic support</li> <li>- Reduced need for opioids</li> <li>- Shorter ventilation</li> </ul>	<ul style="list-style-type: none"> <li>- Malignant hyperthermia</li> </ul>	No	N/A	Use for prolonged sedation is experimental and not FDA approved



### **Analgo-sedation of Covid-19 intensive care patients. Special aspects during the pandemic**

J. Herrmann · Q. Notz · T. Schlesinger · B. Schmid · J. Stumpner · M. Kredel ·  
P. Kranke · P. Meybohm · C. Lotz

► **Zitierweise:** Herrmann J, Notz Q, Schlesinger T, Schmid B, Stumpner J, Kredel M et al: Analgo-sedierung bei Covid-19-Intensivpatienten. Besondere Aspekte während der Pandemie. *Anästh Intensivmed* 2020;61:S154–S158. DOI: 10.19224/ai2020.S154



**Tabelle 1**

Übersicht über die Vor- und Nachteile verschiedener Sedativa bei COVID-19-Intensivpatienten.

Sedativum	+	-
<b>Propofol</b>	<ul style="list-style-type: none"><li>• gut steuerbar</li><li>• kurz- und mittelfristige Sedierung (&lt;72 h Dauer)</li></ul>	<ul style="list-style-type: none"><li>• eingeschränkte Verfügbarkeit</li><li>• Preisanstieg</li></ul>
<b>Volatile Anästhetika</b>	<ul style="list-style-type: none"><li>• gut steuerbar</li><li>• mögliche organprotektive Effekte im ARDS</li></ul>	<ul style="list-style-type: none"><li>• Systemwechsel und Beendigung mit zahlreichen Konnektions- und Dekonnektionsschritten verbunden</li><li>• erfahrener Anwender nötig</li></ul>
<b>Benzodiazepine</b> <ul style="list-style-type: none"><li>• Midazolam</li><li>• Lormetazepam</li></ul>	<ul style="list-style-type: none"><li>• Langzeitsedierung &gt; 72 h</li><li>• Anxiolyse</li></ul>	<ul style="list-style-type: none"><li>• schlecht steuerbar mit Ceiling-Effekt</li><li>• erhöhtes Delirrisiko</li><li>• ggf. eingeschränkte Verfügbarkeit</li></ul>
<b>Ketamin</b>	<ul style="list-style-type: none"><li>• additive Gabe in allen Phasen der Langzeitsedierung möglich</li><li>• Analgesie</li></ul>	<ul style="list-style-type: none"><li>• bei knappen Ressourcen</li><li>• nicht zur Monosedierung geeignet</li></ul>
<b><math>\alpha</math>2-Adrenozeptor-agonisten</b>	<ul style="list-style-type: none"><li>• geeignet zur Monosedierung oder additiven Gabe</li><li>• Reduktion des Delirrisikos</li></ul>	<ul style="list-style-type: none"><li>• kardiovaskuläre Nebenwirkungen</li></ul>

# intensive care in Covid patients I.

- dexametazon 6 mg i.v.
- striktní individualizovaná antikoagulace (dle FXa)
- neinvazivní ventilační techniky (O<sub>2</sub>, HFNO<sub>2</sub>, NIV)
- invazivní ventilace
- *prone position* rutinně u všech při *response*
- NO, ECMO
- individualizovaná sedace
- neinvazivní TTM (ArcticSun vs ThermoGuard)







...děkuji Vám za pozornost