Traitements adjuvants en douleur chronique

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23 avril 2026

Plan

1) Agents topiques
2) Kétamine en perfusion IV, PO ou IN
3) Lidocaïne en perfusion IV
4) Agonistes α-2 adrénergiques

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Agents topiques

Agents topiques

- Besoin grandissant de mieux **cibler la zone douloureuse**, surtout en présence d'une douleur neuropathique chronique périphérique

- **Soucis multiples et justifiés** concernant
  - Mécanisme de **sensibilisation périphérique**
  - Profil d'**innocuité: action directe et locale**
  - **Préférence** clinique: **facilité** d'usage, compliance
  - **Absorption systémique**
  - **Interactions médicamenteuses**

Casale R et al. Curr Pain Headache Rep 2017; 21(15): 1-9

Agents topiques en douleur neuropathique localisée

- Douleur neuropathique est directement liée à une lésion ou à un dysfonctionnement du SNC ou périphérique

- En général, signes et symptômes peuvent varier selon la présence et la localisation d'une atteinte périphérique

- Douleur neuropathique localisée («Localized Neuropathic Pain») → raisonnement clinique approprié pour usage des agents topiques

Casale R et al. Curr Pain Headache Rep 2017; 21(15): 1-9

Agents topiques en douleur neuropathique localisée

Curr Pain Headache Rep (2017) 21: 15
DOI 10.1007/s11916-017-0615-y

NEUROPATHIC PAIN (E EISENBERG, SECTION EDITOR)

Topical Treatments for Localized Neuropathic Pain

Roberto Casale[1] · Z. Symeonidou[1,2] · M. Bartolo[3]

«**Douleur SUPERFICIELLE consistante et circonscrite** dans une **zone précise** de douleur maximale, associée **avec des signes négatifs ou positifs** et/ou **symptômes spontanés caractéristiques de douleur neuropathique**»

Anh Nguyen, 2026 *Extrait de Casale R et al. Curr Pain Headache Rep 2017; 21(15): 1-9*

Agents topiques en douleur neuropathique localisée

Curr Pain Headache Rep (2017) 21: 15
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NEUROPATHIC PAIN (E EISENBERG, SECTION EDITOR)

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Roberto Casale[1] · Z. Symeonidou[1,2] · M. Bartolo[3]

Niveau d'évidence

- Haut (grade 1)
- Moyen (grades 2 et 3)
- Bas (grades 4 et 5)

Anh Nguyen, 2026 *Extrait de Casale R et al. Curr Pain Headache Rep 2017; 21(15): 1-9*

Agents topiques en douleur neuropathique localisée

- **Analyse systématique** des agents topiques séparément selon plusieurs aspects pertinents
  - **Efficacité**
  - **Mécanisme d'action individuel**
  - **Pathologies étudiées**
  - **Qualité des études**

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Casale R et al. Curr Pain Headache Rep 2017; 21(15): 1-9

Agents topiques en douleur neuropathique localisée

Table 1 Topical agents for the treatment of LNP

Topical agent (active compound content)	Mechanism of action	Site of action	Pathology	Efficacy, level of evidence (references)
Lidocaine 5%	- Anaesthetic features: Nav channels blockade (especially 1.7 and 1.8) - Non-anaesthetic features: TRPA1 blockade	Aδ and C fibres	PHN; DPN Post-traumatic NP; cervical RP NOP	E, HLE [24, 26–30] E, MLE [33, 34] E, LLE [31, 32]
Ketamine: - 0.5–5% - 0.5% - 0.093–9.33 mg/kg - 10% - 10–50 mg/ml; 0.25–1.5%	NMDA blockade with consequent reduction of glutamate production	Aδ and C fibres	PHN; DPN; post-traumatic NP PHN CRPS, PHN and RP CRPS CRPS	NE, MLE [48–51] E, MLE [52] E, LLE [53] E, MLE [54] E, LLE [55, 56]
Baclofen 5%	GABAb receptor agonist	C fibres	NP related to: acromegaly; RP	E, LLE [62•, 63•]
Capsaicin 8%	TRPV1 receptor agonist with reversible superficial degeneration	Aδ and C fibres	PHN; HIV-DSP Cervical RP; lumbar RP DPN	E, HLE [69] E, MLE [70] E, H&MLE [72, 73]

Extrait de Kocok-Kepska M et al. Pharmaceutics 2021; 13(450): 1-37

Agents topiques en douleur neuropathique localisée

Diclofenac 1.5%	- Topical inflammation - Topical antinociception: TRPV1, TRPA1	- Superficial tissues - Aδ and C fibres	PHN; CRPS	E, MLE [81]
Salicylates	Topical inflammation	Superficial tissues	AHN and PHN	E, MLE [83•, 84•]
Antidepressants: • Amitriptyline - 1–5% - 5–10% • Doxepin 3.3%	Blockade of Na^+, K^+, Ca^{2+} channels, muscarinic, cholinergic, nicotinic, H^+, α2, adenosine, NMDA receptors	Aδ and C fibres	PHN; DPN; post-traumatic NP; peripheral neuropathy CIAP; CRPS; post-traumatic NP Chronic NP; CRPS	NE, MLE [50, 51, 93] E, LLE [94–96] E, M&LLE [98, 99]
Clonidine 0.1%	- α2 receptor agonist - I2 imidazoline receptor agonist	Aδ and C fibres	DPN	E, MLE [105–107]
Ambroxol 20%	Na_V channels blockade (especially 1.8)	C fibres	LNP	E, LLE [116•]

E effective, *NE* non-effective, *HLE* high level of evidence, *MLE* medium level of evidence, *LLE* low level of evidence, *PHN* post-herpetic neuralgia, *DPN* diabetic peripheral neuropathy, *NP* neuropathic pain, *RP* radiculopathy, *NOP* neuropathic orofacial pain, *CRPS* complex regional pain syndrome, *HIV-DSP* HIV distal sensory polyneuropathy, *AHN* acute herpetic neuralgia, *CIAP* chronic idiopathic axonal polyneuropathy, *LNP* localized neuropathic pain

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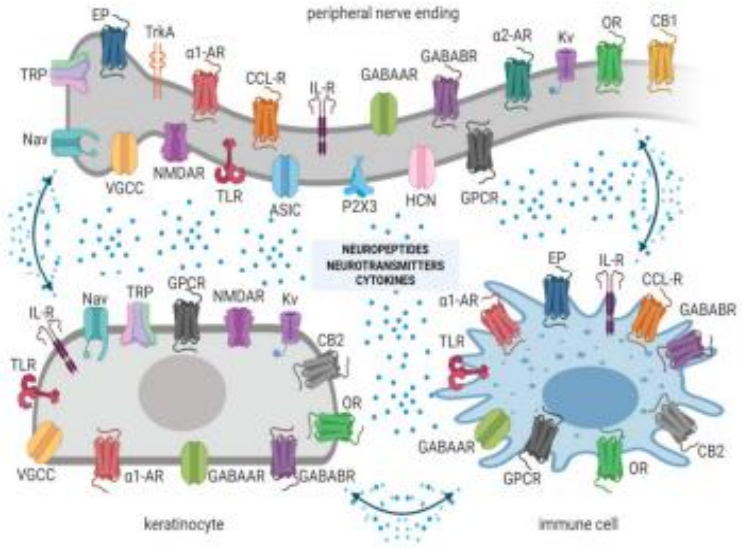
Extrait de Kocok-Kepska M et al. Pharmaceutics 2021; 13(450): 1-37

Agents topiques
Mécanismes d'action potentiels



Interactions complexes entre neurones périphériques avec cellules immunocompétentes et kératinocytes via neuropeptides, neurotransmetteurs, cytokines, divers canaux et récepteurs

Figure 1. Peripheral nerve endings, keratinocytes, and immune cells express ion channels and receptors and release numerous signaling molecules to create a complex interaction, involved in physiological nociception and neuropathic pain (NP) generation. Abbreviations: Nav—voltage-gated sodium channels, TRP—transient receptor potential channels, VGCCs—voltage-gated calcium channels, NMDAR—N-methyl-D-aspartate receptors, ASIC—acid-sensing ion channels, TLR—Toll-like receptors, α1-AR—α1 adreno receptors, α2-AR—α2 adreno receptors, EP—prostaglandin E2 receptors, GABAAR—gamma-aminobutyric acid receptors A, GABABR—gamma-aminobutyric acid receptors B, Kv—voltage-gated potassium channels, OR—opioid receptors, CB1, CB2—cannabinoid receptors type 1 or 2, CCL-R—chemokine receptors, IL-R—interleukin receptors, TrkA—tropomyosin receptor kinase A, HCN—hyperpolarization-activated cyclic nucleotide-gated channels, P2X3—P2X purinoceptors 3, GPCR—G protein-coupled receptors, TLR—Toll-like receptors. Created with BioRender.com.

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Extrait de Kocok-Kepska M et al. Pharmaceutics 2021; 13(450): 1-37

Agents topiques en douleur neuropathique loicalisée

- **Molécules plus petites que 500 daltons peuvent traverser facilement la peau**

- Presque toutes les molécules actives sont plus petites que 500 daltons → **application topique** permet diffusion à travers la peau et influence potentielle de l'épiderme (nocicepteurs, kératinocytes…)

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Agents topiques
Mécanismes d'action potentiels

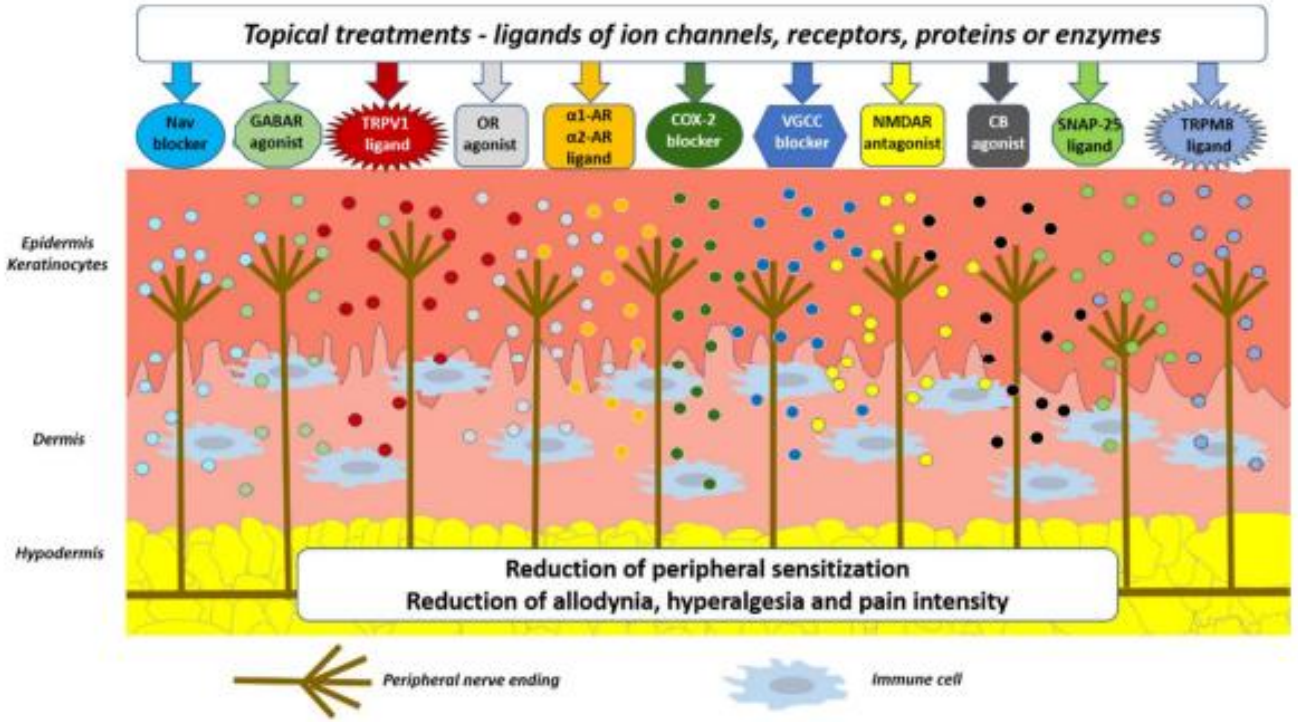

Figure 2. Topical treatments utilized in clinical practice and their molecular/cellular mechanisms in patients suffering from localized NP (LNP). Active molecules from topically applied drug formulations modulate the corresponding ion channels, receptors, enzymes, or proteins on neuronal and non-neuronal cells. Abbreviations: Nav—voltage-gated sodium channels, TRPV1—transient receptor potential vanilloid 1, VGCCs—voltage-gated calcium channels, NMDAR—N-methyl-D-aspartate receptors, α1-AR—α1 adreno receptors, α2-AR—α2 adreno receptors, GABAR—gamma-aminobutyric acid receptors, CB—cannabinoid receptors, COX-2—cyclooxygenase 2, SNAP-25—synaptosome associated protein 25, OR—opioid receptors, TRPM8—transient receptor potential melastatin 8.

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Extrait de Kocok-Kepska M et al. Pharmaceutics 2021; 13(450): 1-37

Agents topiques en douleur neuropathique loicalisée

- **Actions potentielles** sur plusieurs canaux, récepteurs, protéines ou enzymes exprimés **a/n des cellules neuronales et non-neuronales**

- **Interruption du processus d'intensification et de stimulation mutuelle en boucle** → ↓ **sensibilisation périphérique** → ↓ **douleur neuropathique** (allodynie, hyperalgésie) chez patients ayant douleur neuropathique localisée

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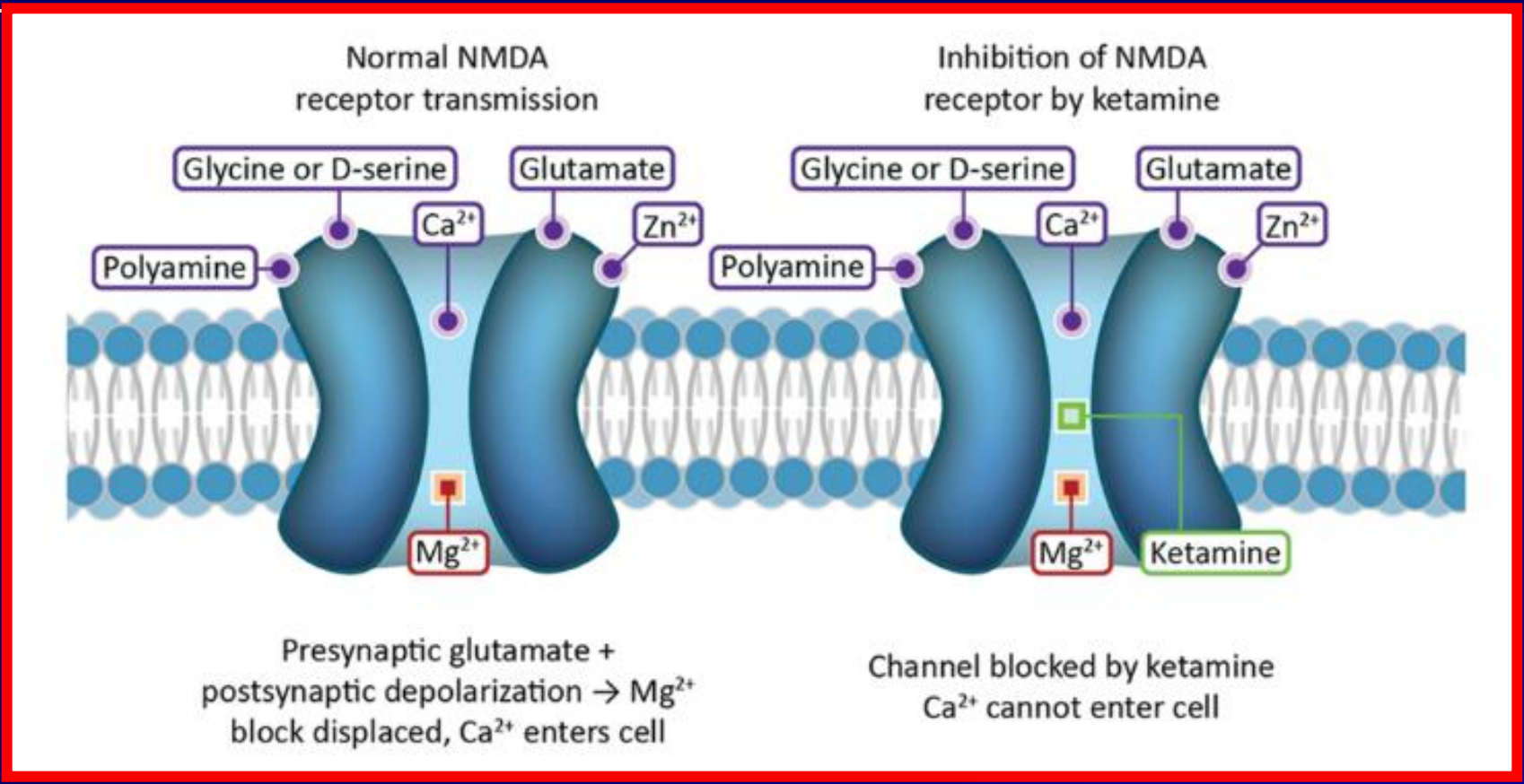
Kocok-Kepska M et al. Pharmaceutics 2021; 13(450): 1-37

Kétamine

Kétamine - Mécanisme d'action



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Kétamine - Antagoniste NMDA
Analgésie multimodale

- **Liaison de la kétamine au récepteur NMDA**
  - → **Blocage** non compétitif du **canal ionique central**
  - → **Inhibition** de **l'entrée intracellulaire du calcium**
  - → **Inhibition** de la **dépolarisation du neurone post-synaptique**
  - → **Arrêt de l'activité neuronale excitatrice**

- Formulation racémique, très liposoluble
- Demi-vie d'élimination courte (2-3h)

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Marchant et al. Rev Med Liège 2010; 65(1): 29-34

Kétamine - Particularités

Ketamine - More mechanisms of action than just NMDA blockade

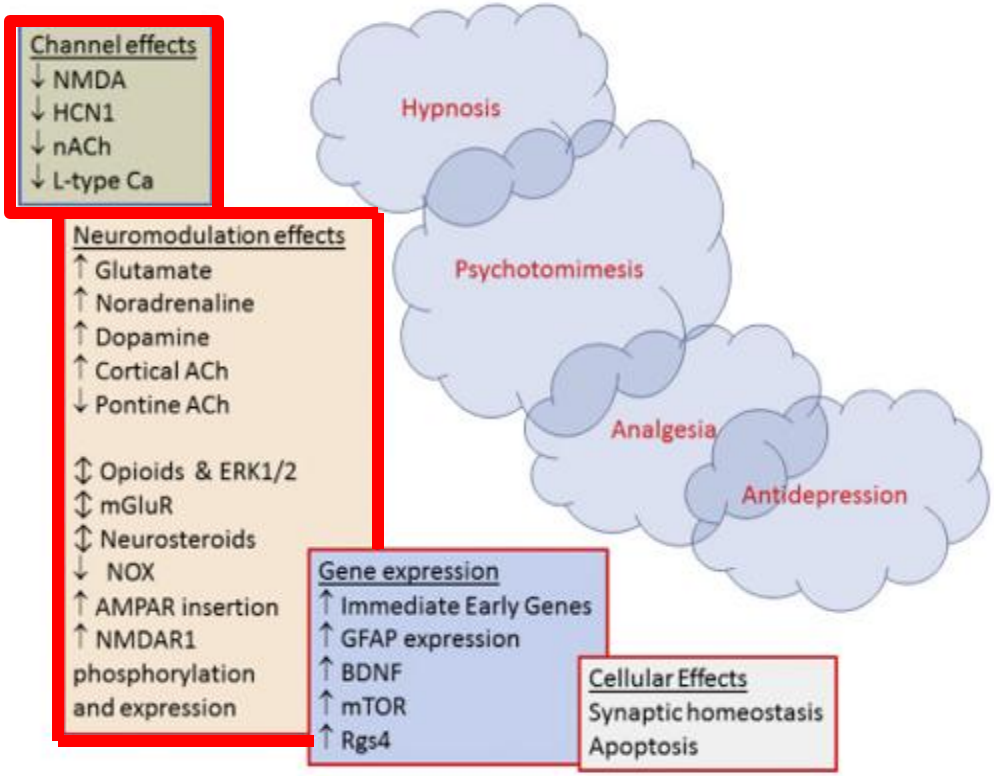

Fig. 1. Summary diagram of the neuropharmacological actions of ketamine, and the resultant clinical effects. The rapid effects and actions are represented at the top left, and the more delayed and prolonged effects and actions represented towards the bottom ri...

Anh Nguyen, 2026 *Extrait de Sleigh J al. Trends in Anesthesia and Critical Care 2014; 4: 76-81*

Kétamine
Propriétés pharmacocinétiques

Table 2. Pharmacokinetic of ketamine hydrochloride[1,3,5,10,11,13]	
Peak effect	10-15 min (intramuscular)
	15-30 min (oral)
	15-20 min (intranasal)
Bioavailability	Oral (16-20 percent)
	Intramuscular (90-93 percent)
	Intranasal (25-50 percent)
Volume of distribution	3 L/kg
Model of metabolism	3-Compartment model
α-Elimination phase	4-5 min
β-Elimination half-life	2-3 h
Plasma clearance	1,000 mL/min
Metabolism	80 percent hepatic
Cytochrome P450 system	CYP2B6, 2C9, and 3A4
Metabolites	Norketamine (N-demethylation)
Pharmacokinetic in pediatrics	Faster peak effect after intramuscular administration
	Higher norketamine concentration

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Extrait de Tawfic QA. J Opioid Manage 2013; 9(5): 379-388

Kétamine - Antagoniste NMDA

- Anesthésique intraveineux doté de
  - → Propriétés analgésiques puissantes et
  - → Profil hémodynamique particulier

- Usage souvent limité par **effets secondaires** parfois très **déplaisants**, regroupés en **3 groupes**
  - → **Effets psychodysleptiques** (à l'émergence)
  - → Pression intracranienne
  - → Hypersympathicotonie

Marchant et al. Rev Med Liège 2010; 65(1): 29-34

Kétamine - Antagoniste NMDA
Effets secondaires

Effets psychodysleptiques de la kétamine

→ Impression de flottement

→ Décorporation

→ Rêves éveillés

→ Hallucinations visuelles, auditives

→ Confusion

→ Délires

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Marchant et al. Rev Med Liège 2010; 65(1): 29-34

Kétamine - Antagoniste NMDA
Effets psychodysleptiques

Facteurs de risque

→ Âge (moins fréquent chez enfants)

→ Sexe (plus fréquent **chez hommes**)

→ **Troubles psychiatriques préexistants**

→ **Éthylisme chronique**

→ **Dose élevée** ou **bolus rapides**

Midazolam peut permettre de prévenir la survenue de ces manifestations

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Marchant et al. Rev Med Liège 2010; 65(1): 29-34

Kétamine en douleur chronique
Recommandations récentes

CHRONIC AND INTERVENTIONAL PAIN

SPECIAL ARTICLE

OPEN

Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Chronic Pain From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists

Steven P. Cohen, MD,† Anuj Bhatia, MBBS, MD,‡ Asokumar Buvanendran, MD,§ Eric S. Schwenk, MD,|| Ajay D. Wasan, MD, MSc,** Robert W. Hurley, MD, PhD,†† Eugene R. Viscusi, MD,|| Samer Narouze, MD, PhD,‡‡ Fred N. Davis, MD,§§|||| Elspeth C. Ritchie, MD, MPH,***††† Timothy R. Lubenow, MD,§ and William M. Hooten, MD‡‡‡*

Extrait de Cohen SP et al. Reg Anesth Pain Med 2018; 43: 521-546

Kétamine en douleur chronique
Recommandations récentes

TABLE 1. Pharmacokinetics of Ketamine for Different Routes of Administration[38,91]

Route of Administration	Typical Dosing	Bioavailability, %	Time of Onset	Duration of Action After Dosing
Intravenous	1–4.5 mg/kg for general anesthesia induction; 1–6 mg/kg per hour for anesthesia maintenance; 0.5–2 mg/kg for 1-d outpatient or 3- to 5-d inpatient awake ketamine infusions in chronic pain (higher dosages titrated to effect from lower doses); 0.2–0.75 mg/kg for procedural analgesia, can be repeated; 0.1 mg/kg for IV infusion test; 5- to 35-mg/h continuous infusion for acute traumatic or postoperative pain, 1–7 mg/demand dose mixed with opioids in patient-controlled analgesia	N/A	30 s	5–10 min for bolus doses
Intramuscular	2–4 times IV dosing; 5–10 mg/ kg for surgical anesthesia; 0.4–2 mg/kg for procedural analgesia; bolus and treatment dosing 0.10–0.5 mg/kg for chronic pain	75–95	2–5 min	30–75 min
Intranasal	0.2–1 mg/kg for chronic pain and sedation; 3–6 mg/kg for procedural analgesia and anesthetic premedication	25–50	5–10 min	45–120 min
Subcutaneous	0.1–1.2 mg/kg per hour for chronic pain; bolus and treatment dosing 0.10–0.6 mg/kg	75–95	10–30 min	45–120 min
Oral	0.3–1.25 mg/kg for chronic pain; up to 3 mg/kg for procedural analgesia and anesthetic premedication	10–20	5–20 min	2–4 h
Rectal	5–10 mg/kg for anesthesia premedication and procedural analgesia	25–30	5–15 min	2–3 h
Topical	1%–10% cream for chronic pain	<5	<2 d	NA

Kétamine IV en douleur chronique:
0,5-2 mg/kg/hre pour admisson d'un jour ou si patient hospitalisé pendant 3 à 5 jours
Dosage plus haut peut être titré

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Extrait de Cohen SP et al. Reg Anesth Pain Med 2018; 43: 521-546

Kétamine IV en douleur chronique
Recommandations récentes

TABLE 2. Randomized Placebo-Controlled Trials Evaluating Intravenous Ketamine for Chronic Pain With a Minimum of 48 Hours of Follow-Up

First Author, Year	Patients	Ketamine Regimen	Follow-Up	Results	Comments
Amr,[155] 2010	40 patients with neuropathic pain after spinal cord injury	80 mg over 5 h per day × 1 wk	4 wk	Ketamine better than placebo for 2 wk	All patients also received gabapentin
Eichenberger,[117] 2008	20 patients with PLP	0.4 mg/kg over 1 h with 48 h minimum interval between infusions	48 h	Ketamine better than placebo and calcitonin. No difference between ketamine alone and combination for worst pain reduction, but combination superior for mean pain reduction. Mixed results for QST	Crossover study comparing ketamine to calcitonin to combination of both to placebo
Schwartzman,[123] 2009	19 patients with CRPS types 1 and 2	Up to 100 mg over 4 h for 10 consecutive weekdays	9–12 wk	Ketamine better than placebo for pain, but no improvement in QST and no correlation between response and serum levels	Study halted at midpoint because of lack of improvement in ketamine group
Sigtermans,[161] 2009	60 patients with CRPS type 1	0.43 mg/kg per hour continuously over 4.2 d	12 wk	Ketamine better than placebo, but results were not statistically significant beyond 11 wk	Blinding ineffective
Noppers,[160] 2011	24 patients with fibromyalgia	0.5 mg/kg over 30 min	8 wk	Ketamine better than placebo only up to 3 h	Blinding ineffective
Mitchell,[162] 2002	35 patients with ischemic limb pain	0.6 mg/kg over 4 h	2–9 d (mean, 5 d)	Ketamine better than placebo	All patients also received opioids
Salas,[164] 2012	20 patients with cancer pain	0.5 mg/kg per day increased to 1 mg/kg per day × 2 d for persistent pain	48 h	No difference between treatment groups	All patients received morphine

QST indicates quantitative sensory testing.

- **Grande variété de pathologies** (lésion de moëlle épinière, douleur de membre fantôme, CRPS, fibromyalgie, douleur ischémique, douleur cancéreuse), de méthodologies, **de posologies** (dose, durée d'administration), **de F/U**
- **Petit nombre d'échantillon**

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Cohen SP et al. Reg Anesth Pain Med 2018; 43: 521-546

Kétamine IV en douleur chronique
Recommandations récentes

En résumé,

- **Douleur post-lésion médullaire**: **évidences faibles** pour supporter soulagement **à court terme** (**recommandation de grade C**)

- **CRPS**: **évidences modérées** pour supporter soulagement **ad 12 semaines** (**recommandation de grade B**)

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Kétamine IV en douleur chronique
Recommandations récentes

En résumé,

- Douleur neuropathique mixte, douleur de membre fantôme, NPH, fibromyalgie, douleur cancéreuse, douleur ischémique, migraine, lombalgie chronique: **peu ou pas d'évidence** (**recommandation de grade D**)

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Cohen SP et al. Reg Anesth Pain Med 2018; 43: 521-546

Kétamine en douleur chronique
Contre-indications/Précautions

TABLE 5. Contraindications to and Precautions for Use of Subanesthetic Doses of Ketamine for Chronic Pain

Category	Contraindication/Precaution
Cardiovascular	• Unstable angina • Poorly controlled hypertension • High-risk coronary vascular disease
Neurological and ophthalmic	• Elevated intracranial pressure, including secondary traumatic brain injury or tumor • Elevated intraocular pressure, acute globe injury, or glaucoma
Endocrinological (due to possible potentiation of sympathomimetic effects)	• Hyperthyroidism • Pheochromocytoma
Metabolic	• Severe liver disease
Gastrointestinal	• Full stomach aspiration risk
Pregnancy	• Lack of data on safety
Psychiatric	• Intoxication with alcohol or other substances • Active substance abuse • Delirium • Psychosis • Refusal or inability to consent

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Extrait de Cohen SP et al. Reg Anesth Pain Med 2018; 43: 521-546

Kétamine IV en douleur chronique
Recommandations récentes

TABLE 6. Summary of ASRA/AAPM/ASA Recommendations for Ketamine Infusions for Chronic Pain

Recommendation Category	Recommendation	Level of Evidence*
Indications	(1) For spinal cord injury pain, there is weak evidence to support short-term improvement	(1) Grade C, low certainty
	(2) In CRPS, there is moderate evidence to support improvement for up to 12 wk	(2) Grade B, low to moderate certainty
	(3) For other pain conditions such as mixed neuropathic pain, fibromyalgia, cancer pain, ischemic pain, headache, and spinal pain, there is weak or no evidence for immediate improvement	(3) Grade D, low certainty
Dosing range and dose response	(1) Bolus: up to 0.35 mg/kg	(1) Grade C, low certainty
	(2) Infusion: 0.5 to 2 mg/kg per hour, although dosages up to 7 mg/kg per hour have been successfully used in refractory cases in ICU settings	(2) Grade C, low certainty
	(3) There is evidence for a dose-response relationship, with higher dosages providing more benefit. Total dosages be at least 80 mg infused over a period of >2 h	(3) Grade C, low certainty
Relative contraindications	(1) Poorly controlled cardiovascular disease, pregnancy, active psychosis	(1) Grade B, low certainty
	(2) Severe hepatic disease (avoid), moderate hepatic disease (caution)	(2) Grade C, low certainty
	(3) Elevated intracranial pressure, elevated intraocular pressure	(3) Grade C, low certainty
	(4) Active substance abuse	(4) Grade C, low certainty
Role of oral NMDA receptor antagonist as follow-on treatment	(1) Oral ketamine or dextromethorphan, and intransal ketamine can be tried in lieu of serial infusions in responders	(1) Grade B, low certainty for oral preparations, moderate certainty for intranasal ketamine

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Extrait de Cohen SP et al. Reg Anesth Pain Med 2018; 43: 521-546

Kétamine IV en douleur chronique
Recommandations récentes

Preinfusion tests	(1) No testing is necessary for healthy individuals	(1) Grade C, low certainty
	(2) In individuals with suspected or at high risk of cardiovascular disease, baseline ECG testing should be used to rule out poorly controlled ischemic heart disease.	(2) Grade C, low certainty
	(3) In individuals with baseline liver dysfunction or at risk of liver toxicity (eg, alcohol abusers, people with chronic hepatitis), and those who are expected to receive high doses of ketamine at frequent intervals, baseline and postinfusion liver function tests should be considered on a case-by-case basis	(3) Grade C, low certainty
Positive response	(1) A positive response should include objective measures of benefit in addition to satisfaction such as ≥30% decrease in pain score or comparable validated measures for different conditions (eg, Oswestry Disability Index for back pain)	(1) Grade C , low-to-moderate certainty
Personnel and monitoring	(1) Supervising clinician: a physician experienced with ketamine (anesthesiologist, critical care physician, pain physician) who is ACLS certified and trained in administering moderate sedation	(1) Grade A, low certainty
	(2) Administering clinician: registered nurse or physician assistant who has completed formal training in safe administration of moderate sedation	(2) Grade A, low certainty
	(3) Setting: at dosages exceeding 1 mg/kg per hour, a monitored setting containing resuscitative equipment and immediate access to rescue medications and personnel who can treat emergencies should be used, although this dose may vary based on individual characteristics	(3) Grade A, low certainty

*Evidence was evaluated according to the US Preventive Services Task Force grading of evidence, which defined levels of evidence based on magnitude and certainty of benefit.[5]

ACLS indicates Advanced Cardiac Life Support; ICU, intensive care unit.

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Extrait de Cohen SP et al. Reg Anesth Pain Med 2018; 43: 521-546

Kétamine IV en douleur chronique
Recommandations récentes

Considérant les évidences cliniques dans ce contexte, il serait raisonnable de

- **Débuter** la perfusion IV de kétamine à la dose maximale **de 80 mg sur une durée de ≥2h**
- Ajuster cliniquement selon réponse et tolérance
- **Usage potentiel de kétamine PO/IN** comme thérapie de suivi post-perfusion de kétamine. Soucis sérieux concernant faible biodisponibilité de la voie PO, potentiel d'abus de la voie IN, profil d'innocuité surtout en terme d'hallucinations, de jugement, de perception et d'habilités psychomotrices…

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Cohen SP et al. Reg Anesth Pain Med 2018; 43: 521-546

Kétamine IV en douleur chronique
Recommandations récentes

- **Pas besoin de test de laboratoire en particulier chez patients en bonne santé**
- **Surveillance nécessaire si bolus ≥ 0,35 mg/kg et/ou perfusion ≥ 1mg/kg**
- Bénéfices justifiant son utilisation devrait être ≥ 3 semaines pour perfusion unique et ≥ 6 semaines pour perfusion sériée
- **Décision selon réponse du patient** (maximum de **6-12 traitements par année**)

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Cohen SP et al. Reg Anesth Pain Med 2018; 43: 521-546

Kétamine IV ou PO en douleur neuropathique

REVIEW ARTICLE

A Systematic Review of NMDA Receptor Antagonists for Treatment of Neuropathic Pain in Clinical Practice

Rohit Aiyer, MD, Neel Mehta, MD,† Semih Gungor, MD,‡ and Amitabh Gulati, MD§*

- Kétamine IV: 13 études
- **Kétamine PO**: **3 études**
- Kétamine topique: 5 études

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Extrait de Aiyer R et al. Clin J Pain 2018; 34(5): 450-467

Kétamine PO en douleur neuropathique

Rigo et al. (2017) (n = 42)	**Kétamine 30 mg PO TID** **Bénéfice** observé **avec kétamine** (Comparaison avec méthadone à 30 mg PO TID)
Furuhashi-Yonaha et al. (2002) (n = 8)	**Kétamine PO 0,5 mg/kg QID** vs placebo (total de 7 jours) **Soulagement pour 6-8h**
Haines et Gaines (1999) (n = 21)	**Kétamine 20 mg PO die, ↑ tous les jours selon réponse et tolérance ad** dose de **100 mg** (effet chez 3 pts)

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Aiyer R et al. Clin J Pain 2018; 34(5): 450-467

Kétamine IN
en douleur cancéreuse

Intranasal Ketamine and Its Potential Role in Cancer-Related Pain

Ad 1mg/kg au total
Viser ≤ 0,5 ml/narine

Vinita Singh,[1] Theresa W. Gillespie,[2] and Robert Donald Harvey[3,4*]
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Grande biodisponibilité de la voie IN pour **kétamine**

- Haute perméabilité
- Température uniforme
- Vascularisation étendue
- Pas de premier passage hépatique
- Grande surface d'absorption (nez, sinus, muqueuse)

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Extrait de Singh V et al. Pharmacotherapy 2018; 38(3): 390-401

Lidocaïne

Lidocaïne en perfusion IV
Mécanismes d'action

Mechanisms of Action of Intravenous Lidocaine Infusion

Effect	Mechanism of Action	Reference
Antinociceptive	Blockade of sodium gated channels	16, 17, 30, 47
	Blockade of presynaptic muscarinic and dopamine receptors	18, 19, 31, 32
	Blockade of potassium current	17
	Reduce excitability and conduction of unmyelinated C fibers	20
	Decreased excitability of the spinal dorsal horn	20, 34
	Modulation of NMDA-receptors	21, 35
	Increased in CSF acetylcholine aggravating the descending inhibitor pain pathways	31
	Inhibiting release of endogenous opioids	33
Anti-hyperalgesic	Inhibition of NMDA receptor	21
	Affecting mechanoinsensitive nociceptors	36, 37
Anti-inflammatory	Inhibits leukotriene B4	22
	Inhibiting release of superoxide anion	48, 49
	Blocking of interleukin 1	22–24
	Inhibiting histamine release	25
	Reduction of pro-inflammatory cytokines	38–41
	Inhibiting prostaglandin release	26–29, 45, 46
	Attenuating vascular inflammation	42
	Increase in cell mediated immunity	43, 44

Anh Nguyen, 2026 *Extrait de Chu R et al. Psychopharmacol Bulletin 2020; 50 (4, Suppl 1): 216-258*

Lidocaïne en perfusion IV

Lidocaine Infusion: A Promising Therapeutic Approach for Chronic Pain

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Abstract

Opioid abuse is a national epidemic in the United States, where it is estimated that a prescription drug overdose death occurs every 19 minutes. While opioids are highly effective in acute and subacute pain control, their use for treatment of chronic pain is controversial. Chronic opioids use is associated with tolerance, dependency, hyperalgesia. Although there are new strategies and practice guidelines to reduce opioid dependence and opioid prescription drug overdose, there has been little focus on development of opioid-sparing therapeutic approaches. Lidocaine infusion has been shown to be successful in controlling pain where other agents have failed. The opioid sparing properties of lidocaine infusion added to its analgesic and antihyperalgesic properties make lidocaine infusion a viable option for pain control in opioid dependent patients. In this review, we provide an overview of the opioid abuse epidemic, and we outline current evidence supporting the potential use of lidocaine infusion as an adjuvant therapeutic approach for management of chronic pain.

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Extrait de Kandil E et al. J Anesth Clin Res 2017; 8(1): 1-29

Lidocaïne IV et douleur neuropathique réfractaire Mécanismes potentiels

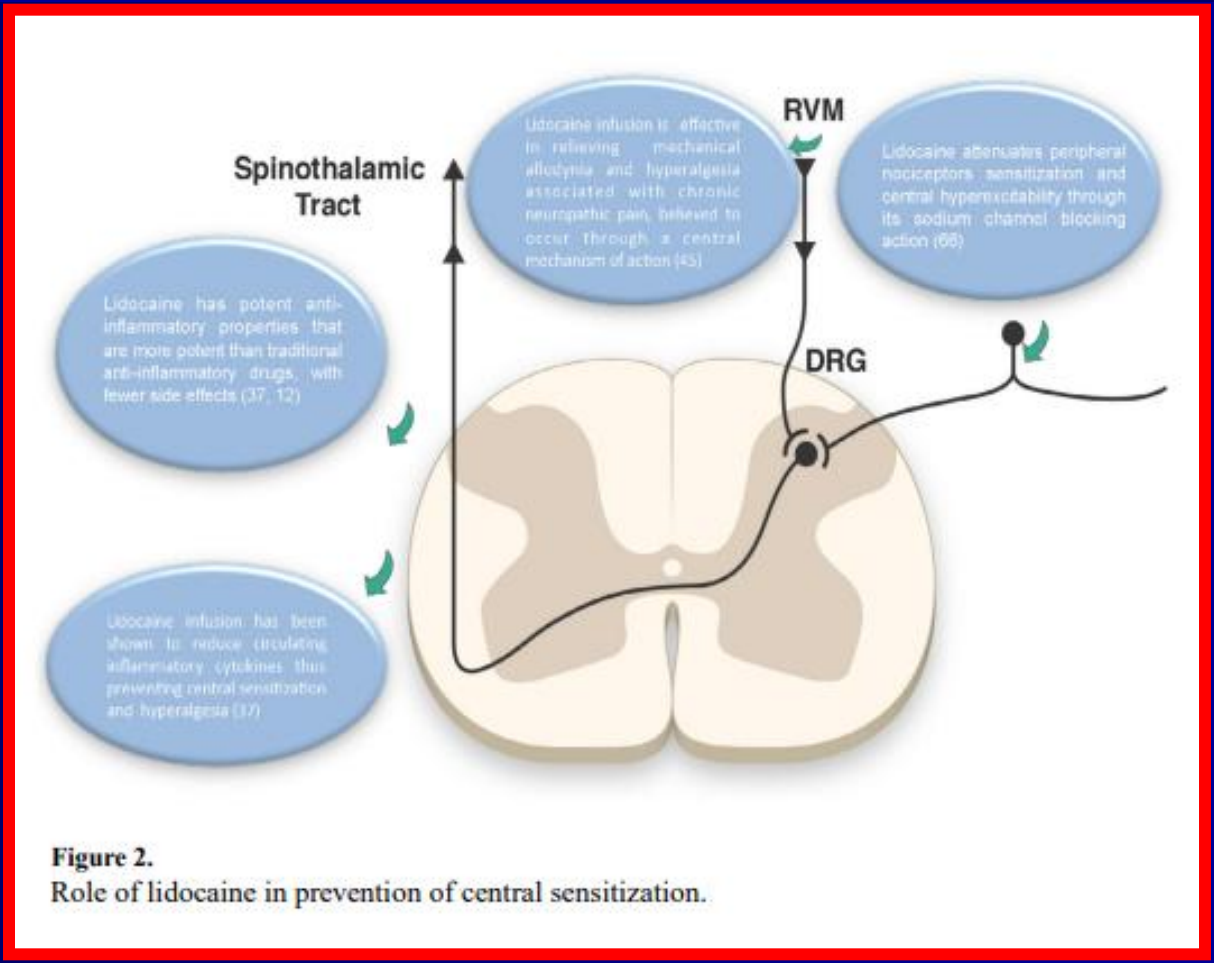

Figure 2.
Role of lidocaine in prevention of central sensitization.

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Lidocaïne IV et douleur neuropathique réfractaire Mécanismes potentiels

Effet anti-nociceptif

Blocage des canaux sodiques mène à

- ↓ de la sensibilisation des nocicepteurs périphériques
- ↓ de l'hyperexcitabilité centrale

Effet anti-inflammatoire

Activité anti-inflammatoire considérée comme puissante

- ↓ **niveau des cytokines inflammatoires circulantes**

(Rôle crucial des cytokines inflammatoires reconnu dans processus d'hyperalgésie secondaire et de sensibilisation centrale)

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Lidocaïne IV et douleur neuropathique réfractaire Mécanismes potentiels

Effet anti-hyperalgésique

Via mécanisme central impliquant **antagonisme des récepteurs NMDA**

- ↓ allodynie mécanique
- ↓ hyperalgésie

Kandil E et al. J Anesth Clin Res 2017; 8(1): 1-29

Summary of randomized trials of lidocaine infusion for neuropathic pain.

Type of pain	Study	Condition treated	Method	Number of subjects	Intervention	Outcome	Conclusion	Adverse events
Central	Attal et al.	Neuropathic pain	Randomized double blind Crossover, 3-wk washout	16	IV Lidocaine, 5 $mg.kg^{-1}$, 30 min	Intensity of spontaneous ongoing pain	Lidocaine > Placebo Supraspinal mechanisms of lidocaine actions are demonstrated by its effectiveness in hemispheric lesions and central pain.	Lightheadedness (44%)
Central	Kvarnstrom,	Spinal Cord Injury with Pain Below Injury Level	Randomized, double-blind three treatment Crossover	10	IV lidocaine 2.5mg.kg^{-1}, 40 min Ketamine (0.4 mg/kg IV) vs. Lidocaine (2.5 mg/kg IV) vs. Placebo (NS) over 40 min	visual analogue scale (VAS). Sensory function, sensory tests and temperature thresholds.	Lidocaine = Placebo No significant difference in response between both groups in VAS spontaneous pain scores and evoked allodynia.	4/10 Drowsiness, perioral paresthesia 5 somnolence, 1 dizziness, 2 out of body sensation, change in hearing, 2 paresthesias.
Peripheral	Kvarnstrom	Long lasting, Posttraumatic, neuropathic pain	Randomized double blind, crossover	12	Ketamine (0.4 mg/kg IV) vs. Lidocaine (2.5 mg/kg) vs. placebo infused over 40 min	Visual analogue scale (VAS) Warm and cold perception as well as heat and cold pain thresholds Sensibility to touch was also tested	Lidocaine = Placebo No significant difference in VAS resting score between lidocaine and placebo; no significant difference in any evoked VAS scores	9 somnolence, 5 light-headedness,4 "out of body sensation", 3 nausea, 2 pruritus, 2 paresthesia.
Central	Finnerup	Spinal cord injury	Crossover Double-blind Placebo controlled	24	IV Lidocaine 5 $mg.kg^{-1}$ or placebo, 30 min	Visual Analog Scale and quantitative sensory testing.	Lidocaine > Placebo For pain at and below the level of injury irrespective of the presence or absence of evoked pain.	11 somnolence, 7 dizziness, 7 dysarthria, 7 lightheaded, 3 blurred visions.
Peripheral	Tremont-Lukats	Peripheral neuropathic pain	Parallel	32	1, 3, and 5 $mg.kg.hr^{-1}$, 6 h		Lidocaine > Placebo	Placebo: 6/7 lidocaine (all doses): 21/23.
Peripheral	Wallace	Complex regional pain syndrome (CRPS I and II) with a prominent allodynia	Crossover 1 week washout	16	IV lidocaine and diphenhydramine separated by 1 week by increases in plasma levels of lidocaine of 1, 2, and 3 $\mu g.ml^{-1}$.	Spontaneous and evoked pain scores, neurosensory testing within the painful area was measured.	Lidocaine caused a significant elevation of the hot pain thresholds in the painful area and decreased response to stroking and cool stimuli in the	Delirium, nausea

Type of pain	Study	Condition treated	Method	Number of subjects	Intervention	Outcome	Conclusion	Adverse events
							allodynic area. Significant decrease in pain scores to cool stimuli at all plasma levels and the spontaneous pain at the highest plasma level.	
Peripheral	Wu	Post-amputation pain: phantom limb or stump pain	Crossover, 24-h washout	32 11 cases Stump pain alone, 9 cases phantom pain alone, and 11 with both	IV Lidocaine 1 $mg.kg^{-1}$ bolus, followed a 4 $mg.kg^{-1}$ infusion vs. morphine 0.5 $mg.kg^{-1}$ bolus 0.02 $mg.kg^{-1}$ infusion vs. active placebo diphenhydramine, 10 mg bolus IV 40 mg infusion). All infusions lasted 40 min.	Phantom and stump pain ratings, sedation scores, and 0–100 visual analog scale (VAS).	Lidocaine > Placebo for stump but not phantom pain. Lidocaine = Morphine > Placebo in self-reported ratings of pain and satisfaction for stump pain.	No adverse events reported. 1/32 withdrawn because of no pain before treatment.
Peripheral	Attal	Pain-related to postherpetic neuralgia or traumatic nerve injury	Randomized controlled double-blind, Crossover	22	IV Lidocaine 5 mg.kg-1 30 min vs. placebo while 16 patients subsequently received mexiletine on an open basis titrated from 400 to 1,000 mg per day (mean 737 mg/day).	Spontaneous pain and Quantitative sensory testing. Change in mechanical dynamic allodynia and static (punctate) mechanical allodynia/ hyperalgesia, but not thermal allodynia and hyperalgesia.	Five of 22 patients were pain free with lidocaine, 11 of 22 had 50% reduction of spontaneous pain, and 12 of 22 had 33% reduction of spontaneous pain.	Somnolence, lightheadedness and perioral numbness, which were present in 16 of 22 patients.
Peripheral	Lemming	PNP Whiplash disorder	Crossover	33	IV Lidocaine 5 mg.kg-1 30 min Ketamine (0.3 mg/kg infused over 30 min) vs. Lidocaine vs. morphine vs. placebo (NS)		No significant difference in response between all treatment arms; all treatment arms did illicit partial response	No reported adverse events
Peripheral	Viola	Diabetic PNP Previous responders to lidocaine	Crossover Double-blind, Placebo controlled 4 week wash out	15	5 and 7.5 $mg.kg^{-1}$, 4 h Lidocaine (5	Pain perception with McGill	Lidocaine > Placebo Both doses of lidocaine decreased	1 patient reported lightheadedness with 7.5 mg/ml infusion

Type of pain	Study	Condition treated	Method	Number of subjects	Intervention	Outcome	Conclusion	Adverse events
					mg/ml IV) vs. Lidocaine (7.5 mg/ml IV) vs. placebo (NS), 5ml/kg over 4 h × 1 each four week washout.	Pain Questionnaire (MPQ), hours of sleep, fasting blood glucose, and use of other pain-relieving medication.	MPQ resting pain scores compared to placebo; effect lasted up to 28 days post-infusion.	
Peripheral	Gottrup	Nerve injury pain	Randomized Placebo-controlled Crossover	20	IV infusion of ketamine (0.24 mg.kg^{-1}), lidocaine (5 mg. kg^{-1}), or saline for 30 min.	Effects on spontaneous and mechanical evoked pain.	Lidocaine only reduced evoked pain to repetitive pinprick stimuli. Ketamine was superior to lidocaine in reducing spontaneous pain.	Sixteen patients (84%) experienced side effects from lidocaine, compared with 11% in the placebo group.
Peripheral	Gormsen	PNP chronic neuropathic pain (peripheral nerve injury)	Randomized double-blind, placebo-controlled, three-way crossover	13	IV lidocaine 5 mg/kg vs. NS1209 (AMPA Receptor antagonist 322 mg total) vs. placebo (NS) over 4 h	Spontaneous current pain and pain evoked by brush, pinprick, cold, and heat stimulation	No difference in any treatment arms of spontaneous current pain, both NS1209 and lidocaine exhibited significant effects on resting pain compared to placebo	Drowsiness, perioral paresthesia, headache, dizziness, fatigue, discomfort, dry mouth, nausea, muscle spasm.
Peripheral	Schafranski	PNP Fibromyalgia	Open	23	IV lidocaine 2–5 mg/kg 2 h. Five sequential intravenous 2% lidocaine infusions with rising dosages (2–5 mg/kg, days 1–5).	Fibromyalgia Impact Questionnaire (FIQ), Health Assessment Questionnaire, and a visual analog scale (VAS) for pain were applied before the first lidocaine infusion, immediately after the fifth infusion, and 30 days after the fifth infusion.	A significant improvement was observed in the FIQ scores after the fifth infusion and maintained after 30 days.	No adverse events reported.
Peripheral	Park	Failed back surgery syndrome (FBSS)	Randomized controlled double-blind Crossover, 2 weeks wash out	18	Patients received each of following intravenous infusion over 1 hour at 2 weeks apart: normal	VAS and neuropathic pain questionnaire.	Lidocaine = Placebo in controlling neuropathic pain-related to FBSS.	No adverse events reported.

Type of pain	Study	Condition treated	Method	Number of subjects	Intervention	Outcome	Conclusion	Adverse events
					saline placebo, lidocaine 1 mg/kg, and lidocaine 5 mg/kg at 60 ml/hr initially, and then titrated infusion speed while keep the heart rate <130 rates/minor 160 mmHg >systolic blood pressure >85 mmHg.			
Peripheral	Schipper	Peripheral neuropathic pain	prospective, uncontrolled, open-label	16	IV lidocaine (5 $mg.kg^{-1}$) within 30 min followed by long-term oral Oxcarbazepine (900–1,500 $mg.day^{-1}$)	Daily numeric pain scores for a period 28 days.	Prematurely aborted due to ethical reason.	Lidocaine infusion well tolerated with slight paresthesias and dizziness. 6 out of 16 participants (38%) discontinued oxcarbazepine treatment due to side effects.
Peripheral	Tanen	Acute radicular back pain	Randomized controlled double-blind Crossover	21 lidocaine, 20 ketorolac	100 mg lidocaine or 30 mg ketorolac intravenously over 2 min.	A 100-mm visual analog scale (VAS) at Time 0 (baseline), and 20, 40, and 60 minutes and 1 week.	Intravenous lidocaine failed to clinically alleviate the pain associated with acute radicular low back pain.	1 in the ketorolac and 1 in the lidocaine group withdrew at the 20-min time point due to a lack of improvement in symptoms.

Bolus de 1mg/kg (sur 10-15 minutes)
Perfusion de 3-5 mg/kg (sur 30-60 minutes)

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Extrait de Kandil E et al. J Anesth Clin Res 2017; 8(1): 1-29

Lidocaïne en perfusion IV et douleur cancéreuse réfractaire

Summary of case reports and studies of lidocaine infusion for cancer pain.

Author	Condition treated	Study method	Number of subjects	Intervention	Outcome	Conclusion	Adverse events
Buchanan	Opioid refractory metastatic renal cell cancer	Case report	1 case	Lidocaine 1.8 mg/kg at a rate of 0.8 mg/kg/h.	Treatment of opioid refractory cancer pain	Lidocaine improved patients pain and end of life care	Infusion needed to be repeated after 3 weeks due return of pain.
Ferrini	Neuroectodermal tumor Breast cancer Rectal adenocarcinoma	Retrospective cases series	6 cases	Lidocaine ranging from 10–80 mg/h. 2 cases subcutaneous, 4 case intravenous	Treatment of opioid refractory cancer pain	Lidocaine improved patients pain and end of life care	Lightheadedness which improved after dose reduction.
Thomas	Refractory cancer pain	Retrospective chart review 0f 768 hospice patients	82 receiving intravenous lidocaine, 61 patients data was analyzed.	Lidocaine 1–2 mg/kg bolus followed by an infusion of 1 mg/kg/h in 56 patients. 5 patients had no bolus	Treatment of opioid refractory cancer pain	50 patients had major improvement in pain out of which 44% had complete resolution of their pain 5 patients had partial response 6 patients had no benefit	No serious side effects reported, 26% had lethargy and somnolence.
Sharma	Refractory cancer pain	Randomize double blinded placebo controlled crossover	50	Lidocaine 2 mg/kg bolus over 20 min. followed by 2 mg/kg over 1 h.	Magnitude and duration of pain relief.	Significant improvement in pain relief of mean duration of 9.3 ± 2.58 days Significant reduction in analgesic requirements.	Self-limited side effects in the form of perioral numbness, tinnitus, sedation, lightheadedness and headache.

Mais PAS d'étude RCT

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Extrait de Kandil E et al. J Anesth Clin Res 2017; 8(1): 1-29

Lidocaïne en perfusion IV et douleur chronique réfractaire

Conclusions

- **Lidocaïne en perfusion IV largement étudiée** mais dans **différents modèles d'études**, **populations**, **méthodes d'évaluation de la douleur et devenirs cliniques!!!**

- **Bénéfices rapportés malgré faibles doses** utilisées chez plusieurs conditions de douleur chronique réfractaire

- **Rx peu coûteuse**, avec **peu d'effets secondaires**

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Extrait de Kandil E et al. J Anesth Clin Res 2017; 8(1): 1-29

Lidocaïne en perfusion IV et douleur chronique réfractaire

Conclusions

- Bien de **questions non parfaitement répondues**:
  - Régime précis de posologie
  - Durée de la perfusion
  - Critères appropriés de sélection des patients

Extrait de Kandil E et al. J Anesth Clin Res 2017; 8(1): 1-29

α-2 agonistes

Agonistes α-2 adrénergiques et leurs actions physiologiques

Table 1. Adrenergic Receptor Subtypes and Their Physiologic Functions

Receptor	*Physiologic Action (Agonism)*
α1	Constriction of vascular smooth muscle
	Contraction of radial muscle of the eye
	Contraction of the vas deferens smooth muscle
α2	Inhibition of norepinephrine release from presynaptic neuron
	Centrally induced sedation via locus ceruleus
	Centrally mediated pain modification via dorsal horn
	Inhibition of insulin release from pancreatic β cells
β1	Increased cardiac output (increased chronotropy, dromotropy, inotropy)
	Increased renin release from kidney
β2	Bronchial smooth muscle relaxation
	Vascular smooth muscle relaxation (vasodilation)
	Reduction of mast cell degranulation and histamine release
β3	Increased adipose tissue lipolysis

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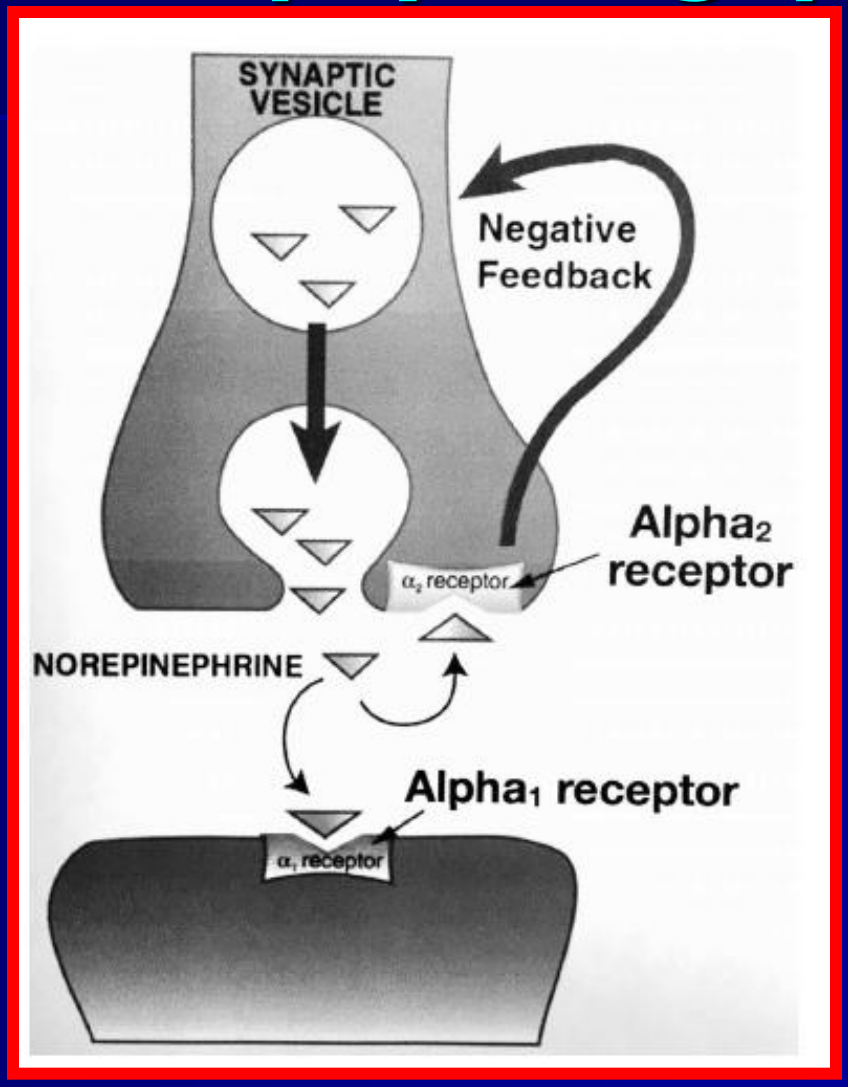
Extrait de Giovannitti JA et al. Anesth Prog 2015; 62: 31-38

Agonistes α-2 adrénergiques et leurs actions physiologiques

3 sous-types de récepteurs α-2 adrénergiques

α-2B a/n périphérique (muscles lisses)

α-2A et α-2C a/n cerveau et moëlle épinière



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Agonistes α-2 adrénergiques et leurs actions physiologiques

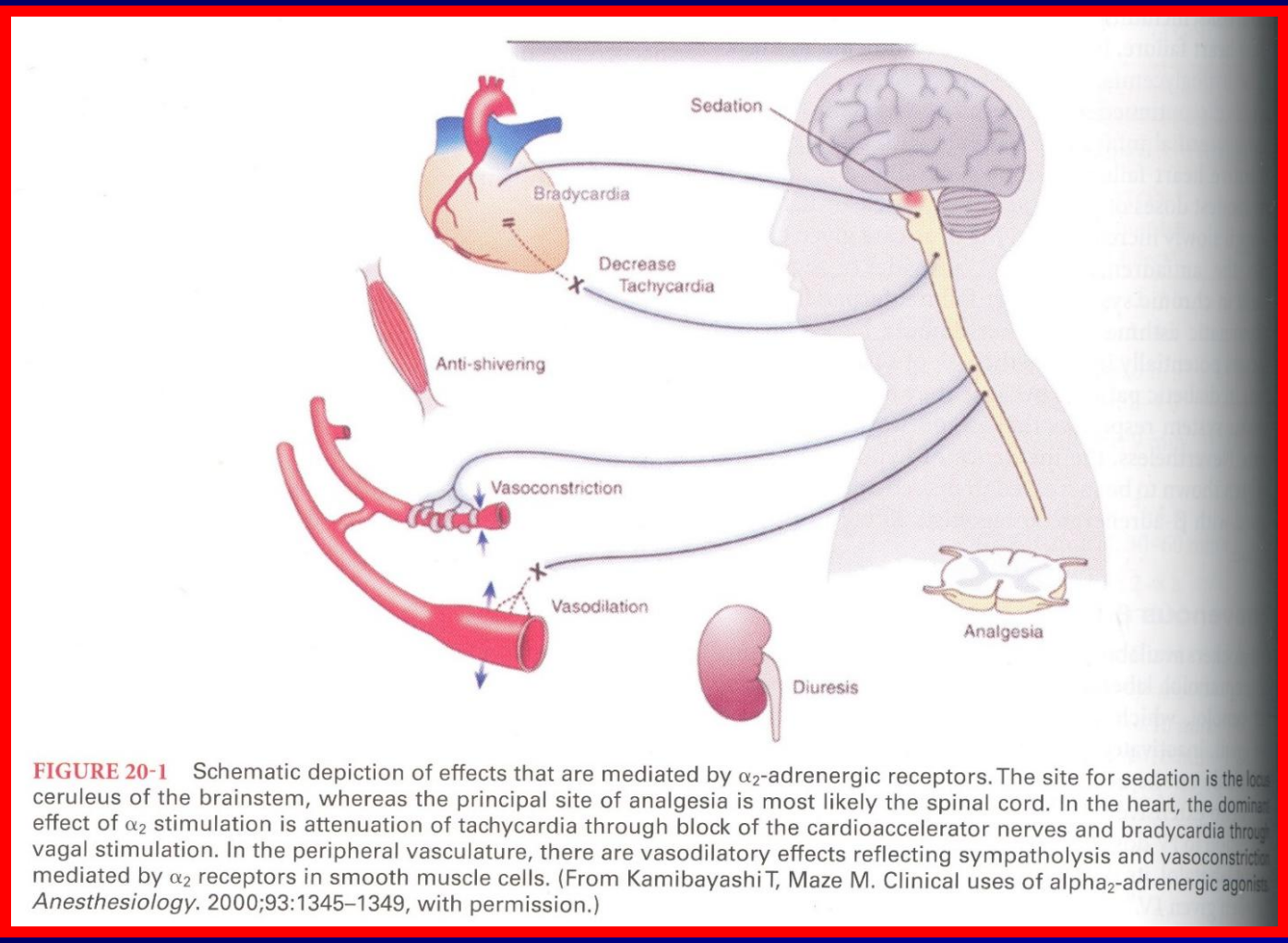

FIGURE 20-1 Schematic depiction of effects that are mediated by α_2-adrenergic receptors. The site for sedation is the locus ceruleus of the brainstem, whereas the principal site of analgesia is most likely the spinal cord. In the heart, the dominant effect of α_2 stimulation is attenuation of tachycardia through block of the cardioaccelerator nerves and bradycardia through vagal stimulation. In the peripheral vasculature, there are vasodilatory effects reflecting sympatholysis and vasoconstriction mediated by α_2 receptors in smooth muscle cells. (From Kamibayashi T, Maze M. Clinical uses of alpha$_2$-adrenergic agonists. *Anesthesiology*. 2000;93:1345–1349, with permission.)

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Extrait de Flood, Rathmell, Shafer Pharmacology and Physiology in Anesthetic Practice 5e édition, 2015, Chapitre 20, page 504

Agonistes α-2 adrénergiques Propriétés pharmacologiques

Table 2. Summary of α-2 Receptor Agonists and Pharmacological Properties*

Drug Name	*Trade Name*	*Pharmacokinetics*	*Clinical Uses*	*Precautions*
Clonidine	Catapres, Nexiclon XR, Kapvay	Metabolism: liver (~50%) Excretion: 40–60% unchanged in urine, 20% bile/feces Half-life: 12–16 h	Treatment of: Hypertension Anxiety ADD/ADHD Chronic pain Withdrawal symptoms Postoperative shivering	Transient increases in blood pressure after initial dosing (stimulation of postsynaptic α1 receptors) Rebound hypertension after sudden cessation
Tizanidine	Zanaflex	Metabolism: Liver Excretion: 60% urine, 20% feces Half-life: 2.5 h	Treatment of: Muscle spasm and cramps associated with CNS disorders Myofascial pain disorders of head and neck Spasticity of cerebral palsy	Potential for hepatotoxicity Fluoroquinolone antibiotics increase serum concentration
Dexmedetomidine	Precedex	Metabolism: Liver Excretion: 95% urine, 4% feces Half-life: 2 h	ICU sedation Procedural sedation	Hypotension, bradycardia Tachyphylaxis (if infused >24 h)

* ADD indicates attention-deficit disorder; ADHD, attention-deficit/hyperactivity disorder; CNS, central nervous system; and ICU, intensive care unit.

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Extrait de Giovannitti JA et al. Anesth Prog 2015; 62: 31-38

Agonistes α-2 adrénergiques

Themed Section: Adrenoceptors—New Roles for Old Players

REVIEW ARTICLE

Spinal α_2-adrenoceptors and neuropathic pain modulation; therapeutic target

Zahra Bahari[1,2] | Gholam Hossein Meftahi[1]

Anh Nguyen, 2026

Extrait de Bahari Z et al. Br J Pharmacol 2019; 176: 2366-2381

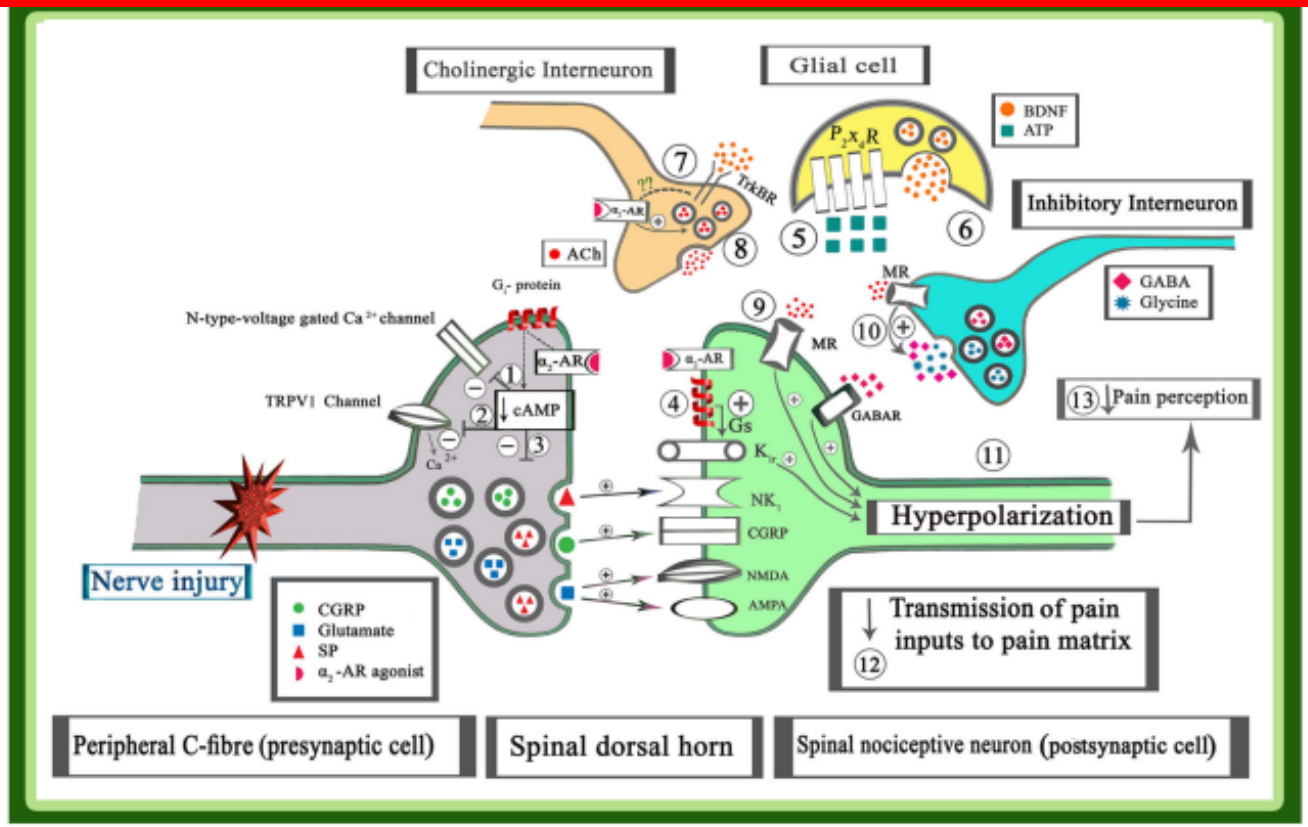

FIGURE 2 Cellular mechanisms for analgesic effects of α_2-adrenoceptor (AR) agonists; α_2-adrenoceptors located both in the peripheral sensory neurons and spinal neurons. The activation of α_2-adrenoceptors on presynaptic cells, using an α_2-adrenoceptor agonist, reduces the activity of AC, suppressing both the production of the cAMP and the activity of PKA. Then, suppressing the activity of PKA inhibited the presynaptic N-type voltage-gated Ca^{2+} channels (1) and TRPV1 channel activity (2); subsequently, the influx of Ca^{2+} ions to presynaptic cell and the release of stimulators neurotransmitters such as glutamate, substance P, and CGRP from primary fibre terminals in the spinal cord are decreased (3). Furthermore, application of α_2-adrenoceptor agonist increases the activity of Gs proteins in the postsynaptic cells. Activation of Gs protein, increased both the production of the cAMP and the activity of PKA, and then the activity of K^+_{ir} channels and efflux of K^+ ions are increased. Efflux of K^+ ions induced hyperpolarization in the postsynaptic neurons (4). Nerve injury increased the release of ATP from the peripheral sensory neuron and also induced an up-regulation of P2X4 receptors on glial cells (5). The activity of P2X4 receptors increased the release of BDNF from glial cells (6). At the same time, activation TrkB receptors on cholinergic interneurons (7) and its interaction with α_2-adrenoceptors via unknown mechanisms elicited the release of ACh (8). Activation of muscarinic receptors directly on the postsynaptic cells (9) or indirectly on the inhibitory GABAergic or glycinergic interneurons (10) can also induce hyperpolarization in the postsynaptic cells (11). Therefore, the application of an α_2-adrenoceptor agonist elicited hyperpolarization in the postsynaptic cell via above-mentioned mechanisms. Hyperpolarization of the neuron decreased transmission of pain inputs to higher centres (12) and suppressed pain perception (13)

Anh Nguyen, 2026

Extrait de Bahari Z et al. Br J Pharmacol 2019; 176: 2366-2381

Agonistes α-2 adrénergiques Mécanismes d'action cellulaire

- **Activation présynaptique des récepteurs α-2 adrénergiques**

  → ↓ **production d'AMPc**

  → **Inhibition présynaptique** des **canaux calciques** (↓ libération de substance P, glutamate et CGRP) et **TRPV1** (récepteur vanilloïde potentiel transitoire de type 1)

  → Activation accrue du fonctionnement des **protéines G a/n postsynaptique** → **Activité accrue des canaux de K**

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Bahari Z et al. Br J Pharmacol 2019; 176: 2366-2381

Agonistes α-2 adrénergiques Mécanismes d'action cellulaire

→ **Sortie massive de K** → **hyperpolarisation du neurone postsynaptique**

→ Uprégulation des récepteurs impliquant les **cellules gliales**

→ Activation des **récepteurs muscariniques postsynaptiques**

→ Activation indirecte des **récepteurs inhibiteurs GABAergiques**

→ **Hyperpolarisation postsynaptique** (résultante finale) (↓ **transmission de la douleur** au SNC et **suppression de la perception de de douleur**)

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Bahari Z et al. Br J Pharmacol 2019; 176: 2366-2381

Dexmédétomidine
Agoniste α-2 adrénergique

- **Indication** → sédation, anxiolyse, **analgésie**

- **Dosage habituellement recommandé**
  - → **Bolus 0,5-1mcg/kg sur 10 minutes**
  - → **Perfusion 0,2-1,0 mcg/kg/h**

- Demi-vie de distribution → 6 minutes
- **Demi-vie d'élimination** → **2h**
- **Élimination** → **95% par voie rénale**

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Bhanan N et al. Drugs 2000; 59(2): 263-268

Dexmédétomidine
Agoniste α-2 adrénergique

- **Grande sélectivité pour récepteurs α-2 adrénergiques (*8 fois plus d'affinité* avec récepteurs adrénergiques présynaptiques que clonidine)**

	Sélectivité α-2	Sélectivité α-1
Clonidine	**200**	**1**
Dexmédétomidine	**1620**	**1**

Giovannitti JA et al. Anesth Prog 2015; 62: 31-38

Dexmédétomidine
Agoniste α-2 adrénergique

Effets secondaires reconnus

- **Hypotension** (surtout si patient hypovolémique)
- **Bradycardie** (sympatholyse)
- **Sédation** (effets centraux a/n du tronc cérébral)

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Giovannitti JA et al. Anesth Prog 2015; 62: 31-38

Dexmédétomidine et douleur cancéreuse réfractaire

Dexmedetomidine as an Adjuvant Analgesic for Intractable Cancer Pain

J Pall Med 2011; 14(3): 371-373

Seth B. Roberts, M.D., Ph.D., Colin P. Wozencraft, M.D., Patrick J. Coyne, R.N., M.S.N., and Thomas J. Smith, M.D.

Dexmedetomidine:
A Novel Analgesic with Palliative Medicine Potential

Kenneth C. Jackson, II
Paul Wohlt
Perry G. Fine

J Pain Pall Care Pharmacother 2006; 20(2): 23-27

Anh Nguyen, 2026

Dexmédétomidine et douleur cancéreuse réfractaire

REPORT

Dexmedetomidine: Exploring Its Potential Role and Dosing Guideline for Its Use in Intractable Pain in the Palliative Care Setting

Patrick J. Coyne, Colin P. Wozencraft, Seth B. Roberts, Barton Bobb, and Thomas J. Smith

J Pain Pall Care Pharmacother 2010; 24(4): 384-386

ABSTRACT

Intractable pain continues to pose problems for patients with life-limiting disease. The authors review the potential role of dexmedetomidine (Precedex), an α_2-adrenergic agonist, as a bridge to obtaining effective analgesia. The authors offer criteria to consider in utilizing this medication within the context of palliative care.

KEYWORDS Dexmedetomidine, guidelines, pain, palliative care, protocol

Anh Nguyen, 2026

VCU/Massey's Thomas Palliative Care Unit Guideline for Dexmedetomidine Infusion

Purpose

Dexmedetomidine is an alpha-2 adrenergic agonist with analgesic properties. It can be used as an adjunctive analgesic for refractory pain, may be opioid sparing, and provides a mild sedative effect. Placing the patient on telemetry should be considered if the goals of care are such that resuscitation is warranted.

Protocol:

- Ordered as 2 x 200 mcg vials for 400 mcg mixed in 100 ml normal saline.
- Check EKG prior to initiation to evaluate for bradycardia, atrial fibrillation, or other arrhythmia.
- Recheck EKG 4 hours after initiation of therapy.
- Usual starting dose is 0.2 mcg/kg/hour, e.g. (0.2)(70 g)=14 mcg/hour
- Check vital signs pre-infusion and every 15 minutes after starting or increasing dose; if stable after 30 minutes check every 30 minutes for 3 hours, then every 4 hours for a 24 hour total.
- Infusion may be increased by 0.1 mcg/kg every 30 minutes until pain is controlled.
- Decrease to previous rate of infusion if heart rate drops below 80, systolic blood pressure drops below 100, or either decreases by > 30% of the pre-infusion baseline unless a physician order is obtained.
- Once analgesia is achieved, or hypotension or bradycardia preclude further increases, continue at current dose.
- After 3 hours, opioid may require decreasing by up to 30% due to opioid sparing effect; consideration of this may help avoid sedation and potential respiratory depression.
- In case of respiratory depression, dilute naloxone (one to two mL of 0.4 mg in 10 mL normal saline) can be utilized to evaluate whether relative opioid sparing is the etiology with minimal risk of heightened pain or withdrawal.

Signed: _____ _____ _____

Medical Director, Thomas Palliative Care Unit | Clinical Director | Date

Anh Nguyen, 2026

Extrait de Coyne PJ et al. J Pain Pall are Pharmacother 2010; 24(4): 384-386

Traitement adjuvant en douleur chronique

- Rôle potentiellement intéressant et pertinent des formulations topiques en présence d'une douleur neuropathique localisée

- Malgré les multiples mécanismes d'action, la perfusion IV de la kétamine demeure un traitement adjuvant de dernier recours

- Perfusion IV de la lidocaïne représente une autre alternative de dernier recours, ayant des effets

Extrait de Kandil E et al. J Anesth Clin Res 2017; 8(1): 1-29

Traitement adjuvant en douleur chronique

anti-nociceptifs, anti-inflammatoires et anti-hyperalgésiques

- Clonidine et dexmédétomidine sont de puissants agents α-agonistes, hautement sélectifs, reconnues pour leur propriété analgésique. Il s'agit également des traitements de dernier recours

Extrait de Kandil E et al. J Anesth Clin Res 2017; 8(1): 1-29

QUESTIONS ?

COMMENTAIRES ?