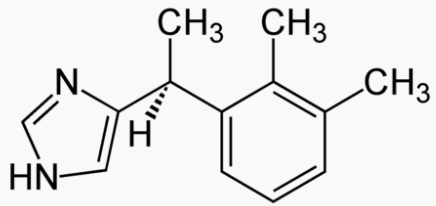
Dexmedetomidine et anesthésie

Dexmédétomidine



Dr Clément Chassery

9 Octobre 2022

Clinique Médi POLE Garonne du sport Médico-Chirurgicale

Déclaration de conflit d'intérêt

Aucun

Dexmedetomidine et Anesthésie

Qu’est-ce que c’est ?

Dexmedetomidine et Anesthésie

Qu’est-ce que c’est ?

Comment cela fonctionne ?

Dexmedetomidine et Anesthésie

Qu'est-ce que c'est ?

Comment cela fonctionne ?

Quelle utilisation lors d'une AG ?

Dexmedetomidine et Anesthésie

Qu'est-ce que c'est ?

Comment cela fonctionne ?

Quelle utilisation lors d'une AG ?

Quelle utilisation lors d'une ALR ?

Dexmedetomidine et Anesthésie

Qu'est-ce que c'est ?

Comment cela fonctionne ?

De quoi faut-il se méfier ?

Quelle utilisation lors d'une AG ?

Quelle utilisation lors d'une ALR ?

Qu’est-ce que la dexmedetomidine ?

Agonistes Récepteurs α2

dci	Clonidine
	Catapressan®
Distribution centrale	20 min
Afinité Récepteurs α2/ α1	200/1
½ vie d’élimination	12-16 h
Métabolisme hépatique	
Dose anesthésie	

*Nguyen, V., et al. (2017). "Alpha-2 Agonists." Anesthesiol Clin **35**(2): 233-245*
*Blaudszun, G., et al. (2012). Anesthesiology **116**(6): 1312-1322.*

Qu'est-ce que la dexmedetomidine ?

Agonistes Récepteurs α2

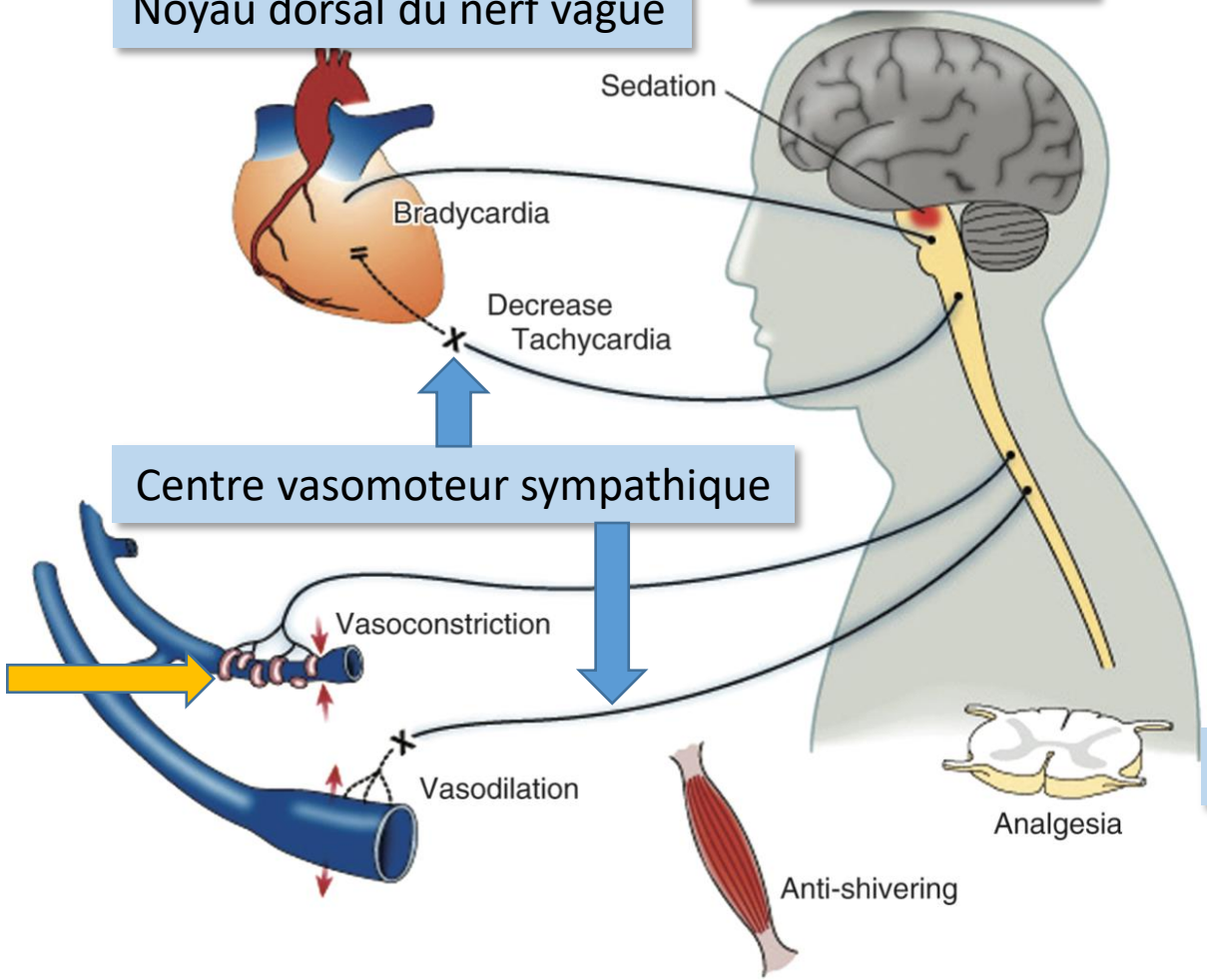
dci	Dexmedetomidine	Clonidine
	Dexdor® Precedex®	Catapressan®
Distribution centrale	6 min	20 min
Afinité Récepteurs α2/ α1	1600/1	200/1
½ vie d'élimination	2 h	12-16 h
Métabolisme hépatique	Dérivé inactif (urines)	
Dose anesthésie	0.5- 1 µg/kg IVLent +/- 0.2-1 µg/kg/h	

*Nguyen, V., et al. (2017). "Alpha-2 Agonists." Anesthesiol Clin **35**(2): 233-245*
*Blaudszun, G., et al. (2012). Anesthesiology **116**(6): 1312-1322.*

Comment cela fonctionne ?

Locus coeruleus

Noyau dorsal du nerf vague



Rα2 Pré synaptiques Centraux

Centre vasomoteur sympathique

Rα2 Post synaptiques périphériques

Muscles lisses

Corne dorsale ME

Anesthetic Pharmacology, 2nd edition, ed. Alex S. Evers, Mervyn Maze, Evan D. Kharasch. Published by Cambridge University Press. © Cambridge University Press 2011.

Comment cela fonctionne ?

Contre-indications

- Bloc cardiaque avancé
  - Bloc sinusal
  - BAV2-3
- HypoTA non contrôlée
- Pathologies cérébrovasculaires aiguës

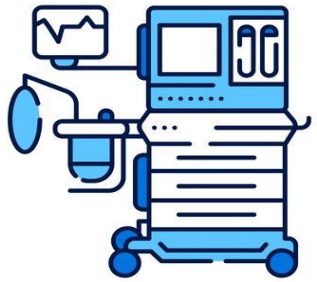
Comment cela fonctionne ?

Contre-indications

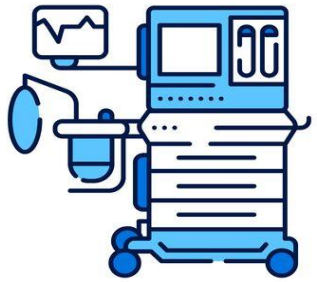
- Bloc cardiaque avancé
  - Bloc sinusal
  - BAV2-3
- HypoTA non contrôlée
- Pathologies cérébrovasculaires aiguës

- Bradycardie
- Risque d'instabilité hémodynamique
- Insuffisance hépatique sévère
- Grossesse
- Allaitement

Médi POLE Garonne
Clinique du sport Médico-Chirurgicale



Quelle utilisation lors d'une AG ?

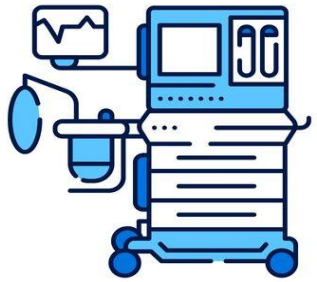


Quelle utilisation lors d'une AG ?

AG balancée

Standardisée
Dose -poids

Hypnotiques
Opioïdes de synthèse
Curares



Quelle utilisation lors d'une AG ?

AG balancée

Standardisée
Dose -poids

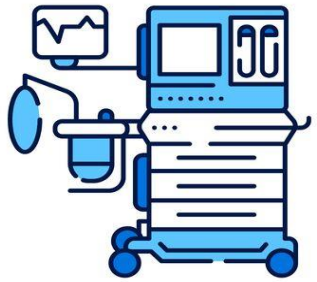
Hypnotiques
Opioïdes de synthèse
Curares

AG multimodale

Sur mesure

Hypnotiques
ALR ou AL
Dexamethasone
Ketamine
Alpha 2 agonistes

+/- opioïdes



Quelle utilisation lors d'une AG ?

AG balancée	AG multimodale
Standardisée Dose -poids	Sur mesure
Hypnotiques Opioïdes de synthèse Curares	Hypnotiques ALR ou AL Dexamethasone Ketamine Alpha 2 agonistes

SOFA
The Society for Opioid Free Anesthesia

Pourquoi diminuer les opioïdes en per op ?

↑ dose Fentanyl® → ↑ NVPO et ↑ douleur à 24 h

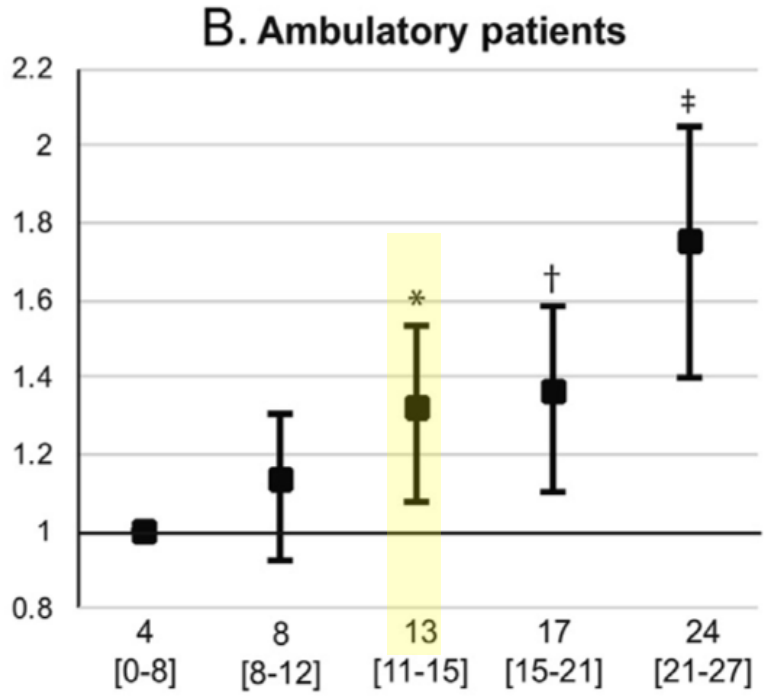
Eckhard Mauermann. Eur J Anaesthesiol 2019 Nov;36(11):871-880

Pourquoi diminuer les opioïdes en per op ?

Au-delà de 300 µg: ↓ 14 min délai douleur aiguë/100 µg de Fentanyl®

Anna rupniewsja-Ladyko. Anesth Pain Med 2019 oct;9(5):e994498

Pourquoi diminuer les opioïdes en per op ?



D R Long. British Journal of Anaesthesia 2018 , 120(5):1090-1102

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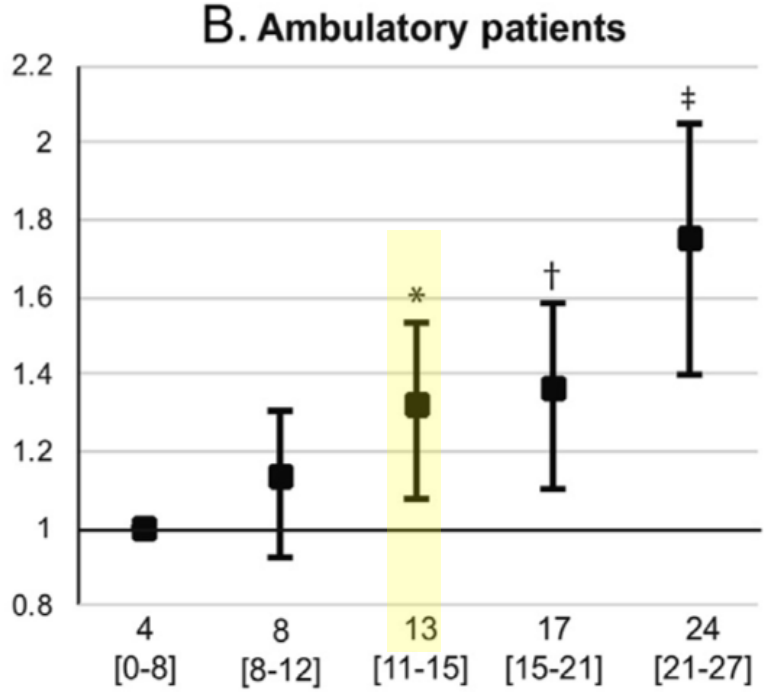

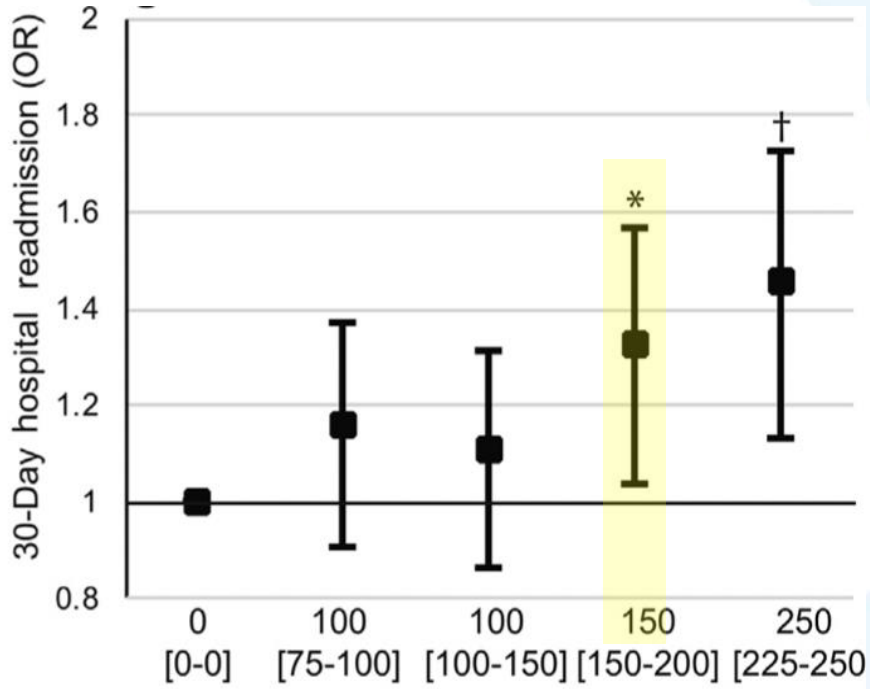

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Quelle utilisation lors d'une AG ?

OFA vs opioïdes

Arthur Salomé, Hakim Harkouk,Dominique Fletcher, Valeria Martinez.J Clin Med 2021,10,2069

Quelle utilisation lors d'une AG ?

	OFA vs opioïdes
EVA 2h	
EVA 24 h	
EVA 48h	
Conso morphine 2 h	
Conso morphine 24h	
Conso morphine 48h	
Nausée à24h	
Vomissement SSPI	
Douleur à 3 mois	

Arthur Salomé, Hakim Harkouk,Dominique Fletcher, Valeria Martinez.J Clin Med 2021,10,2069

Quelle utilisation lors d'une AG ?

	OFA vs opioïdes	
EVA 2h	- O.76/100	Significatif
EVA 24 h	NS	
EVA 48h	NS	
Conso morphine 2 h	-1.61 mg	Significatif
Conso morphine 24h	-1.73 mg	Significatif
Conso morphine 48h	-3.14 mg	Significatif
Nausée à24h	RR 0.55	Significatif
Vomissement SSPI	RR 0.34	
Douleur à 3 mois	NS	

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Quelle utilisation lors d'un bloc périphérique?

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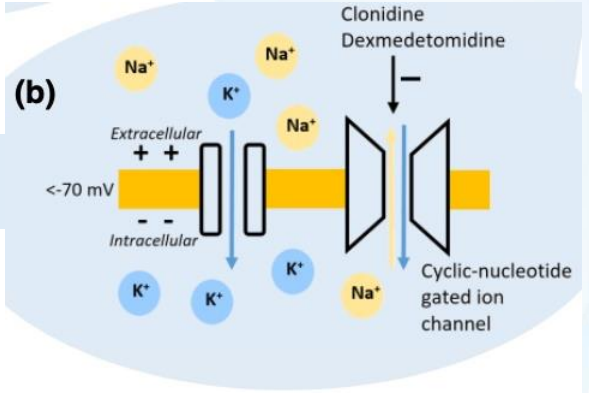
Mode d'action : hyperpolarisation des fibres A Δ et C

Brummett CM, Hong EK, Janda AM, et al. Anesthesiology 2011; 115:836 – 843



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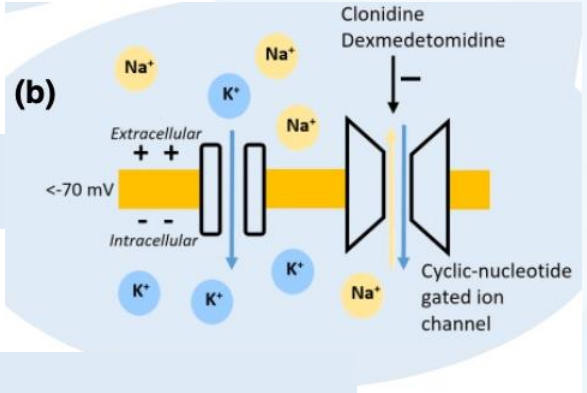

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Yu ZY, Geng J, Li ZQ, et al. British Journal of Anaesthesia 2019; 122: 141–9

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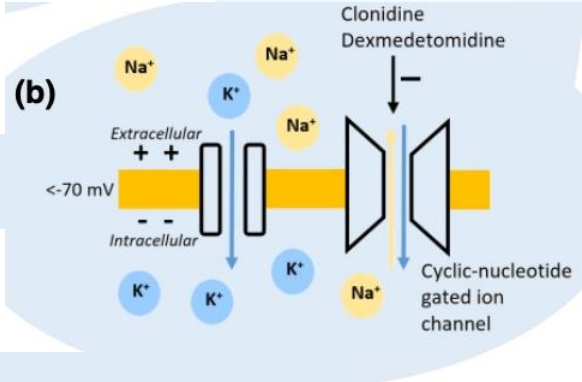

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Yu ZY, Geng J, Li ZQ, et al. British Journal of Anaesthesia 2019; 122: 141–9

Dose optimale ? 50-100 µg : ↑ Durée et ↑ Effets 2ndaires dose dépendante

Keplinger M, Marhofer P. Eur J Anaesth 2015; 32:790 – 796

Desai N. Anaesthesia 2021.76 (suppl1) 100-109

Quelle utilisation lors d'un bloc périphérique ?

Dexmedetomidine vs Dexamethasone

	Durée analgésie	Durée bloc sensitif	Durée bloc moteur	EVA 24 h	Opioïdes 24 h (OME)	Effets secondaires
Dexmedetomidine	+ 4,4 h	+3,8 - 5,7 h	3,2 h	↓	-10 mg	BradyC x 7.4 Sédation x 11.8

N Desai, K R Kirkham, E Albrecht. Anaesthesia 2021,76 (suppl 1)100-109

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Dexamethasone	+ 3,9 - 8 h	3,9 - 8 h	4,8 h	↓	-19 mg	+ Glyc 0.2mMol/l

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Périnerveux: Dexamethasone > Dexmedetomidine

N Desai, K R Kirkham, E Albrecht. Anaesthesia 2021,76 (suppl 1)100-109

Quelle utilisation lors d'un bloc périphérique ?

PN versus IV

*Abdallah, F, Tim Dwyer, Vincent W S Chan. W. Anesthesiology 2016**124**(3): 683-695*

Quelle utilisation lors d'un bloc périphérique ?

PN versus IV

BIS 15 ml Ropi O.5%

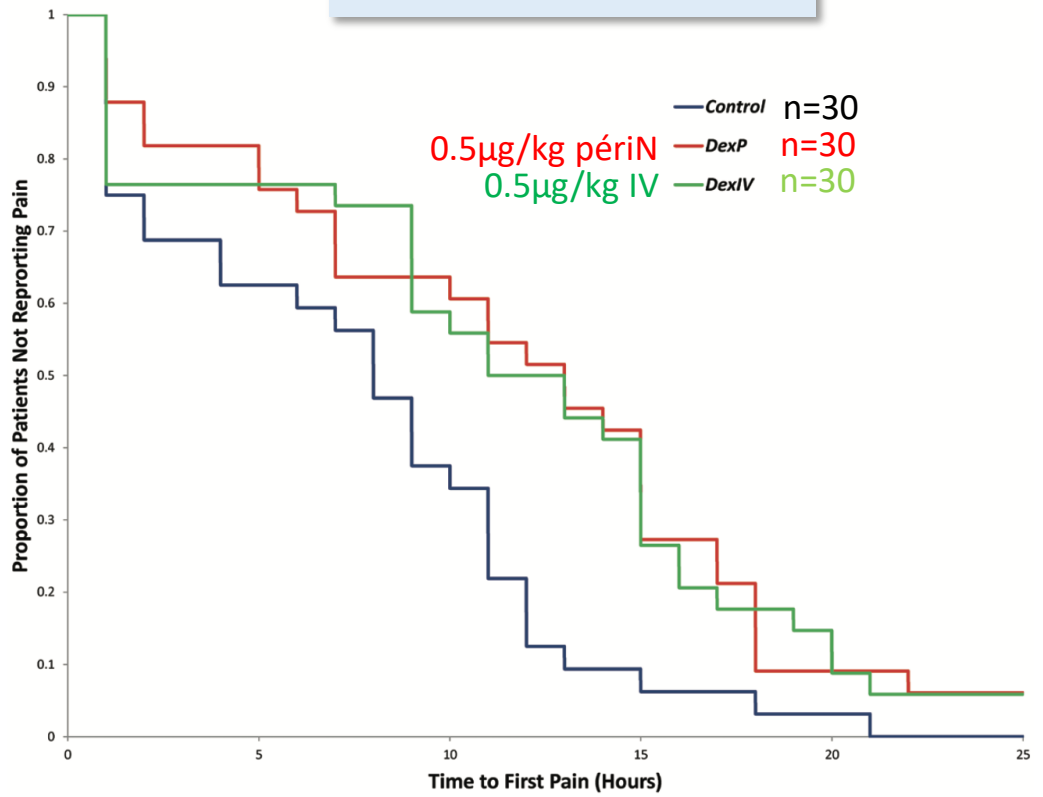

Fig. 2. Kaplan–Meier survival plot representing the duration of analgesia in the three study groups. Dex_{IV} = IV dexmedetomidine; Dex_P = perineural dexmedetomidine.

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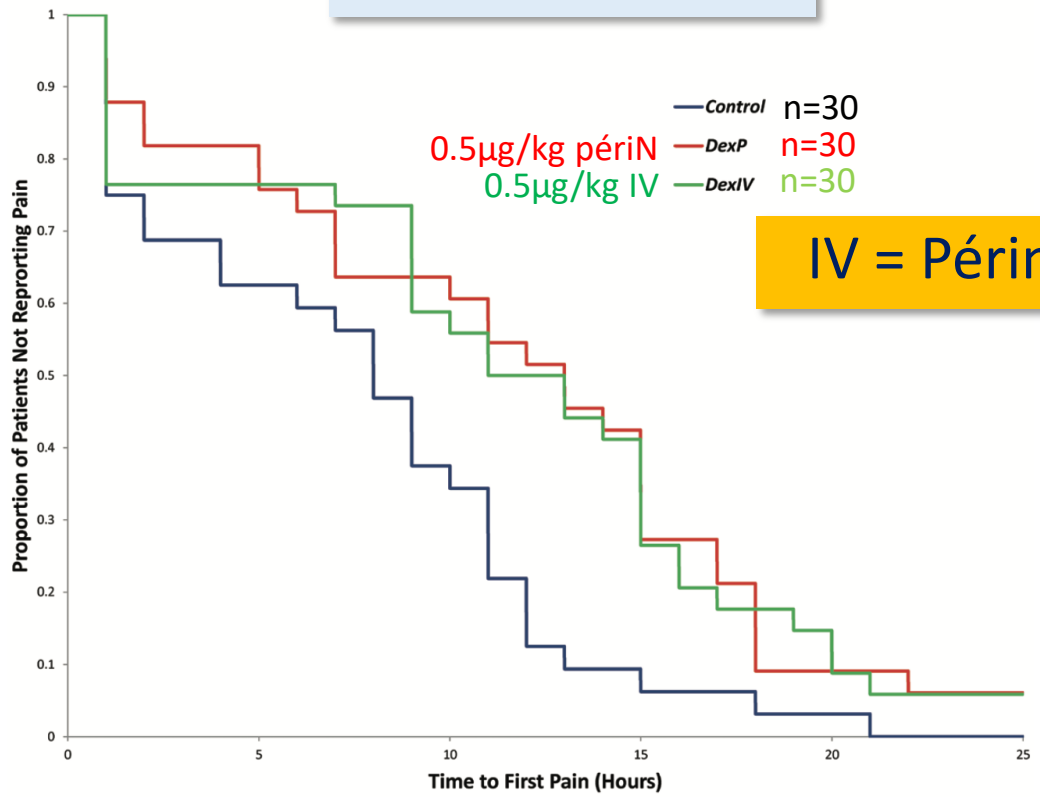

IV = Périnerveux

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Quelle utilisation lors d'un bloc périphérique ?

Quelle dose IV ?

*Kang, R. et al. Reg Anesth Pain Med 2018 **43**(5): 488-495*

Quelle utilisation lors d'un bloc périphérique ?

Quelle dose IV ?

BIS 15 ml Ropi O.5% A

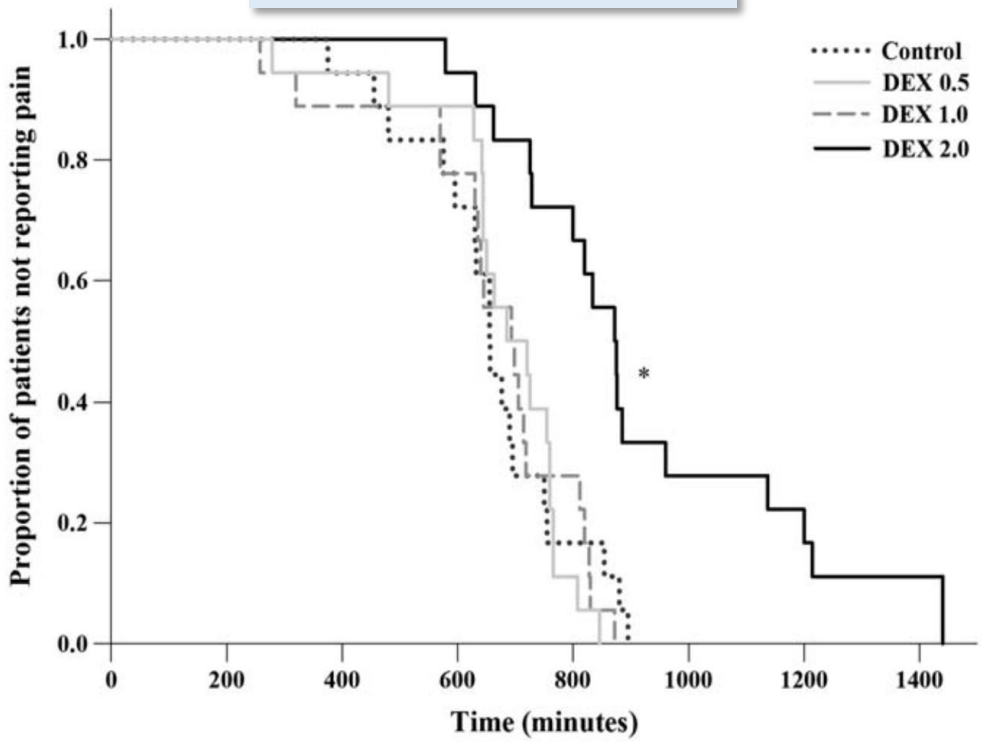

FIGURE 2. Kaplan-Meier survival plot representing the duration of analgesia in the 4 groups. DEX 0.5 = 0.5 µg/kg IV DEX, DEX 1.0 = 1.0 µg/kg IV DEX, DEX 2.0 = 2.0 µg/kg IV DEX. *$P < 0.05$ between DEX 2.0 and other groups.

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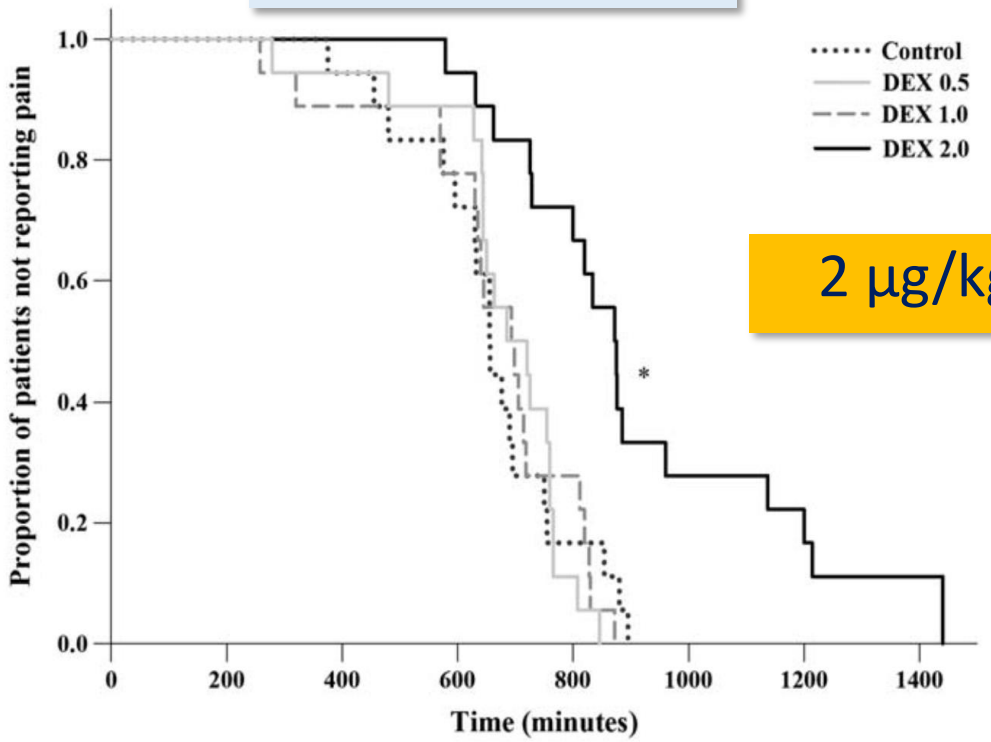

2 µg/kg

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Quelle utilisation lors d'un bloc périphérique ?

Avec Dexa 10 mg IV

Chassery C, *et al*. *Reg Anesth Pain Med* 2020;**0**:1–7. doi:10.1136/rapm-2020-101749

Quelle utilisation lors d'un bloc périphérique ?

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Original research

Total knee arthroplasty under quadruple nerve block with ropivacaine 0.32%: effect of addition of intravenous dexmedetomidine to intravenous dexamethasone on analgesic duration

Clement Chassery,[1] Philippe Marty,[1] Olivier Rontes ,[1] Martine Chaubard,[1] Corine Vuillaume,[1] Bertrand Basset,[1] Mehdi Merouani,[1] Constance Marquis,[1] Anne De Lussy,[1] Marie-Claude Delbos,[1] Julie Casalprim,[1] Benoit Bataille,[2] Cecile Naudin,[3] Fabrice Ferre ,[4] Alain Delbos[1]

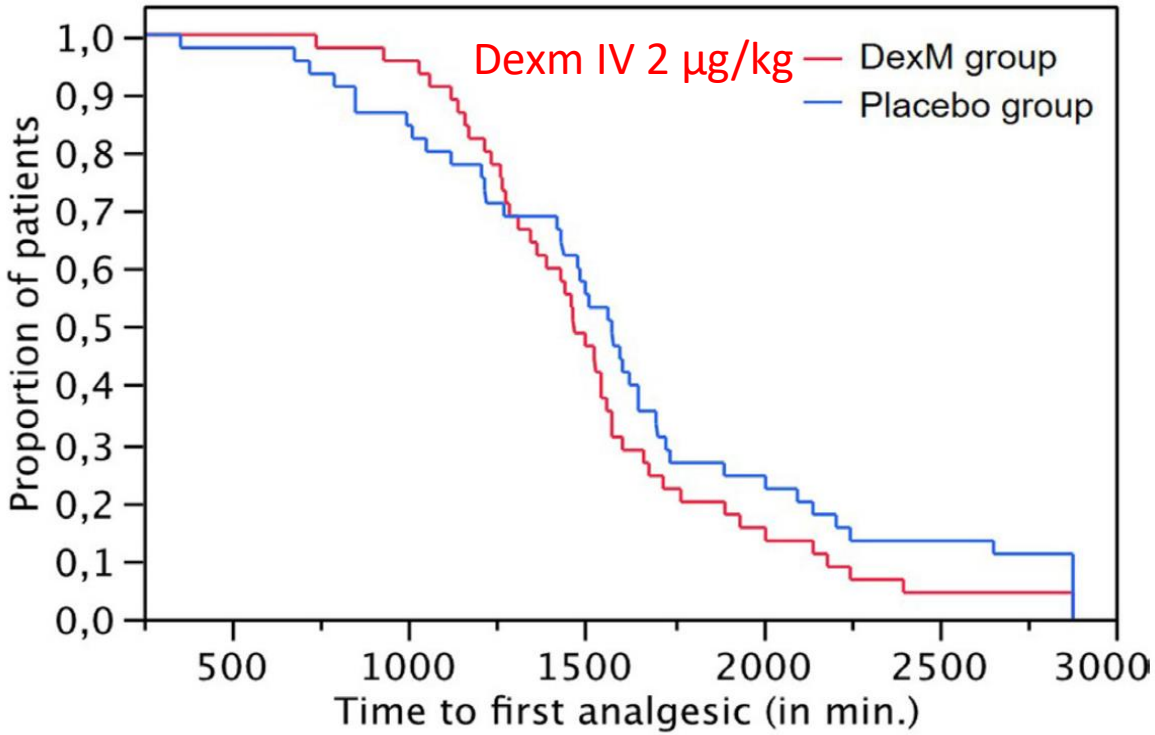

Figure 2 Kaplan-Meier survival plot for duration of analgesia. Log-rank test (p=0.27). DexM, dexmedetomidine.

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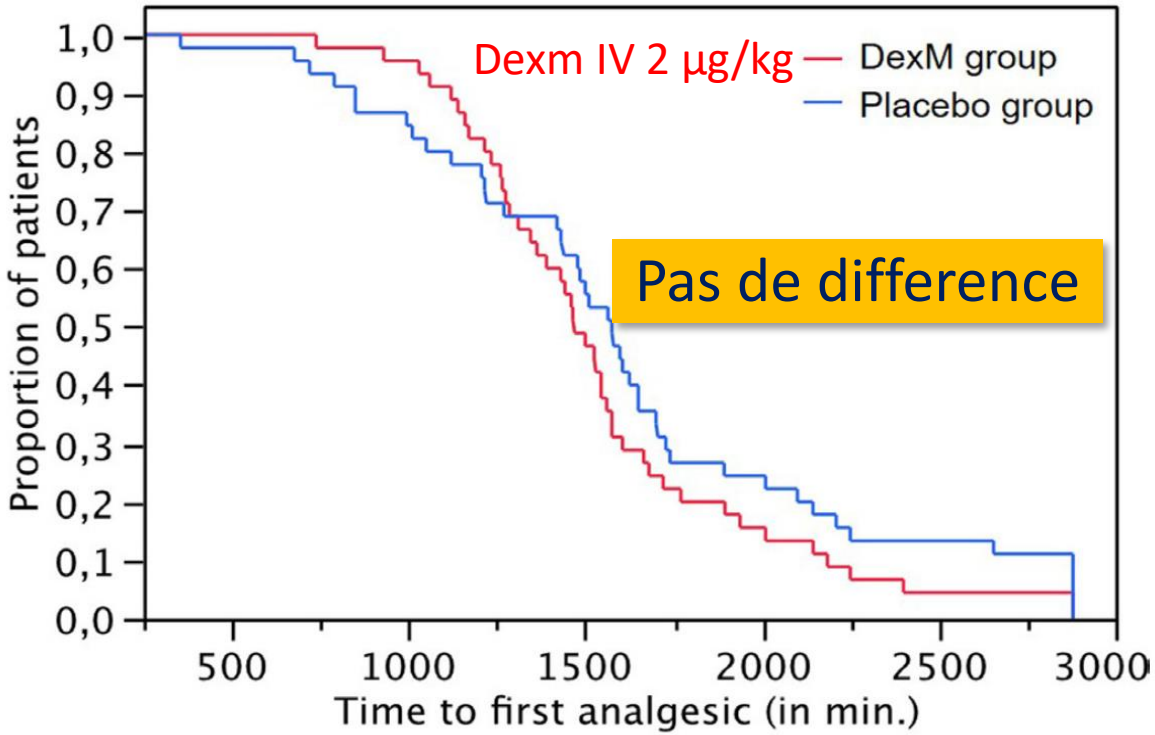

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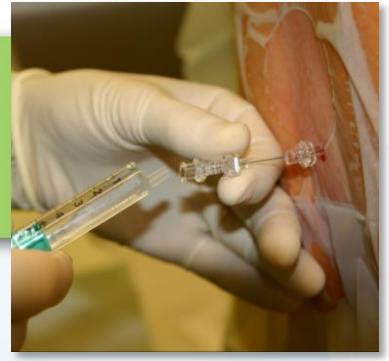
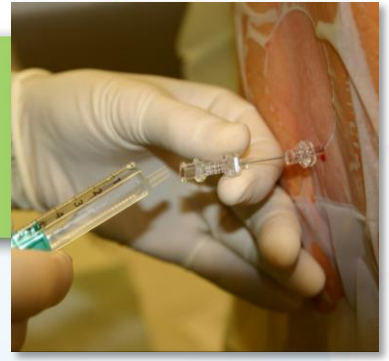
Quelle utilisation IT lors d'une RA ?



Dexm 3- 15 µg

F W Abdallah and R Brull. British Journal os anaesthesia. 110(6):915-25 (2013)

Quelle utilisation IT lors d'une RA ?

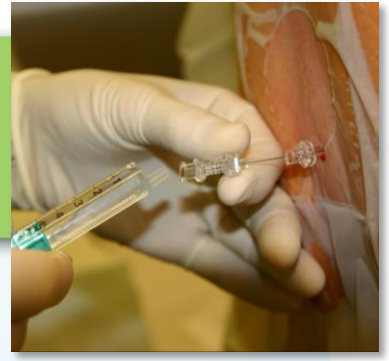


Dexm 3- 15 µg

Durée		IT
Bloc sensitif	+ 72 %	+ 2-3 h
Bloc moteur	+ 88 %	+ 4-6h
Analgésie	+ 127 %	+5-8 h

F W Abdallah and R Brull. British Journal os anaesthesia. 110(6):915-25 (2013)

Quelle utilisation IT lors d'une RA ?



Dexm 3- 15 µg

↑ Dose

↑ Effet

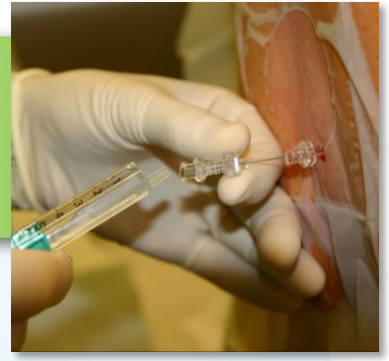
↑ BradyC

↑ Sédation Post op

F W Abdallah and R Brull. British Journal os anaesthesia. 110(6):915-25 (2013)

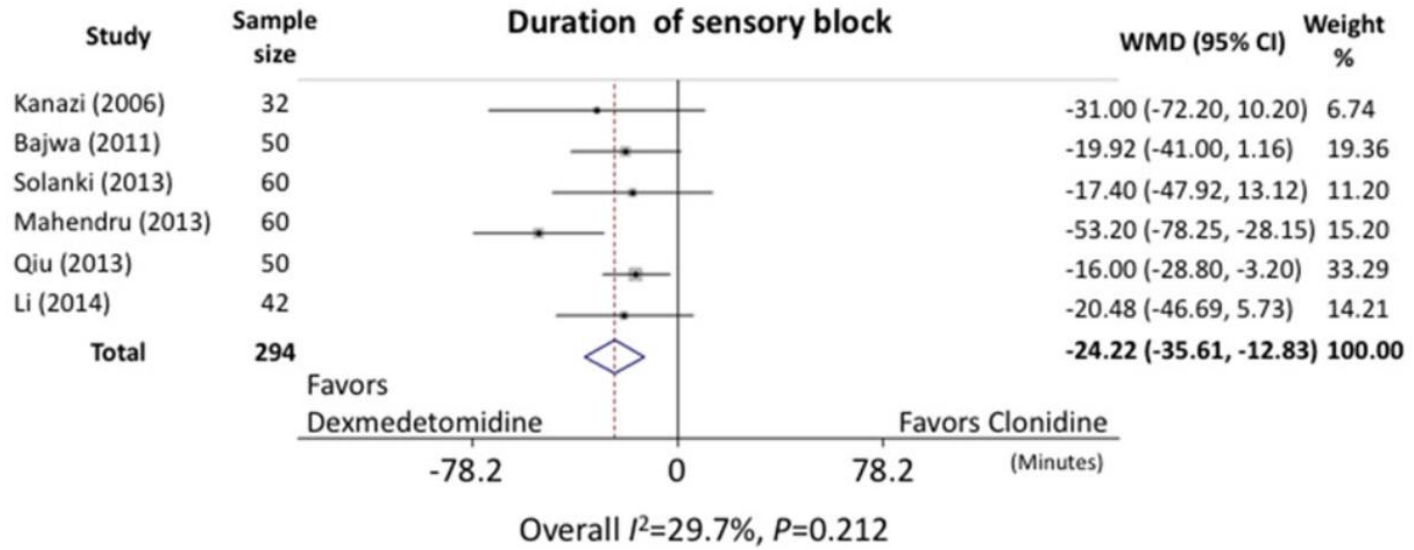
Gupta M. Pain Physician. 2016 Mar;19(3):E411-20

Quelle utilisation IT lors d'une RA ?



Dexm versus clonidine

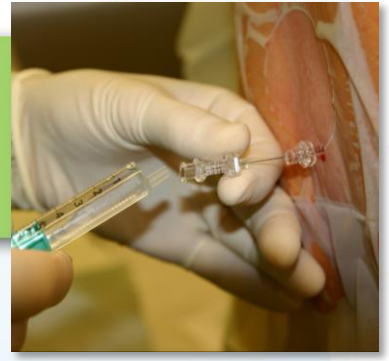
Forest plots comparing the duration of motor block of clonidine with dexmedetomidine as an adjuvant to local anesthetics.



NOTE: Weights are from random effects analysis

Zhang C. J Clin Pharmacol. 2016 Jul;56(7):827-34

Quelle utilisation IV lors d'une RA ?



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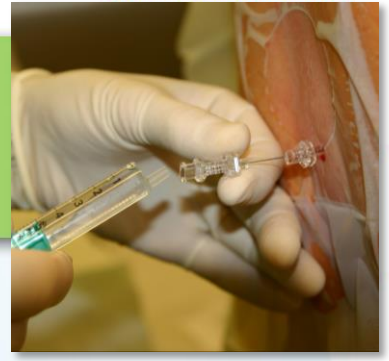
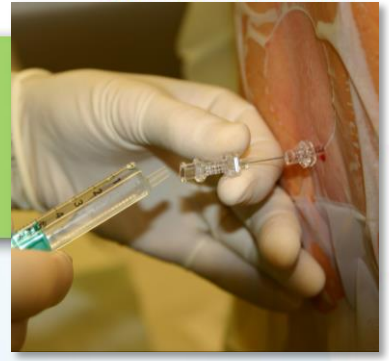


Dexm: 0.5-1 µg/kg IVL +/- 0.2 à 0.5 µg/kg/h

Durée	IT
Bloc moteur +17%	+ 72%
Bloc sensitif + 34 %	+88%
Analgésie + 53%	+127%

Faraj Abdallah. Richard Brull Anesth Analg 2013 jul; (117) 1: 271-8

Quelle utilisation IV lors d'une RA ?



Dexm: 0.5-1 µg/kg IVL +/- 0.2 à 0.5 µg/kg/h

Durée		IT
Bloc moteur	+17%	+ 72%
Bloc sensitif	+ 34 %	+88%
Analgésie	+ 53%	+127%

Bradycardie ↑ (x 3.7)

Faraj Abdallah. Richard Brull Anesth Analg 2013 jul; (117) 1: 271-8

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Clinique du sport Médico-Chirurgicale

Quelle utilisation IV lors d'une RA ?

Sédation per opératoire

Pratibha Jain Sha. Journal of anaesthesiology Clinical Pharmacology.april-june 2016.Vol 32.issue 2

Quelle utilisation IV lors d'une RA ?

Sédation per opératoire

RA bupiV 0.5% 3.5ml

Objectif: *sédation légère*

	Dexm(n=40)	Propofol(n=40)	Placebo(n=40)
	1 µg/kg + 0.5 µg/kg/h	6mg/kg/h + 2.5mg/kg/h	

Pratibha Jain Sha. Journal of anaesthesiology Clinical Pharmacology.april-june 2016.Vol 32.issue 2

Quelle utilisation IV lors d'une RA ?

Sédation per opératoire

	Dexm(n=40)	Propofol(n=40)	Placebo(n=40)
	1 µg/kg + 0.5 µg/kg/h	6mg/kg/h + 2.5mg/kg/h	
Délai d'action			
Douleur inj			
Délai réveil			
Variation FC			
PAm			
Dépression respiR			
analgésie			
Satisfaction			

Pratibha Jain Sha. Journal of anaesthesiology Clinical Pharmacology.april-june 2016.Vol 32.issue 2

Quelle utilisation IV lors d'une RA ?

Sédation per opératoire

	Dexm(n=40)	Propofol(n=40)	Placebo(n=40)
	1 µg/kg + 0.5 µg/kg/h	6mg/kg/h + 2.5mg/kg/h	
Délai d'action	25 min	10 min	
Douleur inj	⌀	+	⌀
Délai réveil	++ long	+long	Nal
Variation FC	↓	Nale	Nale
PAm	Nale	↓	Nale
Dépression respiR	⌀	⌀	⌀
analgésie	+	⌀	⌀
Satisfaction	77,5%	55%	37,5%

Pratibha Jain Sha. Journal of anaesthesiology Clinical Pharmacology.april-june 2016.Vol 32.issue 2

Quelle utilisation IV lors d'une RA ?

Sédation per opératoire

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PAm	Nale	↓	Nale
Dépression respiR	⌀	⌀	⌀
analgésie	+	⌀	⌀
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Pratibha Jain Sha. Journal of anaesthesiology Clinical Pharmacology.april-june 2016.Vol 32.issue 2

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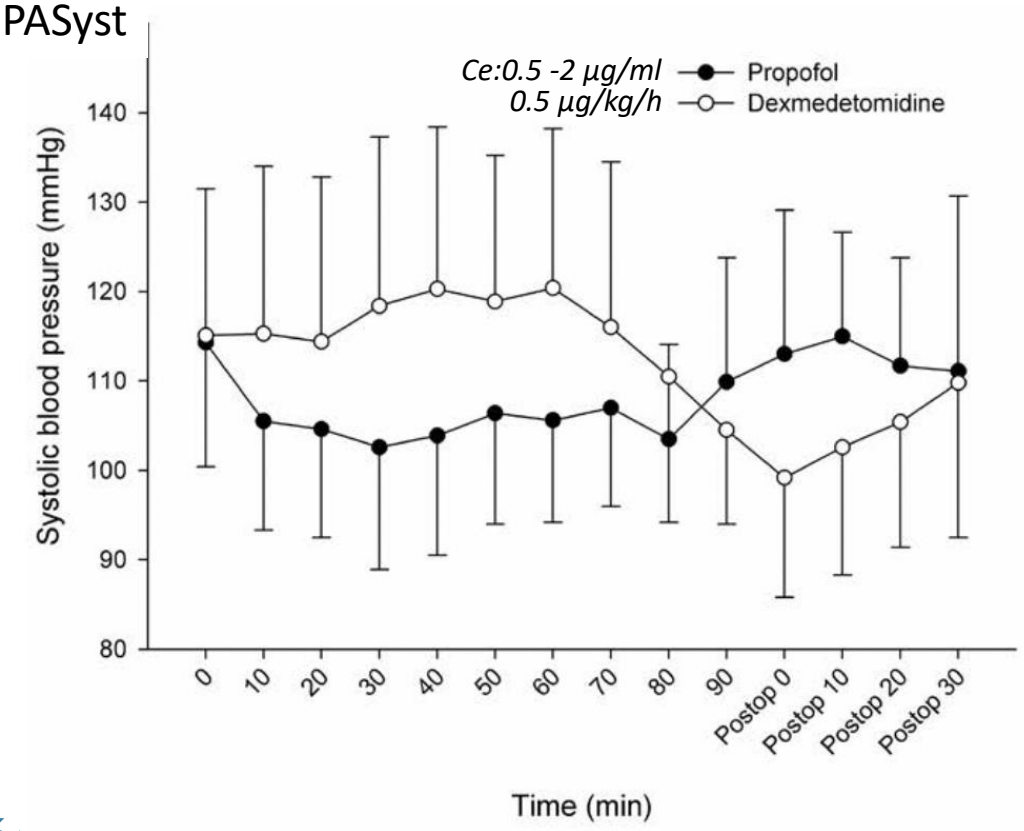
Délai réveil	++ long	+long	Nal
Variation FC	↓	Nale	Nale
PAm	Nale	↓	Nale
Dépression respiR	⌀	⌀	⌀
analgésie	+	⌀	⌀
Satisfaction	77,5%	55%	37,5%

Pratibha Jain Sha. Journal of anaesthesiology Clinical Pharmacology.april-june 2016.Vol 32.issue 2

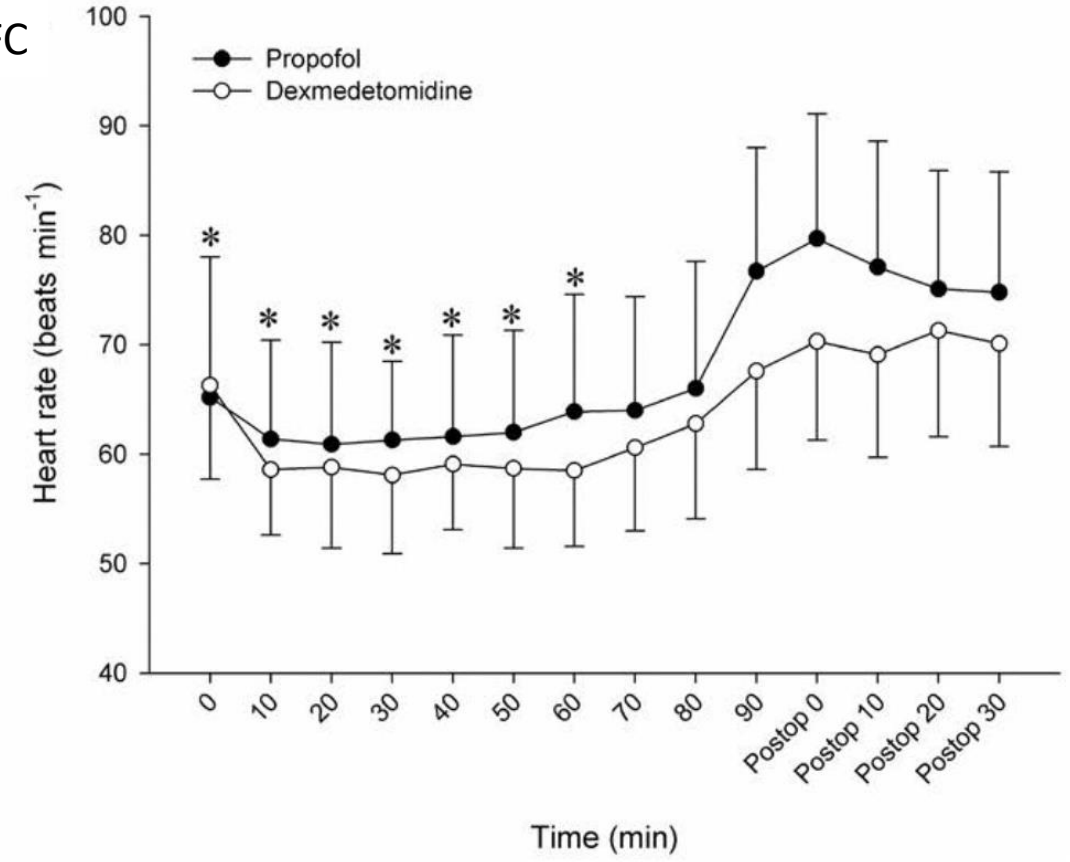
Quelle utilisation IV lors d'une RA ?

Sédation per opératoire

PASyst



FC



Shin, Hyun-Jung. Anesth Analg. 2018 Apr 5

Quelle utilisation IV lors d'une RA ?

Quelle dose pour une sédation IV ?

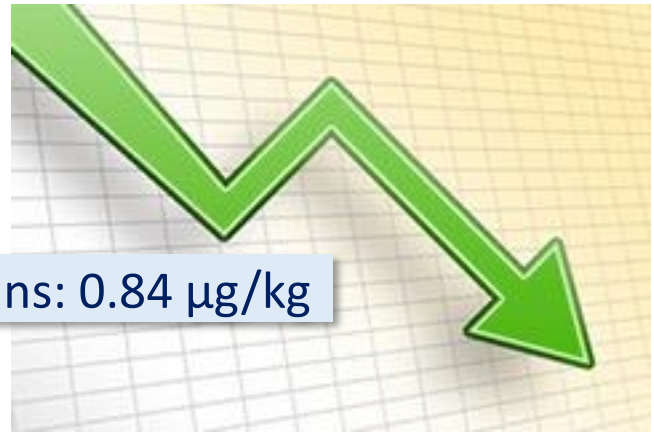
Sun, Q. Pak J Pharm Sci. 2018 Nov;31(6 (Special):2863-2868.

Quelle utilisation IV lors d'une RA ?

Quelle dose pour une sédation IV ?

ED95 Dexm IV pour Sédation légère

18-45 ans: 1,21 µg/kg



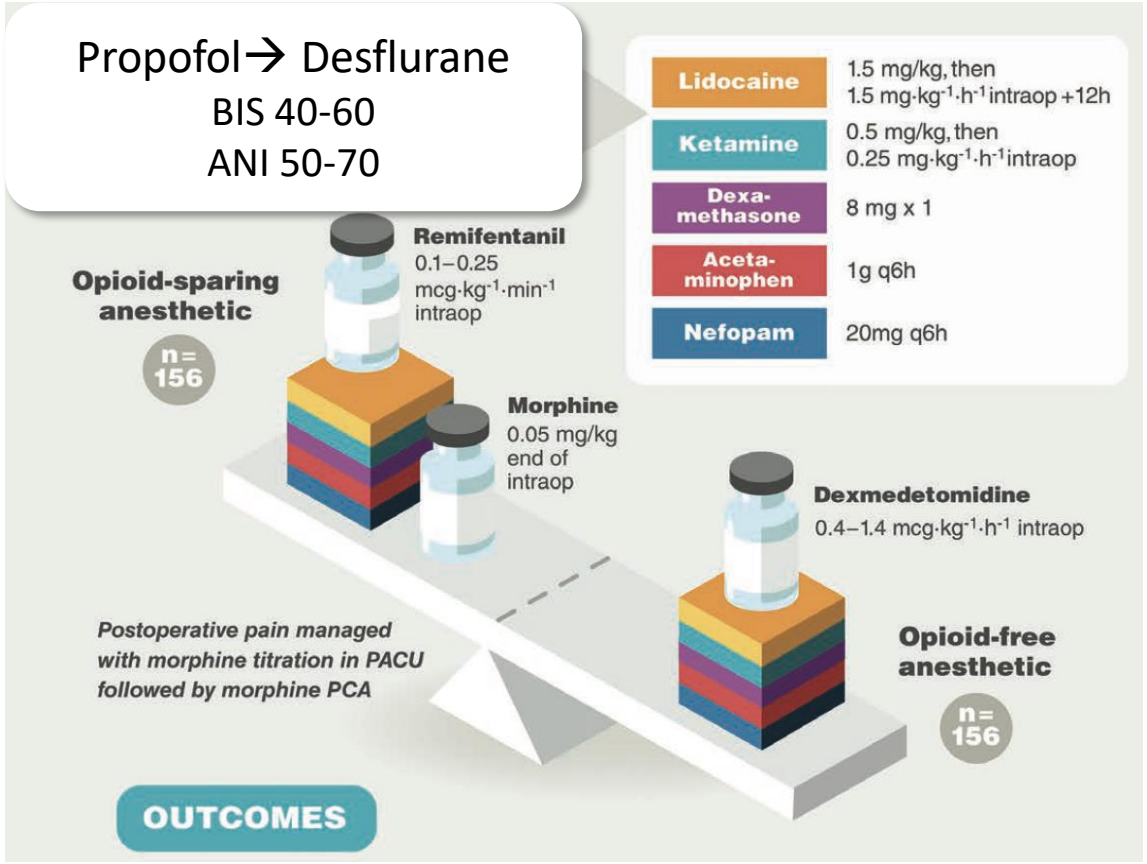
45-65 ans: 0.84 µg/kg

>65 ans: 0.54 µg/kg

Sun, Q. Pak J Pharm Sci. 2018 Nov;31(6 (Special):2863-2868.

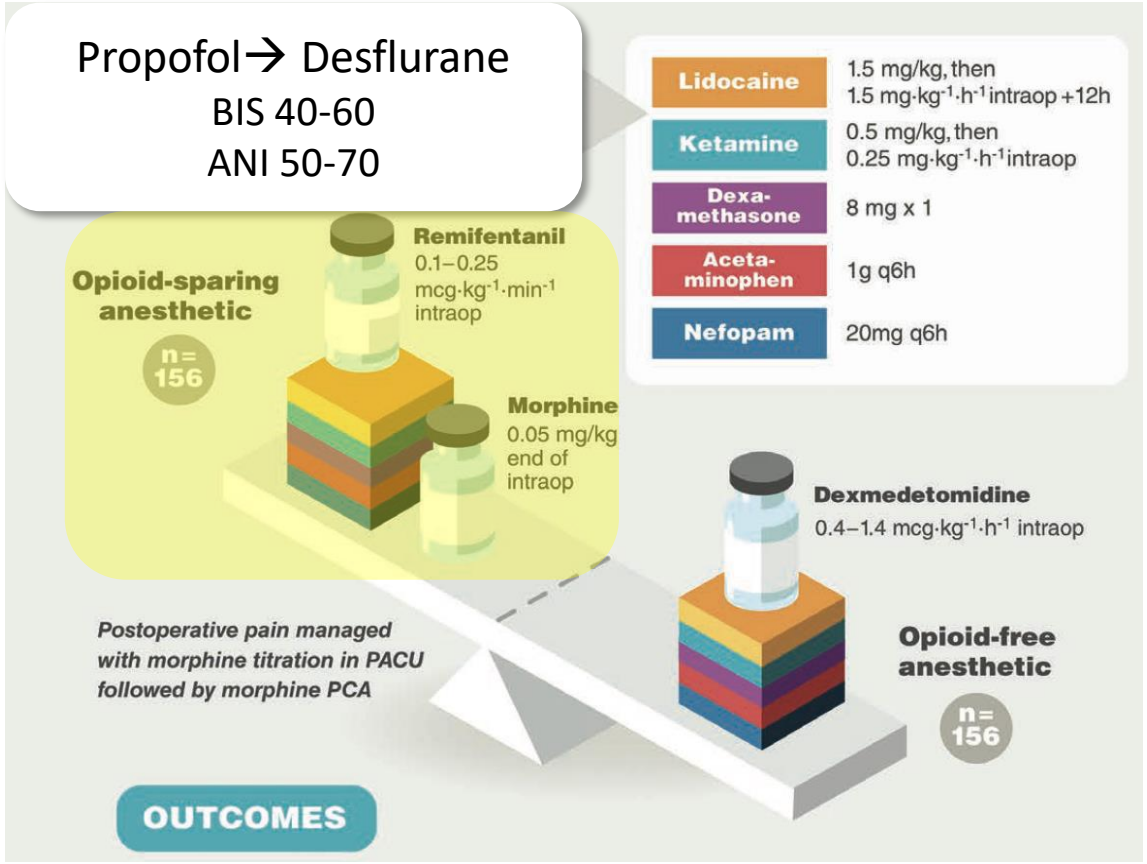
De quoi faut-il se méfier ?

De quoi faut-il se méfier ?



Beloeil H. Anesthesiology. 2021 Apr 1;134(4):541-551.

De quoi faut-il se méfier ?



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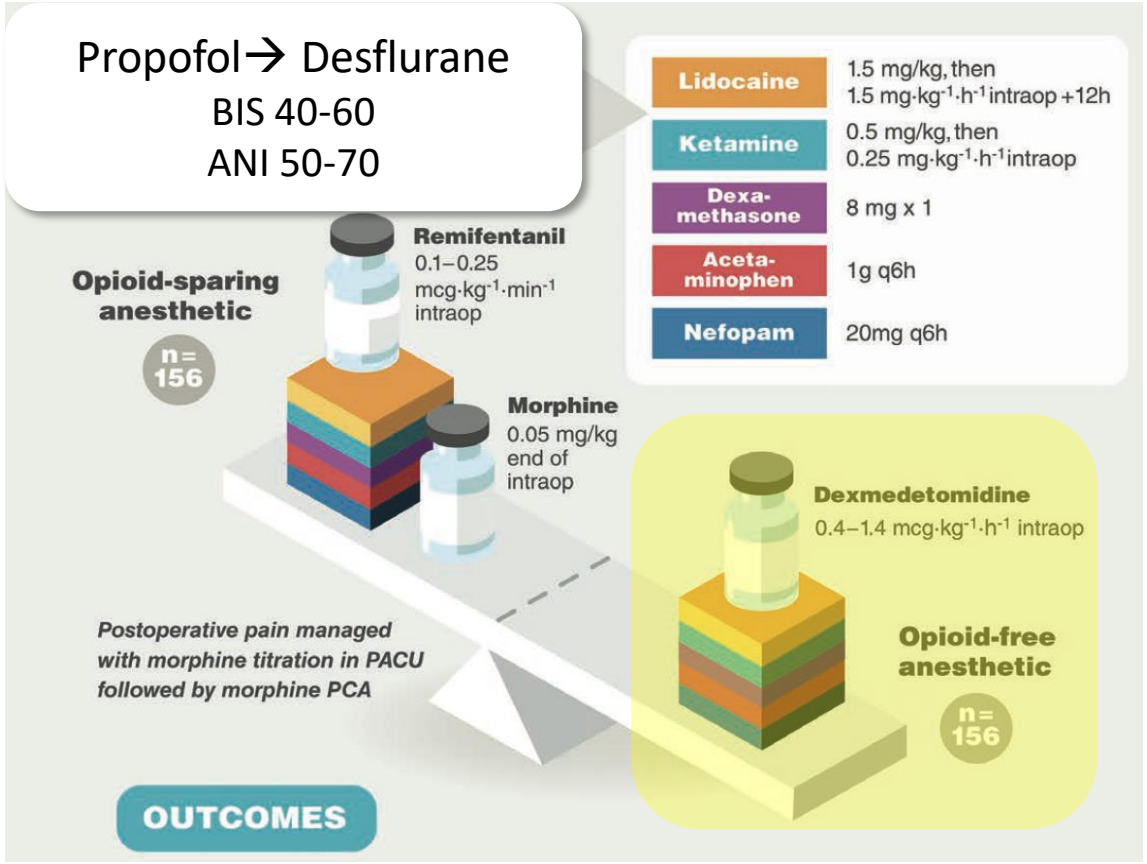

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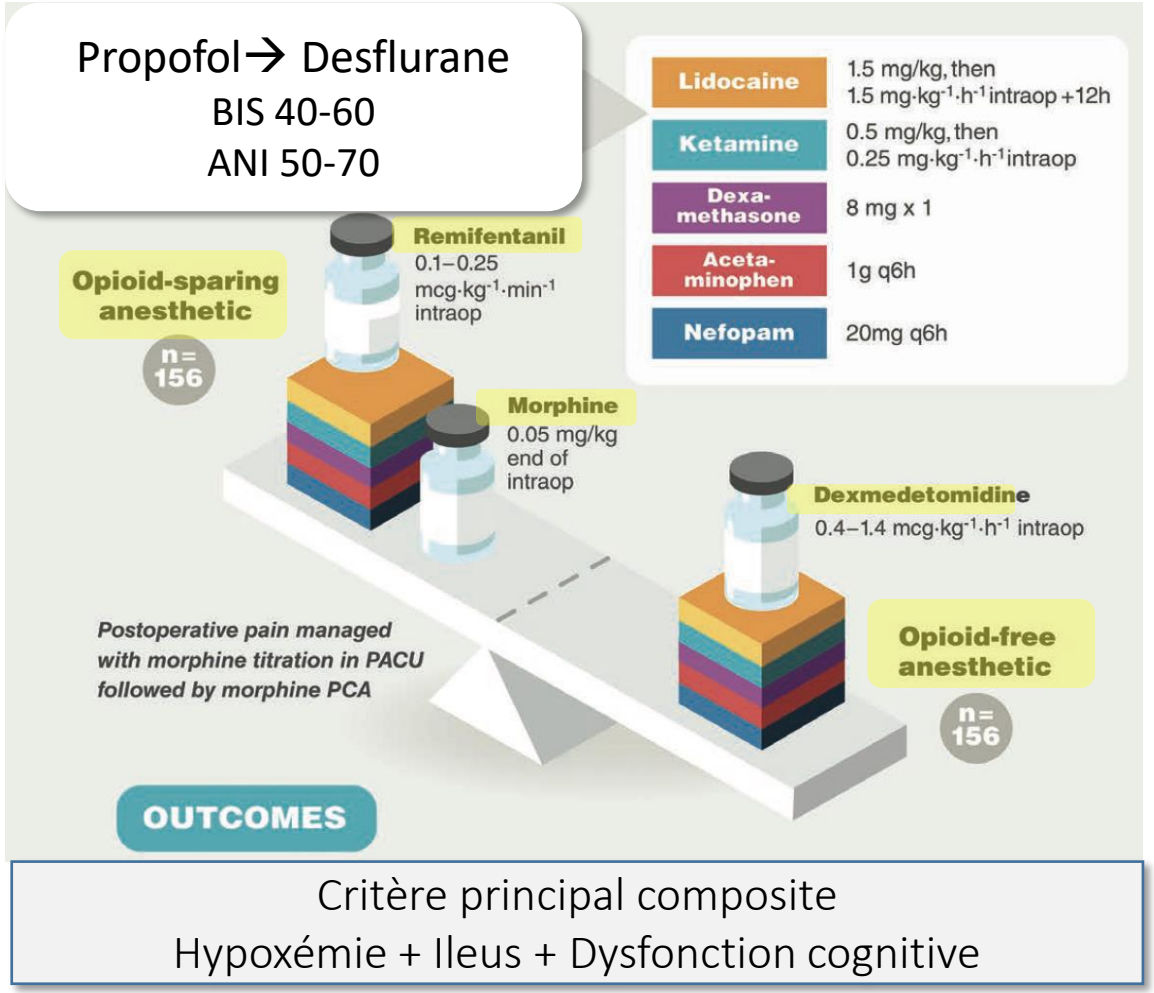

Critère principal composite
Hypoxémie + Ileus + Dysfonction cognitive

Beloeil H. Anesthesiology. 2021 Apr 1;134(4):541-551.

De quoi faut-il se méfier ?

	RemiF	DexM	
Critère Pal	67 %	78%	P=0.031
Hypoxie 48 h	61 %	72%	P=0.03
Morphine 48 h	11 mg	6 mg	p<0.05
Incidence NVPO	37 %	24 %	P<0.05
Durée en SSPI	1h53	2h28	P=0.01
Bradycardie	9 %	19 %	P=0.009

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Hypoxie

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Hypoxie

Sédation

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Hypoxie

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Hypoxie

SpO2< 95% sans apport d'O2

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Hypoxie

Sédation

Association Lidoc IV + Keta IV + Dexmedetomidine

De quoi faut-il se méfier ?

	RemiF	DexM	
Critère Pal	67 %	78%	P=0.031
Hypoxie 48 h	61 %	72%	P=0.03
Morphine 48 h	11 mg	6 mg	p<0.05
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Bradycardie	9 %	19 %	P=0.009

Hypoxie

Sédation

Dexm : Pas d'arrêt anticipé

Dose élevée 1.2 µg/kg/h

De quoi faut-il se méfier ?

	RemiF	DexM	
Critère Pal	67 %	78%	P=0.031
Hypoxie 48 h	61 %	72%	P=0.03
Morphine 48 h	11 mg	6 mg	p<0.05
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Bradycardie	9 %	19 %	P=0.009

De quoi faut-il se méfier ?

5 Bradycardies sévères

Traitement

- Arrêt administration de dexmedetomidine
- 4 injections d'atropine
- 1 injection d'adrénaline

Beloeil H. Anesthesiology. 2021 Apr 1;134(4):541-551.

De quoi faut-il se méfier ?

5 Bradycardies sévères

Traitement

- Arrêt administration de dexmedetomidine
- 4 injections d'atropine
- 1 injection d'adrénaline

Etiologies

1 surdosage

4 laparoscopies

Beloeil H. Anesthesiology. 2021 Apr 1;134(4):541-551.

Bradycardie et dexmedetomidine

Bradycardie et dexmedetomidine

980 patients : Cholecystectomie sous laparoscopie
Bradycardie x 2.81

De Cassai A.Korean J Anesthesiol 2022;75 (3): 245-254

Bradycardie et dexmedetomidine

Asystolie si association avec Néostigmine

Asystolie si association avec Amiodarone

Bell CM. J Pharm Pract 2022. 35 (4):650-653

Ohmori T. J intensive care 2015. 3:43

Dexmedetomidine et anesthésie

Dexmedetomidine et anesthésie

Anesthésie Générale

↓ Modeste opioïdes

↓ Modeste douleur

↓ ↓ Incidence NVPO

Dexmedetomidine et anesthésie

Anesthésie Générale	ALR
↓ Modeste opioïdes	↑ Durée d'analgésie
↓ Modeste douleur	Dexa = référence
↓ ↓ Incidence NVPO	

Dexmedetomidine et anesthésie

Anesthésie Générale	ALR
↓ Modeste opioïdes	↑ Durée d'analgésie
↓ Modeste douleur	Dexa = référence
↓ ↓ Incidence NVPO	Sédation per op utile

Dexmedetomidine et anesthésie

Bradycardie

Dexmedetomidine et anesthésie

Bradycardie

Bon patient

Bonne dose

Dexmedetomidine et anesthésie

Bradycardie

Bon patient

Bonne dose

Pas d'associations dangeureuses

Dexmedetomidine et anesthésie

Bradycardie

Bon patient

Bonne dose

Pas d'associations dangeureuses

Atropine et/ou Ephedrine

Conclusion

“Less may be better, but it is not clear that none is best”

*Kharasch, E. D. "Opioid-free Anesthesia: Time to Regain Our Balance." Anesthesiology 2021 **134**(4): 509-514.*

Merci

Outcomes en chirurgie cardiaque (I)

Clinical Therapeutics/Volume 41, Number 1, 2019

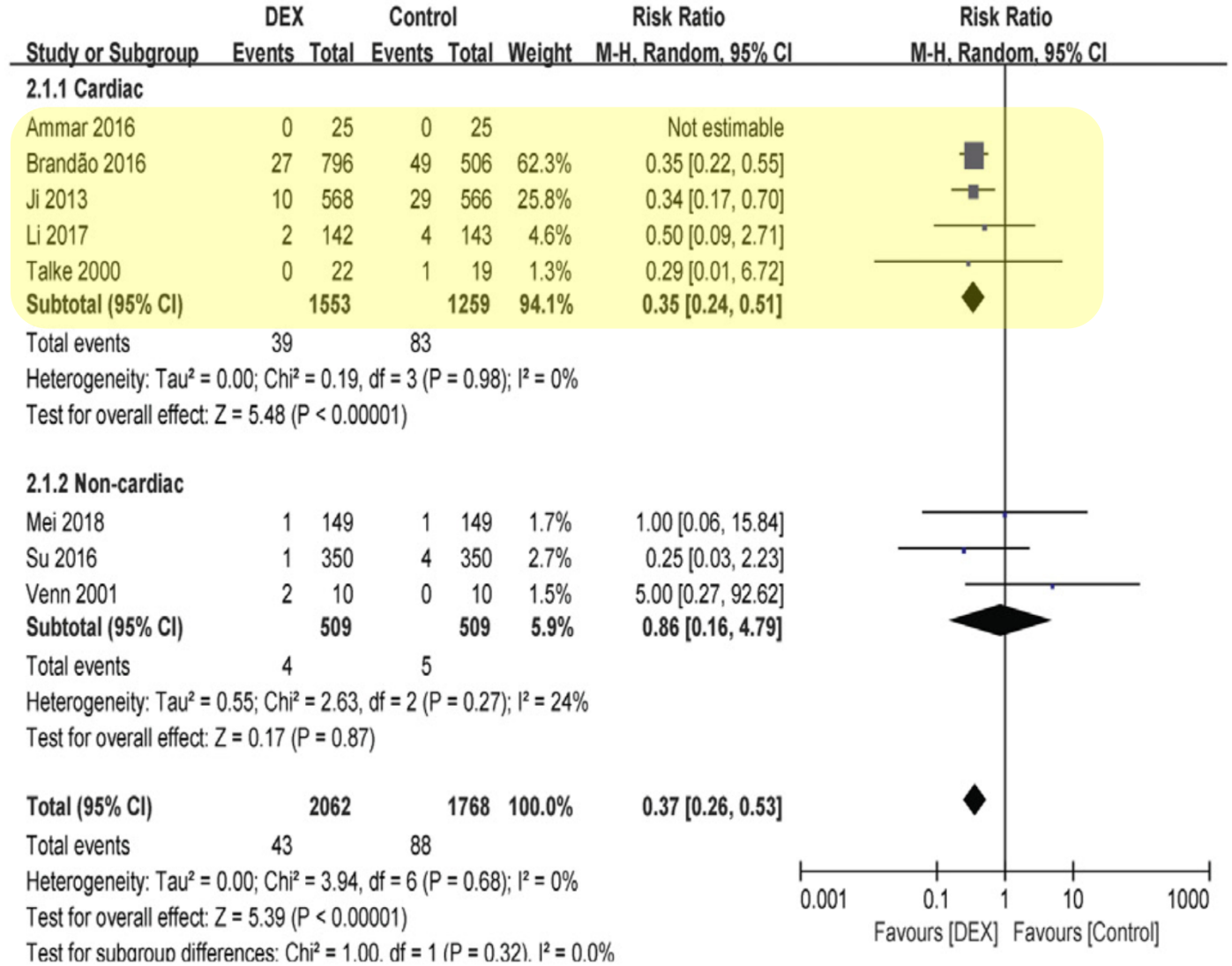
Reviews

Effects of Perioperative Dexmedetomidine on Postoperative Mortality and Morbidity: A Systematic Review and Meta-analysis

Ke Peng, MD; Fu-hai Ji, MD; Hua-yue Liu, MD; Juan Zhang, MD; Qing-cai Chen, MD; and Ya-hui Jiang, MD

Departments of Anesthesiology, Intensive Care Medicine, and Pain Medicine, First Affiliated Hospital of Soochow University, Suzhou, China

- 23 études en chir cardiaque
- ↓ Mortalité, ↓ délirium, ↓ FA, ↓ durée V méca, ↓ durée en ICU
- MAIS: ↑ bradyC et ↑ hypoTA
- MAIS si uniquement 15 RCT : ↓ durée V méca, ↓ durée en ICU



Outcomes en chirurgie cardiaque (II)

Dexmedetomidine for reduction of atrial fibrillation and delirium after cardiac surgery (DECADE): a randomised placebo-controlled trial

Alparslan Turan, Andra Duncan, Steve Leung, Nika Karimi, Jonathan Fang, Guangmei Mao, Jennifer Hargrave, Marc Gillinov, Carlos Trombetta, Sabry Ayad, Manal Hassan, Andrew Feider, Kimberly Howard-Quijano, Kurt Ruetzler, Daniel I Sessler, for the DECADE Study Group*

Lancet 2020; 396: 177–85

- 400 DexM et 398 placebo
- 6 centres USA
- Triple aveugle
- CCV cardioplumonary bypass
  - Dose faible 0.1-0.2 microg/kg/h en per op et 0-4 microg/kg/h en post op pendant 24 h
- Anesthésie standardisée opiacé propofol
- DexM en début de chir et pendant 24 h

	Dexmedetomidine (n=398)		Placebo (n=396)		Relative risk*†	p value†
	Missing	Incidence	Missing	Incidence		
Primary						
Atrial arrhythmia	1	121 (30%)	1	134 (34%)	0·91 (0·72–1·15)	0·34
Delirium	9	67 (17%)	9	46 (12%)	1·48 (0·99–2·23)	0·026
Secondary						
Kidney function‡						
Acute Kidney Injury	9	..	7	..	1·40 (0·84–2·34)	0·14
Network classification						
No risk	..	348 (89%)	..	359 (92%)	..	..
Stage 1	..	33 (8%)	..	29 (7%)	..	..
Stage 2	..	4 (1%)	..	0	..	..
Stage 3	..	4 (1%)	..	1 (<1%)	..	..
90-day pain						
Any pain (Modified Brief Pain Inventory)	109	79 (27%)	96	93 (31%)	0·87 (0·65–1·16)	0·29
Modified Brief Pain Inventory average pain§	..	2 (1–4)	..	1 (1–2)	..	..

Clinique du sport Garonne Médico-Chirurgicale

Meta-Analysis > Br J Anaesth. 2021 Nov;127(5):e168-e170. doi: 10.1016/j.bja.2021.08.009.
Epub 2021 Sep 3.

Meta-analysis of randomised controlled trials of perioperative dexmedetomidine to reduce delirium and mortality after cardiac surgery

Robert D Sanders [1], Jordan Wehrman [2], Joanne Irons [3], Jan Dieleman [4], David Scott [5], Yahya Shehabi [6]

Affiliations + expand

PMID: 34489090 DOI: 10.1016/j.bja.2021.08.009

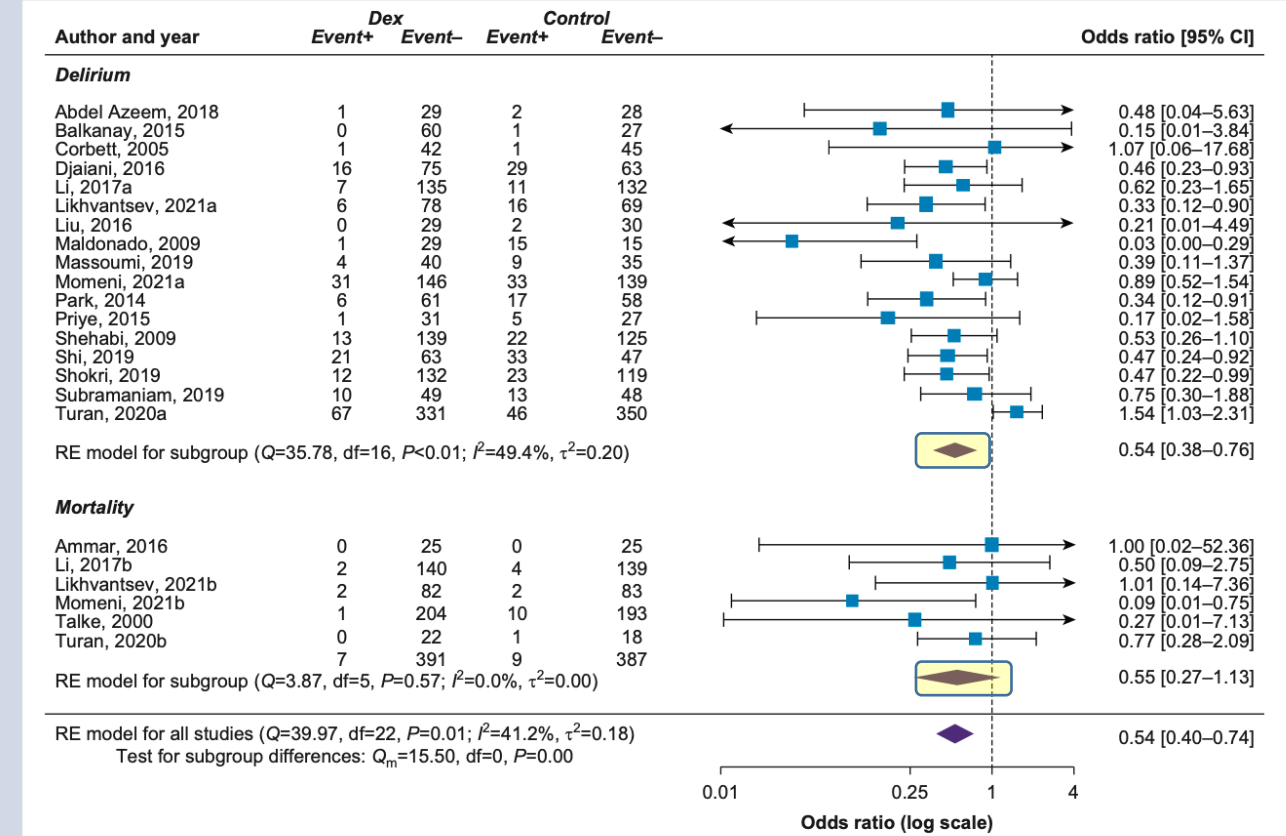


Fig 1. Forest plots showing meta-analyses of cardiac surgery studies comparing dexmedetomidine with a control for delirium and mortality. To facilitate a conservative interpretation, for Momeni and colleagues[1] in-hospital delirium rates were included. CI, confidence interval; Dex, dexmedetomidine; df, degrees of freedom; RE, random effects,

Durée de séjour en SSPI

Meta-Analysis > Anesth Analg. 2022 Jun 1;134(6):1229-1244.
doi: 10.1213/ANE.0000000000005843. Epub 2022 Jan 27.

The Effect of Dexmedetomidine on Postanesthesia Care Unit Discharge and Recovery: A Systematic Review and Meta-Analysis

Jeremy Cheuk Kin Sin [1 2], Alexis Tabah [2 3], Matthys J J Campher [1 4], Kevin B Laupland [5 6], Victoria A Eley [2 7]

33 études qui représentent 2676 patients

- Pas d'augmentation de durée de séjour en SSPI
  - +1 min délai extubation
  - RR 0.38 agitation
  - RR 0.69 toux
  - RR 0.54 NVPO
  - RR 5.39 hypotension`
  - RR 5.13 bradycardie

Médi POLE Garonne
Clinique du sport Médico-Chirurgicale

Prévention des frissons

Review > Cochrane Database Syst Rev. 2015 Aug 10;2015(8):CD011107.
doi: 10.1002/14651858.CD011107.pub2.

Alpha-2 adrenergic agonists for the prevention of shivering following general anaesthesia

Sharon R Lewis [1], Amanda Nicholson, Andrew F Smith, Phil Alderson

Abstract

Background: Shivering after general anaesthesia is common. It is unpleasant but can also have adverse physiological effects. Alpha-2 (α-2) adrenergic agonist receptors, which can lead to reduced sympathetic activity and central regulation of vasoconstrictor tone, are a group of drugs that have been used to try to prevent postoperative shivering.

Objectives: To assess the following: the effects of α-2 agonists on the prevention of shivering and subsequent complications after general anaesthesia in people undergoing surgery; the effects of α-2 agonists on the risk of inadvertent perioperative hypothermia; and whether any adverse effects are associated with these interventions.

Authors' conclusions: There is evidence that clonidine and dexmedetomidine can reduce postoperative shivering, but patients given dexmedetomidine may be more sedated. However, our assessment of the quality of this evidence is very low.

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Clinique du sport Médico-Chirurgicale

Remifentanil

PAIN®

Remifentanil for abdominal surgery is associated with unexpectedly unfavorable outcomes

Sebastian Niedermayer[a], Jens Heyn[a], Felix Guenther[b], Helmut Küchenhoff[b], Benjamin Luchting[a,c,*]

Abstract

Insufficient perioperative pain treatment is known as a highly predictive risk factor for the development of chronic postoperative pain. Remifentanil is an ultrashort-acting opioid that provides quick and efficient analgesia but is associated with the induction of opioid-induced hyperalgesia. Despite these well-known characteristics, this substance is being increasingly used in anesthesia and in a variety of medical fields, such as intensive-care medicine and obstetrics. The aim of our study was to reveal whether remifentanil influences postoperative pain, the requirement for postoperative analgesics, and requirement of antiemetics (as indirect indicator of postoperative nausea and vomiting), as well as the effects on time to extubation and length of stay in the postanesthesia care unit in daily clinical routine. From an electronic medical records database of 55,693 anesthesias, we analyzed data from all patients receiving intraabdominal surgery (visceral, gynecological, and urological) under general anesthesia or combined general-epidural anesthesia by propensity score matching. The administration of remifentanil was associated with higher postoperative pain scores despite a higher requirement of postoperative analgesics. Additional epidural analgesia was not able to avoid this finding. The intraoperative use of remifentanil is associated with a deterioration of pain levels and postoperative analgesic requirement, wherefore the potential benefit of this substance seems to be outweighed by its potential disadvantages. Especially in operative procedures in which high postoperative pain scores are expected, the unreflective use should be critically questioned.

Keywords: Chronic postsurgical pain, Postoperative pain, Anesthesia, Remifentanil, Opioid-induced hyperalgesia

- 55 000 anesthésies
- Chir urologique, viscérale, gynécologique
- Si RemiF : ↑ EVA ↑morphiniques post op
- Même en présence d'une péridurale

Médi POLE Garonne
Clinique du sport Médico-Chirurgicale

OFA et réhabilitation

The effect of opioid-free anesthesia protocol on the early quality of recovery after major surgery (SOFA trial): study protocol for a prospective, monocentric, randomized, single-blinded trial

Maxime Léger[1,2*], Solène Pessiot-Royer[1], Tristan Perrault[1], Elsa Parot-Schinkel[3], Fabienne Costerousse[1], Emmanuel Rineau[1] and Sigismond Lasocki[1]

Abstract

Background: Since the 2000s, opioid-free anesthesia (OFA) protocols have been spreading worldwide in anesthesia daily practice. These protocols avoid using opioid drugs during anesthesia to prevent short- and long-term opioid side effects while ensuring adequate analgesic control and optimizing postoperative recovery. Proofs of the effect of OFA protocol on optimizing postoperative recovery are still scarce. The study aims to compare the effects of an OFA protocol versus standard anesthesia protocol on the early quality of postoperative recovery (QoR) from major surgeries.

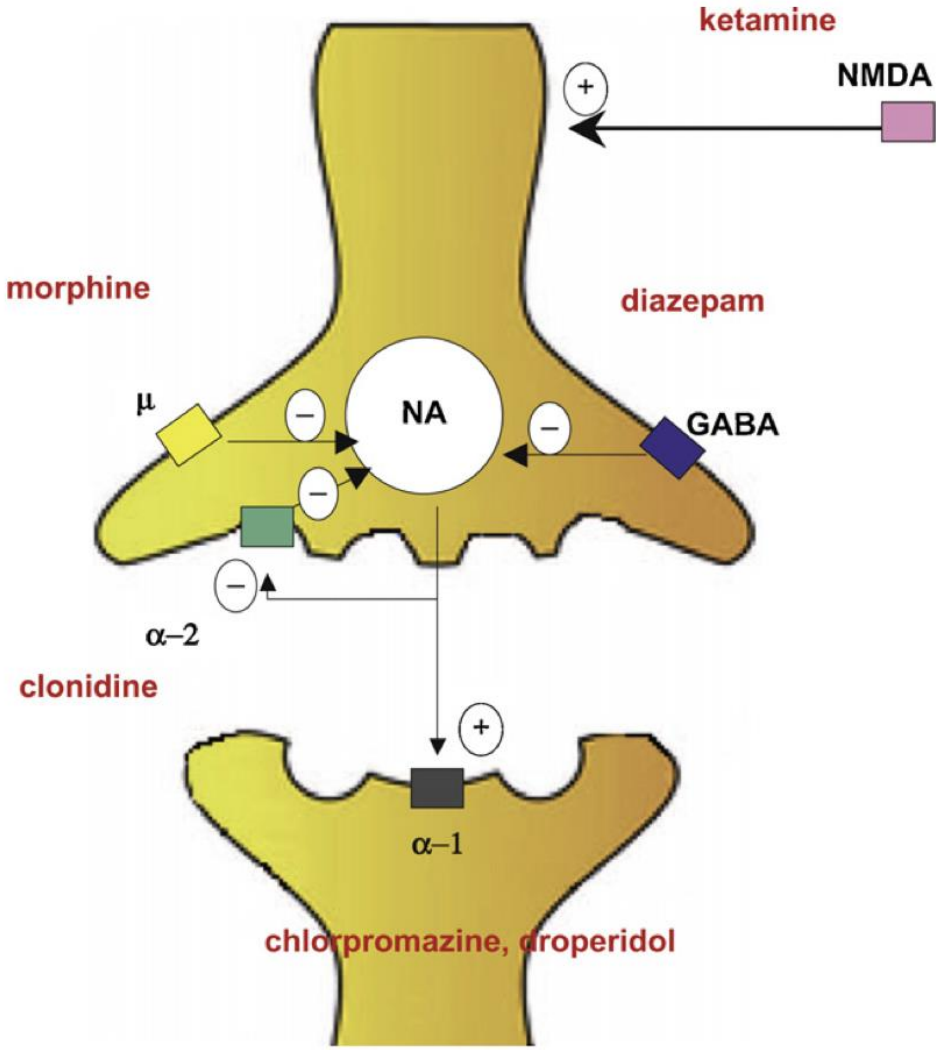
Methods: The SOFA trial is a prospective, randomized, parallel, single-blind, monocentric study. Patients (n = 140) scheduled for major plastic, visceral, urologic, gynecologic, or ear, nose, and throat (ENT) surgeries will be allocated to one of the two groups. The study group (OFA group) will receive a combination of clonidine, magnesium sulfate, ketamine, and lidocaine. The control group will receive a standard anesthesia protocol based on opioid use. Both groups will receive others standard practices for general anesthesia and perioperative care. The primary outcome measure is the QoR-15 value assessed at 24 h after surgery. Postoperative data such as pain intensity, the incidence of postoperative complication, and opioid consumption will be recorded. We will also collect adverse events that may be related to the anesthetic protocol. Three months after surgery, the incidence of chronic pain and the quality of life will be evaluated by phone interview.

Discussion: This will be the first study powered to evaluate the effect of OFA versus a standard anesthesia protocol using opioids on global postoperative recovery after a wide range of major surgeries. The SOFA trial will also provide findings concerning the OFA impact on chronic pain incidence and long-term patient quality of life.

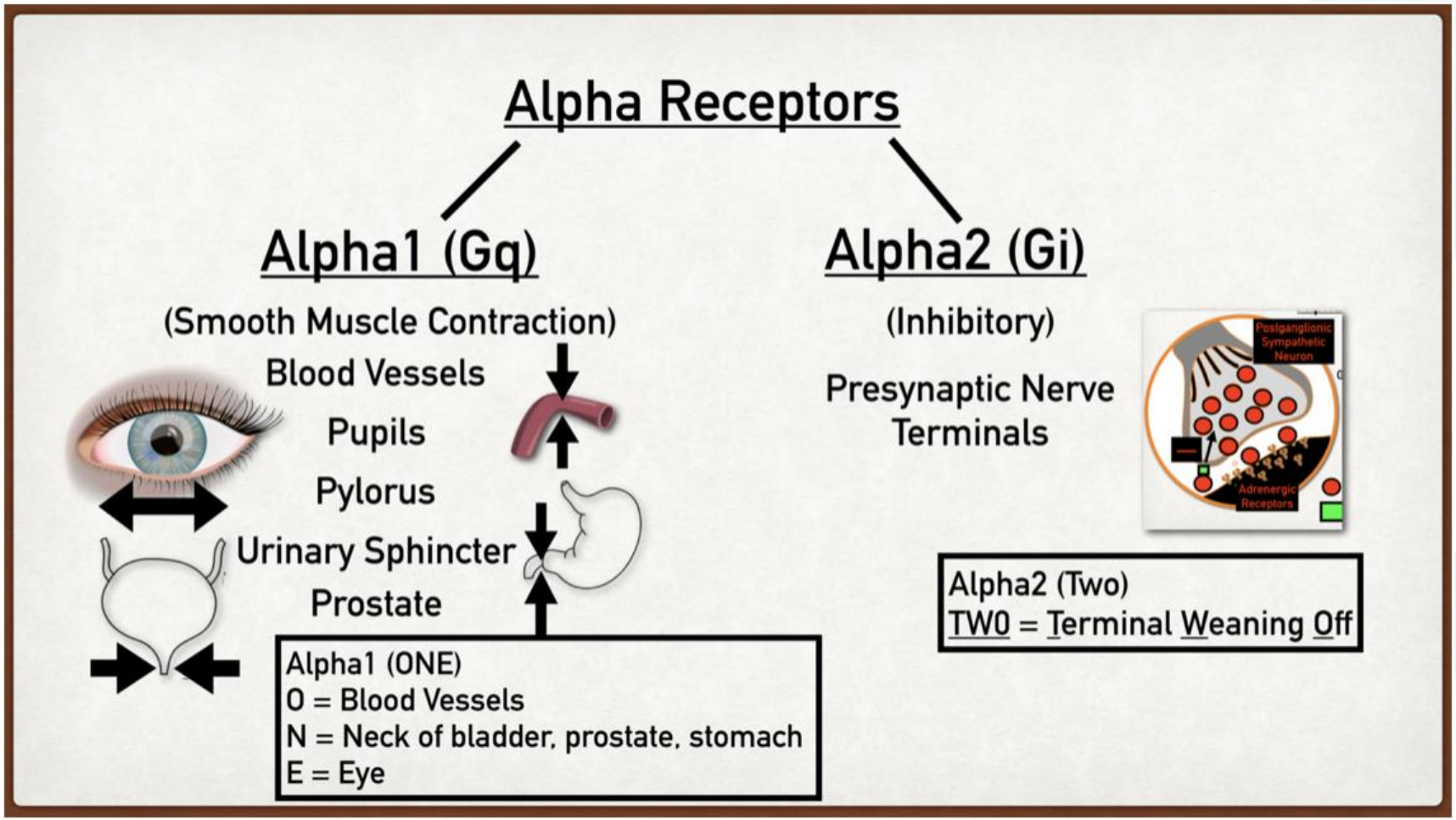
Opioid free anesthesia protocol	Standard anesthesia protocol
Before surgery	
– **CLONIDINE** continuous infusion: start at 50 µg/h, with anesthetic monitoring, and adapt to hemodynamic stability with a maximum infusion rate of 150 µg/h. If patient's weight <50kg, maximum infusion rate of 100µg/h – **Locoregional anesthesia** if needed, but without opioids	– **Locoregional anesthesia** if needed, with or without opioids
Anesthesia induction	
– **Antibiotic prophylaxis** if indicated – **Hypnotic drugs:** left at the discretion of the anesthesiologist – **NO OPIOIDS** – **CLONIDINE** continuous infusion on same infusion rate, adapt to hemodynamic stability – **MAGNESIUM sulfate:** 40 mg/kg, *diluted in 100ml of NaCl 0.9%, IV infusion* Maximum dose: 4 g – **LIDOCAINE:** 1.5 mg/kg in 10 minutes (continuous infusion) (*if loco-regional anesthesia, this dose is not administered*) – **KETAMINE:** 0.5 mg/kg as a bolus (or 0.25 mg/kg if instable coronary disease or instable cardiac failure or pulmonary arterial hypertension) – **Neuromuscular blocking agents** (anesthesiologist's discretion) – **Nausea and vomiting management**	– **Antibiotic prophylaxis** if indicated – **Hypnotic drugs:** left at the discretion of the anesthesiologist – **Opioids:** ○ **Sufentanil** 0.1-0.3 µg/kg IV Or ○ **Remifentanil** via target-controlled infusion, ○ target: 3-6 ng/mL – **KETAMINE:** left at the discretion of the anesthesiologist in charge 0.15 mg/kg IV, can be repeated every 45 min-1hour – **Neuromuscular blocking agents** (anesthesiologist's discretion) – **Nausea and vomiting management**
Intra-operative anesthesia	
– **Hypnotic drugs:** left at the discretion of the anesthesiologist ○ Inhalation anesthetic agents: Desflurane or Sevoflurane with a MAC (Mean Alveolar Concentration) objective of 1-1.5 MAC OR ○ Propofol via target-controlled infusion, target at 3-6 µg/mL – **No Opioids** – **CLONIDINE** on continuous infusion on same infusion rate, adapt to hemodynamic stability – **KETAMINE** 0.2 mg/kg/h on continuous infusion, stopped 30 minutes before end of surgery – **LIDOCAINE** on continuous infusion: 1.5 mg/kg/h, continued up to 1h after the surgery – **Pain management** according to the service protocol: ○ **ACETAMINOPHEN** 1 g IV ○ +/- **NEFOPAM** 20 mg IV ○ +/- **KETOPROFEN** 50 to 100 mg IV ○ **No opioids** – **Neuromuscular blocking agents** left at the discretion of anesthesiologist	– **Hypnotic drugs:** left at the discretion of the anesthesiologist ○ Inhalation anesthetic agents: Desflurane or Sevoflurane with a MAC (Mean Alveolar Concentration) objective of 1-1.5 MAC OR ○ Propofol via target-controlled infusion, target at 3-6 µg/mL – **Opioids** ○ **Sufentanil** 0.1-0.3 µg/kg with bolus intervals left at the discretion of the anesthesiologist in charge OR ○ **Remifentanil** via target-controlled infusion, target: 3-6ng/mL – **Pain management** according to the service protocol: ○ **ACETAMINOPHEN** 1 g IV ○ +/- **NEFOPAM** 20 mg IV ○ +/- **KETOPROFEN** 50 to 100 mg IV ○ +/- **OXYCODONE** or **MORPHINE** 1-5 mg IV – **Neuromuscular blocking agents** left at the discretion of anesthesiologist
Postanesthesia care unit (PACU)	
– **LIDOCAINE** on continuous infusion: 1.5 mg/kg/h, continued up to 1 hour after the surgery in the PACU – **Pain management** (opioids can be used if necessary) – **Nausea and vomiting management**	– **Pain management** (opioids can be used if necessary) – **Nausea and vomiting management**

Fig. 1 Detailed interventional protocols in the opioid-free anesthesia group (OFA group) and in the standard anesthesia group (English translation from our French procedures). IV, intravenous; PACU, postanesthesia care unit

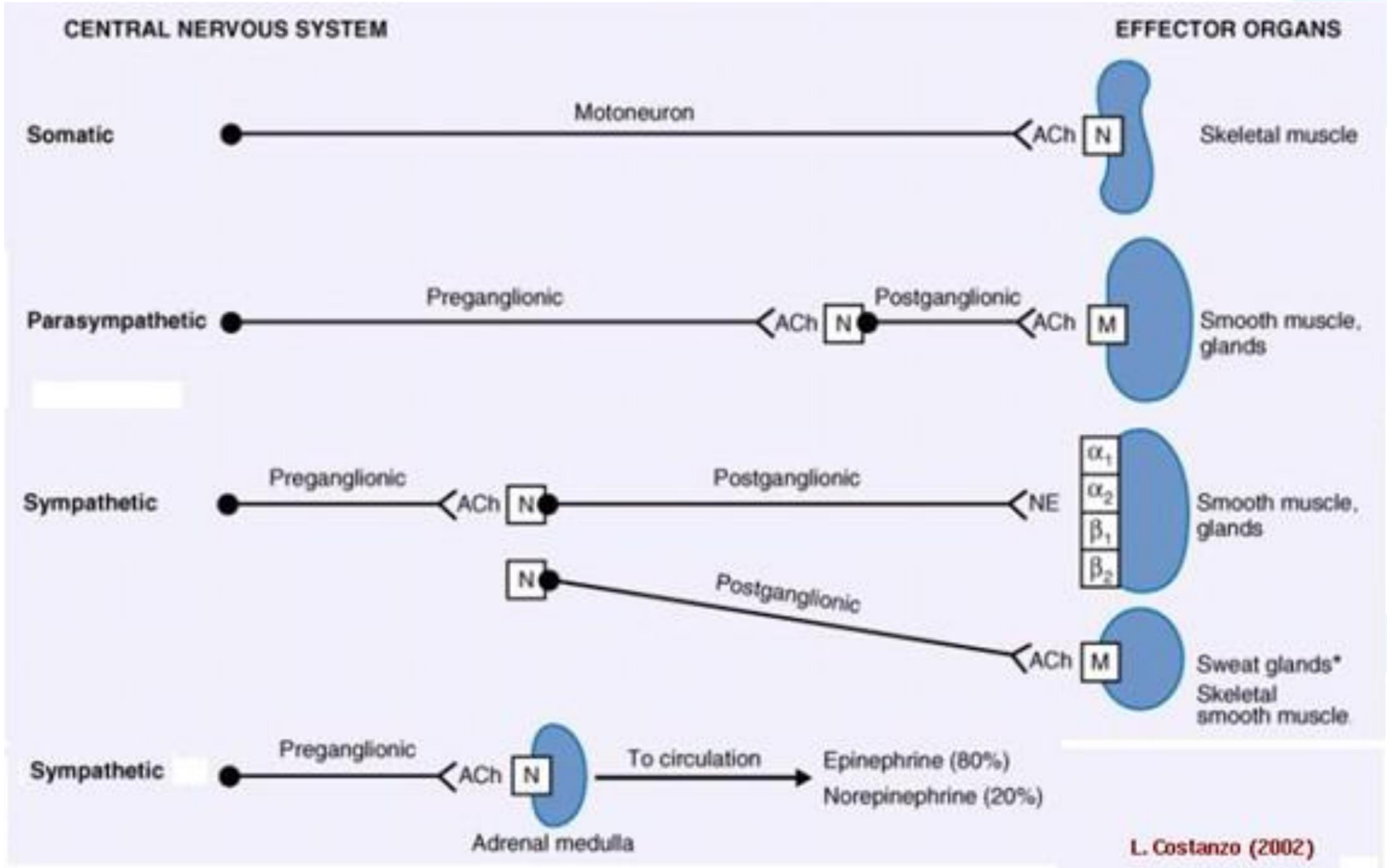
Anti nociception: mécanisme d'action



Récepteurs alpha 1



Neurotransmetteurs



Anesth Analg. 2021 May 01; 132(5): 1254–1264. doi:10.1213/ANE.0000000000005361.

The Neural Circuits Underlying General Anesthesia and Sleep

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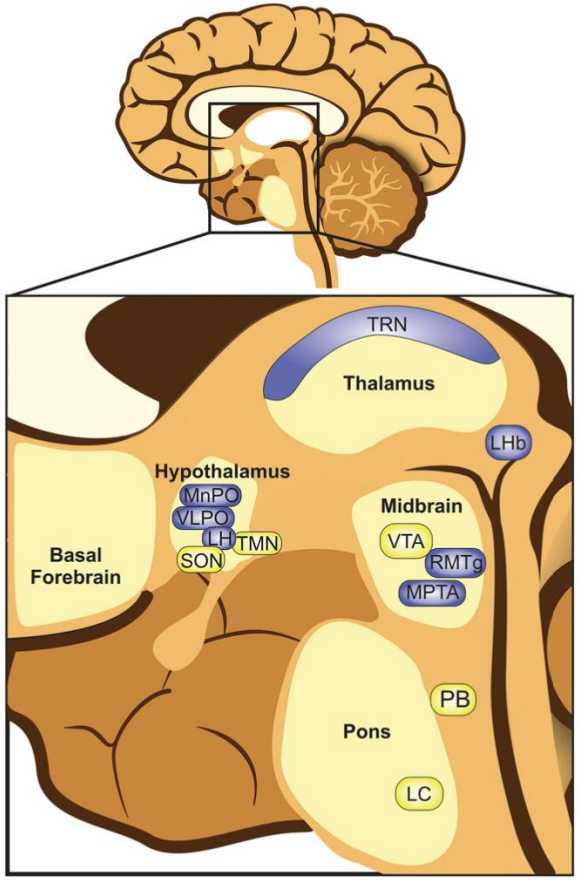


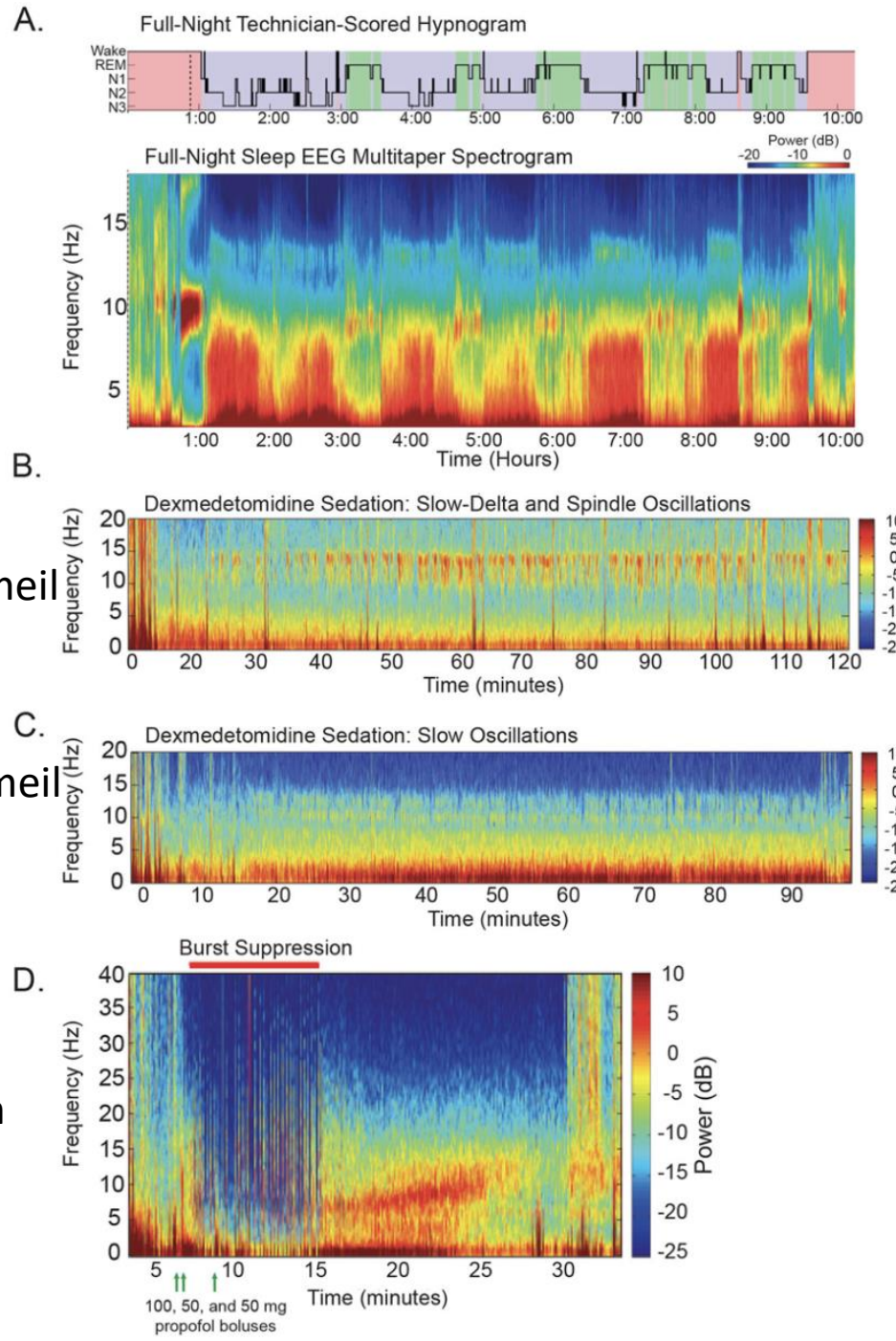
Figure 2.
Subcortical areas implicated in the regulation of sleep and anesthesia-induced loss of consciousness. Subcortical areas are shown in the magnified inset of a human brain. Loss of consciousness generally involves silencing wake-active nuclei (yellow) and stimulating sleep-active nuclei (blue). Hypothalamic nuclei: lateral hypothalamus (LH), ventrolateral preoptic area (VLPO), median preoptic area (MnPO), supraoptic nucleus (SON) and the tuberomammillary nucleus (TMN). Thalamic nuclei: thalamic reticular nucleus (TRN). Lateral habenula (LHb). Midbrain: ventral tegmental nucleus (VTA), rostromedial tegmental nucleus (RMTg), and mesopontine tegmental anesthesia area (MPTA). Pons: locus coeruleus (LC) and parabrachial nucleus (PB). Note: not all structures are located midline. For a

Sommeil naturel

Dexdor low: Stade 2 sommeil
Spindel

Dexdor high:Stade 3 sommeil
Slow delta oscillations

Propofol :Burst suppression



Sédation avec le dexdor®

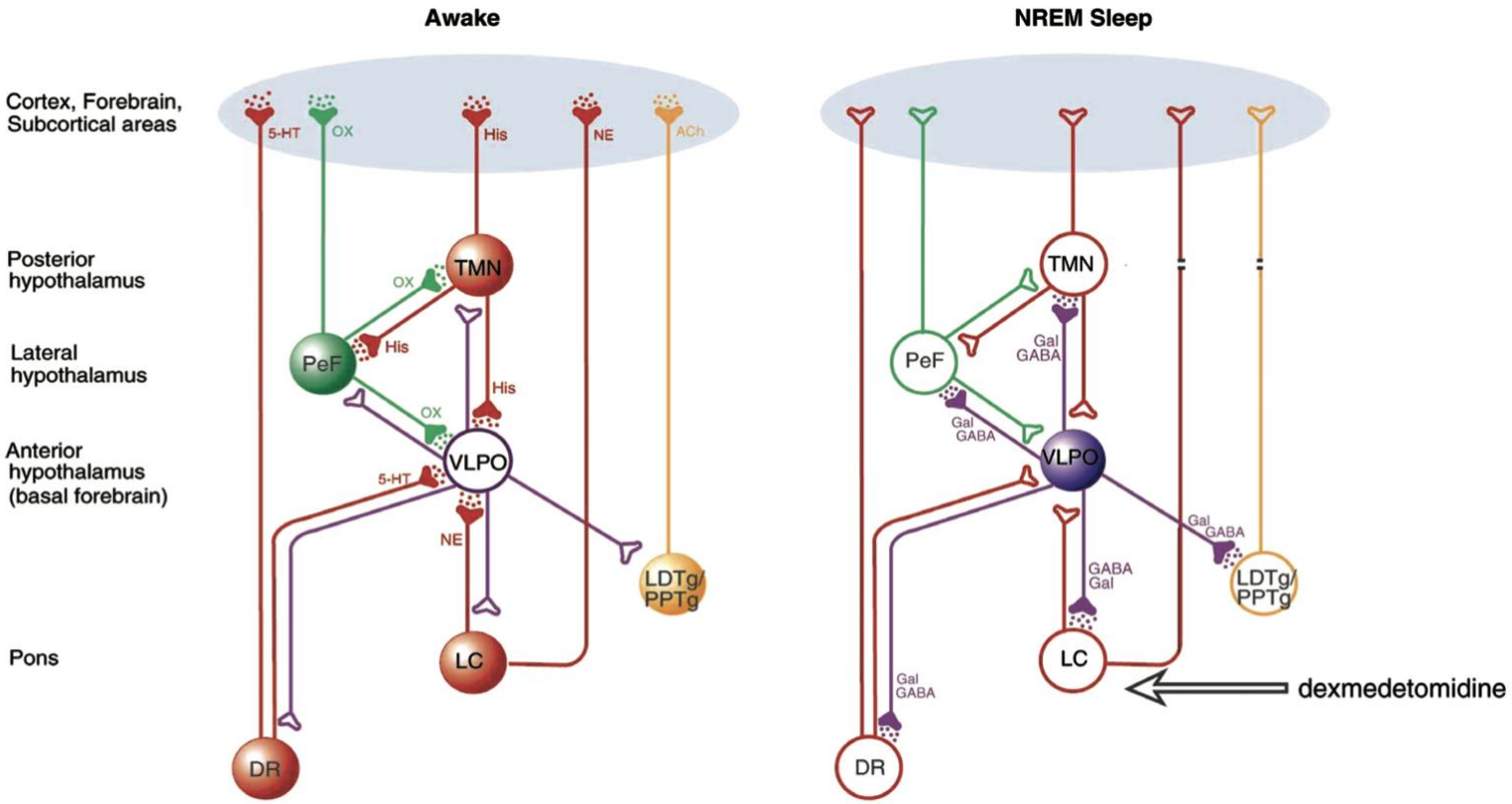


Figure 30.3. Neural substrates for sedative effect. During the hypnotic response induced by α_2-adrenoceptor agonist, a qualitatively similar pattern of neural activation is seen in rats as that observed during normal sleep; there is a decrease in the locus coeruleus (LC) and tuberomammillary nucleus (TMN) and an increase in the ventrolateral preoptic nucleus (VLPO). These changes are attenuated by a selective α_2-adrenoceptor antagonist and are not seen in mice lacking functional α_{2A}-adrenoceptors (which do not show a hypnotic response to α_2-adrenoceptor agonists). There is a hierarchical sequence of changes in which inhibition of the LC disinhibits the VLPO to release γ-aminobutyric acid (GABA) and galanin at the projections that terminate at the TMN. These inhibitory neurotransmitters inhibit firing of the TMN projections to the cortical and subcortical regions. ACh, acetylcholine; 5-HT, serotonin; His, histamine; LDTg, laterodorsal tegmental nucleus; NE, norepinephrine; NREM, non-rapid eye movement; OX, orexin; PPTg, pedunculopontine tegmental nucleus.

Randomized Controlled Trial > N Engl J Med. 2019 Jun 27;380(26):2506-2517.
doi: 10.1056/NEJMoa1904710. Epub 2019 May 19.

Early Sedation with Dexmedetomidine in Critically Ill Patients

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.

Methods: In an open-label, randomized trial, we enrolled critically ill adults who had been undergoing ventilation for less than 12 hours in the ICU and were expected to continue to receive ventilatory support for longer than the next calendar day to receive dexmedetomidine as the sole or primary sedative or to receive usual care (propofol, midazolam, or other sedatives). The target range of sedation-scores on the Richmond Agitation and Sedation Scale (which is scored from -5 [unresponsive] to +4 [combative]) was -2 to +1 (lightly sedated to restless). The primary outcome was the rate of death from any cause at 90 days.

Results: We enrolled 4000 patients at a median interval of 4.6 hours between eligibility and randomization. In a modified intention-to-treat analysis involving 3904 patients, the primary outcome event occurred in 566 of 1948 (29.1%) in the dexmedetomidine group and in 569 of 1956 (29.1%) in the usual-care group (adjusted risk difference, 0.0 percentage points; 95% confidence interval, -2.9 to 2.8). An ancillary finding was that to achieve the prescribed level of sedation, patients in the dexmedetomidine group received supplemental propofol (64% of patients), midazolam (3%), or both (7%) during the first 2 days after randomization; in the usual-care group, these drugs were administered as primary sedatives in 60%, 12%, and 20% of the patients, respectively. Bradycardia and hypotension were more common in the dexmedetomidine group.

Conclusions: Among patients undergoing mechanical ventilation in the ICU, those who received early dexmedetomidine for sedation had a rate of death at 90 days similar to that in the usual-care group and required supplemental sedatives to achieve the prescribed level of sedation. More adverse events were reported in the dexmedetomidine group than in the usual-care group. (Funded by the National Health and Medical Research Council of Australia and others; SPICE III ClinicalTrials.gov number, NCT01728558.).

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PMCID: PMC7939103
PMID: 33686482

Early sedation with dexmedetomidine in ventilated critically ill patients and heterogeneity of treatment effect in the SPICE III randomised controlled trial

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The early use of dexmedetomidine for sedation of ventilated critically ill patients who are older than 65 years, and in those with an operative diagnosis, across broad range of age categories, has a high probability of reduced mortality. Conversely, younger patients with a non-operative diagnosis have a high probability of increased mortality. Thus, the early use of dexmedetomidine in this group of patients, outside controlled research, is not advised.

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