

The efficacy of N-methyl-D-aspartic acid receptor antagonist drugs in patients with chronic neuropathic pain



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Introduction

- Chronic pain is pain experienced for longer than three months and cannot be explained by actual tissue damage
- Neuropathic pain is caused by damage to or a primary lesion in the somatosensory nervous system.
- In Australia, total expenditure in 2007 was \$34 billion¹
- Effect physical and physiological well being of patients
- Managing chronic pain is to target central sensitization induced by NMDAR activation through the use of NMDAR antagonists such as ketamine and memantine

Aim

- The evidence for NMDA receptor antagonists drugs in reducing pain in chronic neuropathic pain patients is unclear
- To clarify the role of NMDAR antagonists in the management of chronic neuropathic pain

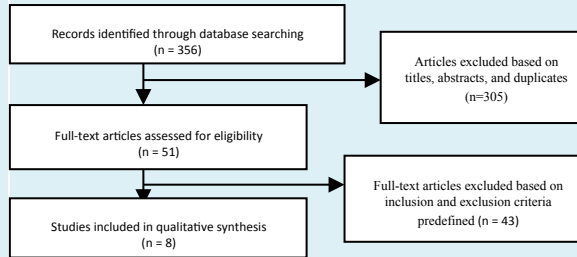
References

- Access Economics (Firm), MBF Foundation., University of Sydney. Pain Management Research Institute. The high price of pain : the economic impact of persistent pain in Australia. Australia: MBF Foundation; 2007. 88 p. p.

Methods

- Inclusion criteria:**
Human subjects, RCT, studies written in English
- Exclusion criteria:**
Systematic reviews, meta-analyses, and case reports, studies before year 2000

Fig. 1 PRISMA Diagram of Selection Process



Study	1	2	3	4	5	6	7	8	9	10	11	Score
Nikolajsen et al(14)	+	+	+	+	+	+	+	+	+	+	+	11/11
Tena et al(28)	+	+	+	+	+	+	+	+	+	+	+	11/11
Maier et al(29)	+	+	+	+	+	+	-	+	-	+	+	9/11
Wiech et al(30)	+	+	+	+	+	-	+	+	-	+	+	9/11
Eichenberger et al(31)	+	+	+	+	+	+	+	+	+	+	+	11/11
Wilson et al(32)	+	+	+	+	+	+	+	+	+	+	+	11/11
Dualé et al(33)	+	+	+	+	+	+	+	+	+	+	+	11/11
Aveline et al(34)	+	+	+	+	+	+	+	+	+	+	+	11/11

Fig. 2 Quality of Trials

Results

Study	Participants (n)	Intervention	Outcome Measures	Main Findings
Nikolajsen et al(13)	15	Oral memantine dosage of 5-20 mg	Numerical Rating Scale (NRS), McGill Pain Questionnaire (MPQ)	Memantine at a dosage of 20 mg/d does not reduce pain in patients with nerve injury pain
Tena et al(27)	104	IV and epidural racemic ketamine 0.5 mg/kg preincisional + 0.25 mg/kg/h	Visual Analog Scale (VAS), Quantitative Sensory Testing (QST), Electronic von Frey, The Catastrophizing Scale	Adding epidural or IV racemic ketamine after thoracotomy did not lead to any reduction in persistent post-surgical pain
Maier et al(28)	36	Oral memantine 5-30 mg (gradually given)	NRS	This trial failed to demonstrate a significant clinical benefit
Wiech et al(29)	8	Oral memantine 10-30 mg (gradually given)	VAS	NMDA receptor antagonist had no effect on the intensity of chronic PLP
Eichenberger et al(30)	20	IV ketamine 0.4 mg/kg	VAS	Ketamine, but not calcitonin, reduced PLP
Wilson et al(31)	53	During surgery: epidural infusion ketamine 3.3 mg/kg/l, post surgery 10-20 ml/h	MPQ, QST, Neuropathic Pain Scale (NPS), Hospital anxiety and depression scale (HADS)	The intrathecal/epidural technique used, with peri-operative sensory attenuation, may have reduced ongoing sensitisation
Dualé et al(32)	86	1 mg/kg at the induction, 1 mg/kg/h during surgery, then 1 mg/kg during 24 h	VAS, NPS	Ketamine given in 24-h infusion failed to prevent chronic neuropathic pain after thoracotomy
Aveline et al(33)	69	0.2mL/kg bolus before surgical, infusion of 120 mg/kg/h	VAS, Knee Injury and Osteoarthritis Outcome Score-Physical Function Shortform (KOOS-PS)	Ketamine do not significantly reduce the incidence of chronic pain

Fig. 3 Characteristics of the Included Articles

Conclusion

- Due to the heterogeneity, it is not possible to conclude whether NMDAR antagonist drugs have or do not have benefit for the chronic neuropathic pain patients
- The heterogeneity in drug dose, treatment duration, mode of administration and small sample sizes indicates a lack of power to detect a difference