JOURNÉE RÉGIONALE DES
Filières

Deuxième édition
PSYCHIATRIE

Prise en charge pharmacologique de l'agitation

Camille Moslard • Reims

27 novembre 2025 • Reims (51)

Est-RESCUE

COMUGE

Déclaration de conflits d'intérêt :

Aucun

I
Introduction
Enjeux et classes thérapeutiques

II
Bibliographie
Que nous dit la littérature ?

III
Intranasale
Quelle place pour l'intranasale ?

IV
Gériatrie
Cas particulier du patient de plus de 65 ans

V
Obstétrique
Cas particulier de la femme enceinte

Introduction

- Situation fréquente.

- Enjeux :
  - Sécurité du patient et des soignants.
  - Quelle étiologie ?
  - Quelle molecule utiliser ?

Classes thérapeutiques

Antipsychotiques typiques

HALOPERIDOL, LOXAPINE, TIAPRIDE

➤ Antagonisme D2 dopaminergiques *: sédation, ↘ hallucinations, ↘ désorganisation*

Antipsychotiques atypiques

OLANZAPINE, RISPERIDONE

➤ Antagonisme D2 + 5HT2A *: sédation, ↘ effets extrapyramidaux*

Benzodiazépines

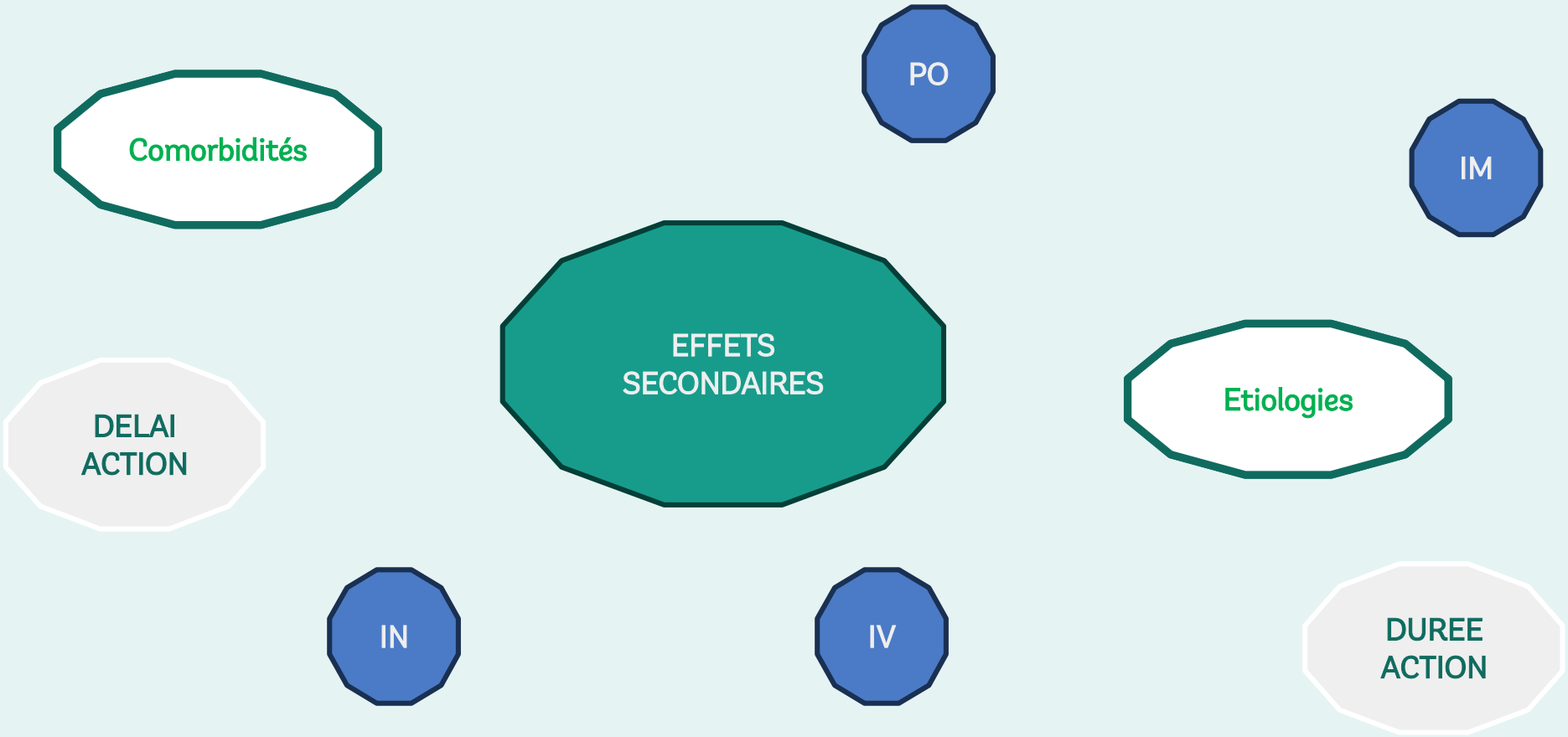
MIDAZOLAM, LORAZEPAM, DIAZEPAM

➤ Potentialisation GABA *: sédation, anxiolyse, myorelaxant, anticonvulsivant*

Anesthésiques dissociatifs

KETAMINE

➤ Antagoniste NMDA *: sédation dissociative rapide, analgésie*


PO
Comorbidités
IM
EFFETS SECONDAIRES
DELAI ACTION
Etiologies
IN
IV
DUREE ACTION

II
Bibliographie

Que dit la littérature ?

Désescalade verbale

Premier recours

Voie orale

A privilégier +++

Voie parentérale

Si patient non-coopérant, refus

Rapid tranquilization of the agitated patient in the emergency department: A systematic review and network meta-analysis☆

Ian S. deSouza, MD [a,*], Henry C. Thode Jr., PhD [b], Pragati Shrestha, MPH [b], Robert Allen, MD [a], Jessica Koos, MLS, MSEd [b], Adam J. Singer, MD [b]

[a] Department of Emergency Medicine, SUNY Downstate Health Sciences University and Kings County Hospital Center, Brooklyn, NY, USA
[b] Department of Emergency Medicine, Stony Brook University, NY, USA

- Efficacité : 11 études pour 11 traitements différents (N= 1142)
- Sécurité : 11 études, 11 traitements (N = 1147)
- Rapidité d'effet : 6 études, 7 traitements (N = 559)

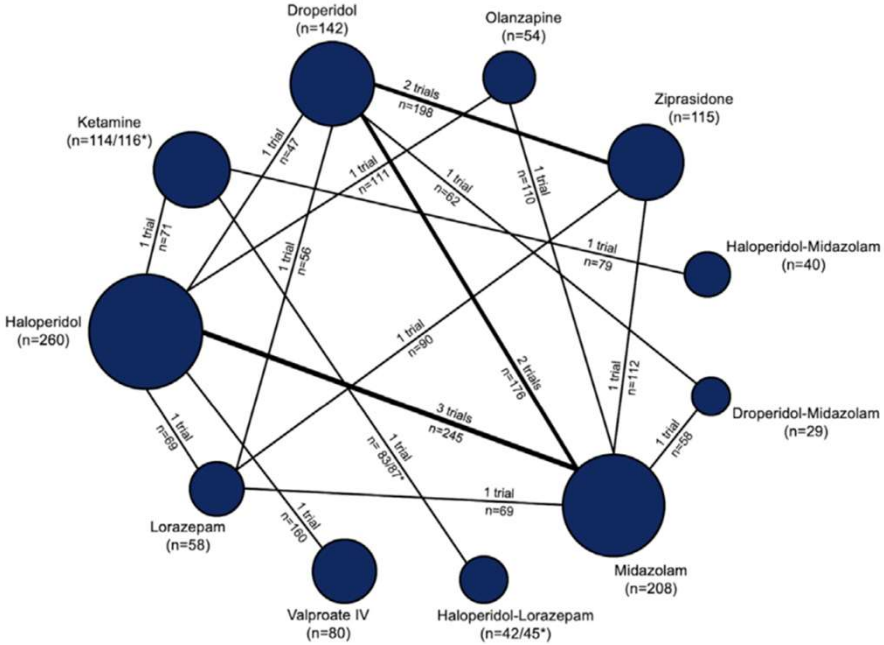


Fig. 2. Network configuration of treatments (11 trials: $n = 1142$ (effectiveness); $n = 1147$ (safety)).

Benzodiazepines for psychosis-induced aggression or agitation

Hadar Zaman[1], Stephanie J Sampson[2], Alison LS Beck[3], Tarang Sharma[4], Fiona J Clay[5], Styliani Spyridi[6], Sai Zhao[7], Donna Gillies[8]

[1]Bradford School of Pharmacy & Medical Sciences, Faculty of Life Sciences, University of Bradford, Bradford, UK. [2]Centre for Reviews and Dissemination, University of York, York, UK. [3]Trust HQ, South London and Maudsley NHS Foundation Trust, London, UK. [4]Nordic Cochrane Centre, Copenhagen, Denmark. [5]Department of Forensic Medicine, Monash University, Southbank, Australia. [6]Department of Rehabilitation Sciences, Faculty of Health Sciences, Cyprus University of Technology, Lemesos, Cyprus. [7]Systematic Review Solutions Ltd, The Ingenuity Centre, The University of Nottingham, Nottingham, UK. [8]Sydney, Australia

<u>Benzodiazépines versus antipsychotiques</u> :

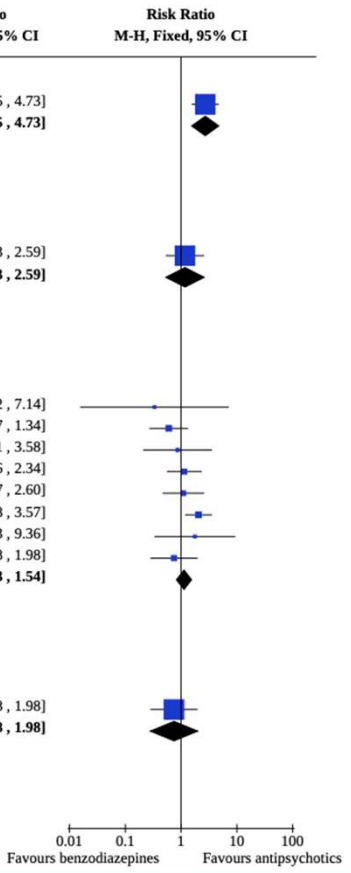
MIDAZOLAM > DROPERIDOL

LORAZEPAM ≈ HALOPERIDOL

19 essais (N = 16 à 301)

Analysis 2.1. Comparison 2: Benzodiazepines versus antipsychotics, Outcome 1: Tranquillisation or asleep: 1. sedation

Study or Subgroup	Benzodiazepine Events	Benzodiazepine Total	Antipsychotics Events	Antipsychotics Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 vs droperidol - short term						
Midazolam 2006, AU	33	74	13	79	100.0%	2.71 [1.55 , 4.73]
Subtotal (95% CI)		**74**		**79**	**100.0%**	**2.71 [1.55 , 4.73]**
Total events:	33		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.50 (P = 0.0005)						
2.1.2 vs haloperidol - short term						
Lorazepam 1989, USA	9	23	7	21	100.0%	1.17 [0.53 , 2.59]
Subtotal (95% CI)		**23**		**21**	**100.0%**	**1.17 [0.53 , 2.59]**
Total events:	9		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.40 (P = 0.69)						
2.1.3 vs haloperidol - medium term						
Clonazepam 1993, CA	0	8	1	8	2.9%	0.33 [0.02 , 7.14]
Diazepam 1979, IL	6	20	10	20	19.5%	0.60 [0.27 , 1.34]
Flunitrazepam 1999, IL	3	15	3	13	6.3%	0.87 [0.21 , 3.58]
Lorazepam 1989, USA	10	23	8	21	16.3%	1.14 [0.56 , 2.34]
Lorazepam 1991, USA	8	27	7	26	13.9%	1.10 [0.47 , 2.60]
Lorazepam 1997a, USA	20	31	11	35	20.2%	2.05 [1.18 , 3.57]
Lorazepam 1997b, USA	3	17	2	20	3.6%	1.76 [0.33 , 9.36]
Lorazepam 2001, RO and USA	5	51	13	99	17.3%	0.75 [0.28 , 1.98]
Subtotal (95% CI)		**192**		**242**	**100.0%**	**1.13 [0.83 , 1.54]**
Total events:	55		55			
Heterogeneity: Chi² = 8.58, df = 7 (P = 0.28); I² = 18%						
Test for overall effect: Z = 0.76 (P = 0.45)						
2.1.4 vs olanzapine - medium term						
Lorazepam 2001, RO and USA	5	51	13	99	100.0%	0.75 [0.28 , 1.98]
Subtotal (95% CI)		**51**		**99**	**100.0%**	**0.75 [0.28 , 1.98]**
Total events:	5		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%						



Benzodiazepines for psychosis-induced aggression or agitation

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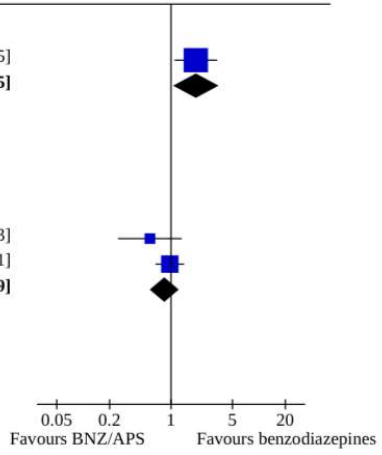
Benzodiazépines versus benzodiazépine + antipsychotiques :
> Association bénéfique à court terme.

Analysis 4.1. Comparison 4: Benzodiazepines plus antipsychotics vs same benzodiazepines, Outcome 1: Tranquillisation or asleep: 1. sedation

Study or Subgroup	BNZ/APS Events	BNZ/APS Total	Benzodiazepines Events	Benzodiazepines Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.1.1 + haloperidol - short term						
Lorazepam 1989, USA	18	24	9	23	100.0%	1.92 [1.10 , 3.35]
Subtotal (95% CI)		**24**		**23**	**100.0%**	**1.92 [1.10 , 3.35]**
Total events:	18		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.28 (P = 0.02)						
4.1.2 + haloperidol - medium term						
Lorazepam 1989, USA	6	24	10	23	33.5%	0.57 [0.25 , 1.33]
Lorazepam 1997a, USA	20	32	20	31	66.5%	0.97 [0.67 , 1.41]
Subtotal (95% CI)		**56**		**54**	**100.0%**	**0.84 [0.59 , 1.19]**
Total events:	26		30			
Heterogeneity: $Chi^2 = 1.36$, df = 1 (P = 0.24); $I^2 = 27\%$						
Test for overall effect: Z = 0.98 (P = 0.32)						
Test for subgroup differences: $Chi^2 = 0.00$, df = 1 (P < 0.00001), $I^2 = 0\%$						



Benzodiazepines for psychosis-induced aggression or agitation

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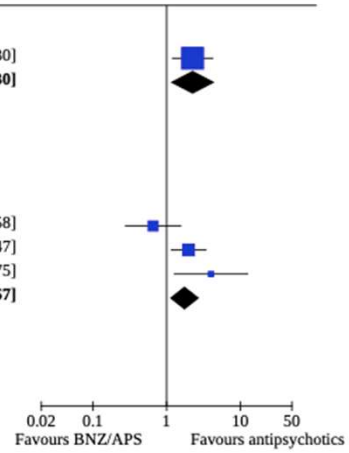
Antipsychotiques seul versus benzodiazépine + antipsychotiques :

> Association bénéfique à court et moyen terme.

Analysis 5.1. Comparison 5: Benzodiazepines plus antipsychotics versus same antipsychotics, Outcome 1: Tranquillisation or asleep: 1. sedation

Study or Subgroup	BNZ/APS Events	BNZ/APS Total	Antipsychotics Events	Antipsychotics Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.1.1 +/vs haloperidol - short term						
Lorazepam 1989, USA	18	24	7	21	100.0%	2.25 [1.18 , 4.30]
Subtotal (95% CI)		**24**		**21**	**100.0%**	**2.25 [1.18 , 4.30]**
Total events:	18		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.45 (P = 0.01)						
5.1.2 +/vs haloperidol - medium term						
Lorazepam 1989, USA	6	24	8	21	38.7%	0.66 [0.27 , 1.58]
Lorazepam 1997a, USA	20	32	11	35	47.7%	1.99 [1.14 , 3.47]
Midazolam 2011, BZ	12	30	3	30	13.6%	4.00 [1.25 , 12.75]
Subtotal (95% CI)		**86**		**86**	**100.0%**	**1.75 [1.14 , 2.67]**
Total events:	38		22			
Heterogeneity: Chi² = 6.90, df = 2 (P = 0.03); I² = 71%						
Test for overall effect: Z = 2.57 (P = 0.01)						



Systematic review of parenteral ketamine for managing acute agitation in emergency settings

Christopher Peter, Satish Suhas, Guru S. Gowda, Deepak Ghadigaonkar, Krishna Prasad Muliyala, Venkata Senthil Kumar Reddi

> Asian J Psychiatr.2025 janv.

29 études (agitation en service d'urgence ou psychiatrie)
N = 1516

- Rapidité d'action : KETAMINE IM 4-5 mg/kg > Midazolam IM, Haloperidol IM, Droperidol IM, combinaisons
- Efficacité : sédation adéquate dès la 1ère dose > neuroleptiques/ benzodiazépines
- Sécurité :
  - EI = tachycardie, HTA transitoire, hypersalivation, vomissement
  - Rare : dépression respiratoire (surtout si association avec BZD), bronchospasme

Qu'en est-il de la LOXAPINE (LOXAPAC®) ?

- Peu d'études sur la LOXAPINE.
- Très utilisée en France (PO/IM).
- A l'international : surtout utilisée en IN aux Etats-Unis.
- Antipsychotique de première génération.
- Effet sédatif important.
- Demi-vie ≈ 8h.

SYSTEMATIC REVIEW | DECEMBER 19, 2023

Efficacy and Safety of Loxapine in Acute Agitation: A Systematic Review of Interventional Studies

Camille Lebel, MD; Francky Teddy Endomba, MD, MSc; Guillaume Chabridon, MD; Jean-Christophe Chauvet-Gélinier, MD, PhD

Prim Care Companion CNS Disord 2023;25(6):23r03552

- 7 essais cliniques
- N = 1276
- Population : troubles bipolaires, schizophrénie *(sauf un essai sur le sevrage de la ventilation mécanique en réanimation)*

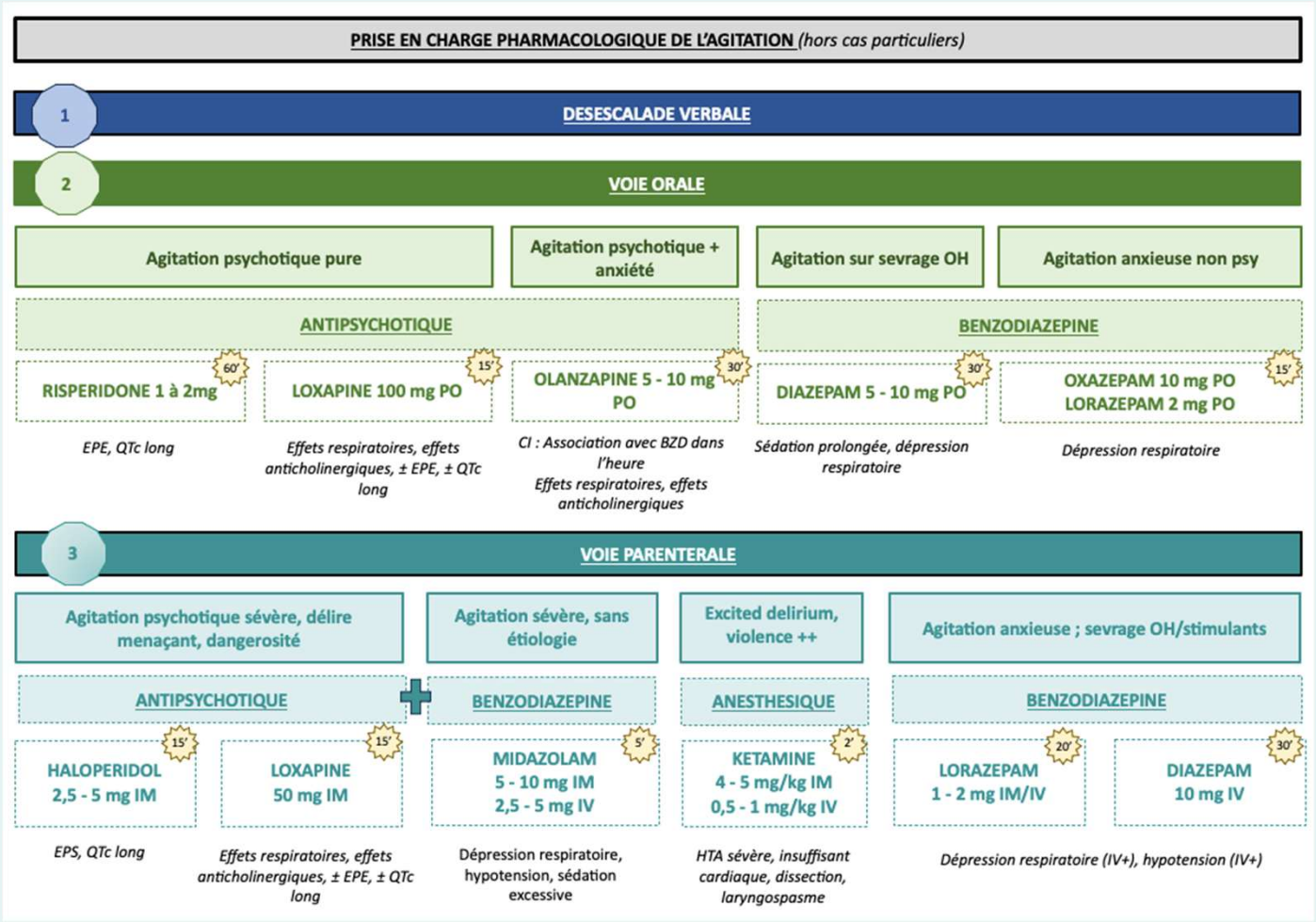
Table 1.
Main Characteristics of the Included Studies

Study/Country/Time Period	Study Design	Participants, N	Diagnosis/Context	Intervention	Duration of Follow-Up	No. of Administrations Allowed	Agitation Scale	Mean Age, y (range)	Baseline Agitation Score (Mean)
Fruensgaard et al, 1977[23] Denmark NA	RCT, multicentric, double-blind	30 (7 male/ 23 female)	Schizophrenia, psychogenic psychosis/ NA	Loxapine IM 25–50 mg vs haloperidol IM 2.5 to 5 mg	84 h (72 h during the treatment period, 6 to 12 h after the last dose)	NA (average daily 130 mg for loxapine and 12 mg for haloperidol)	Agitation/ agression scale, BPRS, CGI	Loxapine: 41.3 (19–65), haloperidol 40.1 (19–61)	Agitation scale: NA BPRS: 56.0 loxapine, 57.7 haloperidol CGI: 3.60 loxapine, 3.73 haloperidol
Gaussares et al, 1989[24] France NA	RCT, monocentric, open-label	15 (all male)	NA/hospital department	Loxapine IM 200 mg vs droperidol IM 100 mg	3 to 5 d	2/d	Analogical scale assessing the state of agitation rated from 1 to 4	31 (20–58)	NA
Allen et al, 2011[25] United States September 2006– January 2007	RCT, multicentric, double-blind	129 (105 male/ 24 female)	Schizophrenia, schizoaffective disorder, and schizophreniform disorders/hospital and emergency departments	Loxapine inhaled 5 mg vs placebo inhaled vs loxapine inhaled 10 mg	24 h	1	PANSS-EC, CGI, BARS	41.2 (21–61)	PANSS-EC: 17.4 ± 2.23 placebo, 17.6 ± 1.94 loxapine 5 mg, 17.4 ± 2.02 loxapine 10 mg CGI: NA BARS: 4.98 ± 0.46 placebo, 4.96 ± 0.6 loxapine 5 mg and 5.00 ± 0.59 loxapine 10 mg
Lesem et al, 2011[26] United States February–June 2006	RCT, multicentric, double-blind	344 (253 male/ 91 female)	Schizophrenia, hospital and psychiatric/emergency departments	Loxapine inhaled 5 mg vs placebo inhaled vs loxapine inhaled 10 mg	24 h	3	PANSS-EC, CGI, ACES	Loxapine 5 mg: 43.2 (16–65), loxapine 10 mg: 42.2 (21–62), placebo: 43.9 (23–69)	PANSS-EC: 17.4 placebo, 17.8 loxapine 5 mg, 17.6 loxapine 10 mg; CGI-S: 3.9 placebo, 4.0 loxapine 5 mg, 4.1 loxapine 10 mg
Kwentus et al, 2012[27] United States July–November 2008	RCT, multicentric, double-blind	314 (156 male/ 158 female)	Bipolar disorder/ hospital and emergency departments	Loxapine inhaled 5 mg vs placebo inhaled vs loxapine inhaled 10 mg	24 h	3	PANSS-EC, CGI, ACES	Loxapine 5 mg: 41.2 (19–62), loxapine 10 mg: 40.5 (19–64), placebo: 40.6 (19–60)	PANSS-EC: NA CGI-I: NA ACES: 2.01 ± 0.4 placebo, 2.11 ± 0.4 loxapine
Gaudry et al, 2017[28] France, November 2011–November 2013	RCT, multicentric, double-blind	87 (66 male/ 21 female)	NA/situation of weaning from mechanical ventilation in intensive care units	Loxapine enteral (NGT) 150 mg vs placebo enteral (NGT)	48 h–14 d	NA	RASS	Loxapine: 59.6 (NA), placebo: 51 (NA)	NA
San et al, 2018[29] Czech Republic, Germany, Spain, Russia December 2014–October 2016	RCT, multicentric, open-label	357 (181 male/ 176 female)	Schizophrenia or bipolar disorder type 1/ hospital and emergency departments	Loxapine inhaled 9.1 mg vs aripiprazole 9.75 mg IM	4–24 h	2	CGI	Loxapine: 40.44 (NA), aripiprazole 40.26 (NA)	CGI-S: 4.42 loxapine, 4.31 aripiprazole

Abbreviations: ACES = Agitation-Calmness Evaluation Scale, BARS = Behavioral Activity Rating Scale, CGI = Clinical Global Impressions, BPRS = Brief Psychiatric Rating Scale, IM = intramuscular, NA = not available, NGT = nasogastric tube, PANSS-EC = Positive and Negative Syndrome Scale Excited Component, RASS = Richmond Agitation Sedation Scale, RCT = randomized clinical trial.

LOXAPINE INH et IM > placebo

LOXAPINE IM > HALOPERIDOL ou DROPERIDOL IM


PRISE EN CHARGE PHARMACOLOGIQUE DE L'AGITATION (hors cas particuliers)
1
DESESCALADE VERBALE
2
VOIE ORALE
Agitation psychotique pure
Agitation psychotique + anxiété
Agitation sur sevrage OH
Agitation anxieuse non psy
ANTIPSYCHOTIQUE
BENZODIAZEPINE
RISPERIDONE 1 à 2mg
60'
LOXAPINE 100 mg PO
15'
OLANZAPINE 5 - 10 mg PO
30'
DIAZEPAM 5 - 10 mg PO
30'
OXAZEPAM 10 mg PO
LORAZEPAM 2 mg PO
15'
EPE, QTc long
Effets respiratoires, effets anticholinergiques, ± EPE, ± QTc long
CI : Association avec BZD dans l'heure
Effets respiratoires, effets anticholinergiques
Sédation prolongée, dépression respiratoire
Dépression respiratoire
3
VOIE PARENTERALE
Agitation psychotique sévère, délire menaçant, dangerosité
Agitation sévère, sans étiologie
Excited delirium, violence ++
Agitation anxieuse ; sevrage OH/stimulants
ANTIPSYCHOTIQUE
BENZODIAZEPINE
ANESTHESIQUE
BENZODIAZEPINE
HALOPERIDOL 2,5 - 5 mg IM
15'
LOXAPINE 50 mg IM
15'
MIDAZOLAM 5 - 10 mg IM 2,5 - 5 mg IV
5'
KETAMINE 4 - 5 mg/kg IM 0,5 - 1 mg/kg IV
2'
LORAZEPAM 1 - 2 mg IM/IV
20'
DIAZEPAM 10 mg IV
30'
EPS, QTc long
Effets respiratoires, effets anticholinergiques, ± EPE, ± QTc long
Dépression respiratoire, hypotension, sédation excessive
HTA sévère, insuffisant cardiaque, dissection, laryngospasme
Dépression respiratoire (IV+), hypotension (IV+)

JOURNÉE RÉGIONALE DES
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Deuxième édition
PSYCHIATRIE

III

L'intranasale

Quelle place pour l'intranasale dans le contexte de l'agitation ?

27 novembre 2025 • Reims (51)

Est-RESCUE

C*MUGE

Intranasal Drug Administration for Psychomotor Agitation as a Safe and Effective Prehospital Intervention: An Integrative Review

Nurs Rep. 2025

Amaya Burgos-Esteban [1,2,3], Valvanera Cordón-Hurtado [2], Marta Giménez-Luzuriaga [3], Maria Peinado-Quesada [4], Laura Gómez-Lage [4], Raúl Juárez-Vela [3,5,*], Michal Czapla [3,6,*], Jorge García-Criado [7], Noelia Navas-Echazarreta [3], Antonio Rodríguez-Calvo [8], Pablo Lasa-Berasain [9], Manuel Quintana-Diaz [4]

- 15 articles + 10 rapports de cas
- Médicaments : MIDAZOLAM, KETAMINE, HALOPERIDOL, OLANZAPINE
- Techniques :
  - Atomiseur
  - Volume : 0,2 à 0,3 mL par narine
  - Délai d'action : 2 à 3 min, effet max 10-15 min

MIDAZOLAM	0,2 mg/kg (max 10mg)
KETAMINE	0,5 à 1 mg/kg

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IV
Zoom gériatrie

Cas particulier du patient de plus de 65 ans

27 novembre 2025 • Reims (51)

Est-RESCUE

COMUGE

Nouvelles recommandations pour la prise en charge des Symptômes Psychologiques et Comportementaux (SPC) dans les maladies neurocognitives

Rédigé par La SFGG / Publié le vendredi 20 septembre 2024

Choix de la molécule en fonction du symptôme prédominant ou du terrain

Si évaluation initiale impossible :
MIDAZOLAM 1 mg PO (si impossible 1 mg SC). Réinjection possible à 1-2h. Max 3 mg.

Maladie de Parkinson ou maladie à corps de Lewy
= CI aux neuroleptiques

Maladie d'Alzheimer, QTc long, ATCD AVC :
= éviter les neuroleptiques

La place de la contention physique : exceptionnelle
- Patient laissé au calme le temps d'action du traitement
- Laisser déambuler si pas de risque
- Prescription médicale tracée + surveillance horaire
- Détacher toutes les 2h + surveillance médicale / 6h

Anxiété aiguë intense
MIDAZOLAM 1 mg PO (1-2 mg S.C.)
Ou **OXAZEPAM 10 mg PO**
Ou **ALPRAZOLAM 0,25 mg PO**
Ou **LORAZEPAM 1 mg PO** (1 mg IM ou 0,025mg/kg, possible réinjection à 2h)

Délire / hallucinations AVEC danger ou agressivité importante :
RISPERIDONE 0,5 à 1 mg PO
Ou **HALOPRIDOL 0,5 à 1 mg PO** (1 à 2 mg IM – possibilité de SC) *Pas en 1ère intension*.
Ou LOXAPINE 25 mg PO ou IM (*pas chez l'insuffisant rénal* !)

Si maladie de Parkinson ou Maladie à corps de Lewy :
CLOZAPINE 12,5 mg PO le soir [prescription par psychiatre, gériatre, neurologie]

Réévaluation à 30 min – 1h – 2h : paramètres vitaux (GCS, FR, T°, douleur...), résolution des symptômes (échelle 4AT), signes de mauvaise tolérance (syndrome malin des neuroleptiques, sédation (RASS), QTc ...)

JOURNÉE RÉGIONALE DES
Filières

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PSYCHIATRIE

IV

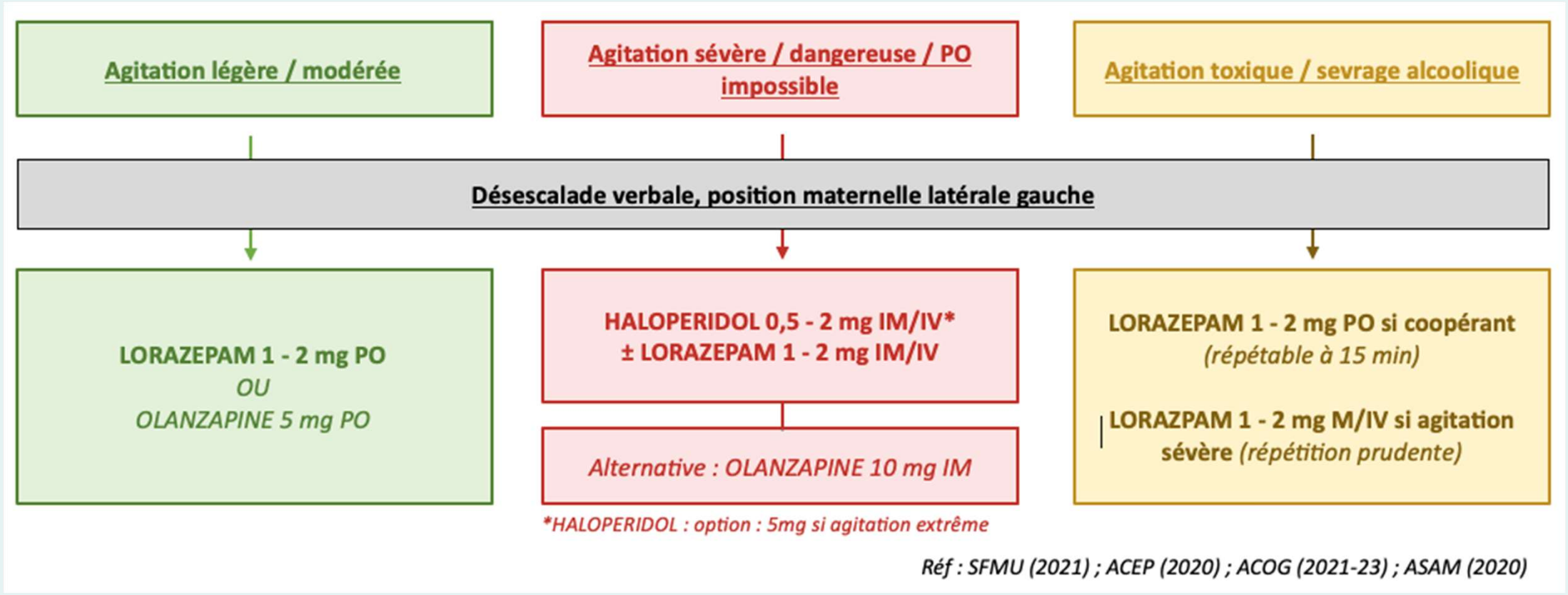
Zoom obstétrique

Cas particulier de la femme enceinte

27 novembre 2025 • Reims (51)

Est-RESCUE

COMUGE



⚠ ***Molécules à éviter : LOXAPINE, KETAMINE, MIDAZOLAM***

CONCLUSION

- Situation fréquente et hétérogène
- Littérature limitée, pas de consensus
- Désescalade verbale > voie orale > voie parentérale
- Adapter la molécule à l'étiologie, au délai d'action et aux comorbidités du patient
- Voie intranasale : piste intéressante mais données limitées

Merci pour votre attention.