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Original study

Intravenous ketamine bolus therapy with or without lidocaine in first-course treatment of chronic pain : a cohort description

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Abstract

Introduction: Refractory chronic pain remains a major challenge in clinical practice. At the Erasme Pain Clinic, intravenous ketamine infusions, alone or combined with an adjuvant analgesic, are proposed in selected complex cases. The primary objective of this retrospective study was to describe the patient management procedure between 2010 and 2024.

Methods: We retrospectively reviewed the records of 89 adult patients. Collected data included demographic characteristics, pre- and post-cycle pharmacotherapy, infusion composition, trajectories of clinical scores (Visual Analogue Scale [VAS], DN4), and reported adverse effects. Results are presented descriptively.

Results: The cohort comprised 74% women, with a mean age of 50 years. The median interval between the first consultation and the first infusion was 92 weeks. Overall, 75% of patients continued treatment, and 70% reported improvement rated as moderate to very good. The most frequent adverse effects were fatigue (33%), nausea (13%), dizziness (19%), and pain exacerbation (18%). Resting pain intensity (VAS) decreased from a median of 7 to 6 after the cycle ($p < 0.001$). The median number of concomitant medications decreased from 4 to 3 ($p = 0.013$).

Conclusion: This study underscores substantial heterogeneity in practices and in patient profiles treated with intravenous ketamine infusions, with or without lidocaine. Despite encouraging trends, the findings should be interpreted cautiously. A standardised protocol and prospective follow-up are warranted to optimise this management.

Key words: **Ketamine, chronic pain, lidocaine, pain clinic.**

Introduction

The management of chronic pain remains a major challenge and profoundly impairs quality of life. Among emerging therapeutic options, intravenous infusions of ketamine and lidocaine have attracted increasing interest for refractory pain. Ketamine, an NMDA receptor antagonist, modulates centrally mediated pain, whereas lidocaine, a local anaesthetic with systemic effects, inhibits nociceptive pathways. Their combination appears particularly relevant for neuropathic pain.

Multiple studies suggest a beneficial effect of ketamine in neuropathic and refractory chronic pain. Bell et al. reported a significant reduction in pain after infusion[1]. In a critical review, Faísco et al. confirmed encouraging results while advising caution, notably regarding psychotomimetic effects that may be mitigated by specific co-medications[2]. Brinck et al. also highlighted the utility of low doses in the perioperative setting[3]. The meta-analysis by McNicol et al. identified a potential analgesic effect, albeit with heterogeneous findings and limited certainty of evidence[4].

Ketamine reduces central sensitisation and hyperalgesia by blocking NMDA receptors, thereby limiting neuronal hyperexcitability and nociceptive transmission. Additional targets include μ- and δ-opioid receptors and monoaminergic systems, conferring a multimodal analgesic profile. Ketamine has also been associated

with neuroprotective properties, including anti-inflammatory effects and modulation of brain networks involved in pain processing. The most frequent adverse effects include hallucinations and vivid dreams, often attenuated by dose adjustments[5]. The long-term toxicity profile remains insufficiently characterised[6]. Faísco et al. note that co-administration of benzodiazepines or α2-agonists may limit psychotropic effects in selected cases[2].

A 2018 U.S. consensus statement issued recommendations for the use of intravenous ketamine infusions in chronic pain, acknowledging potential effectiveness while calling for further research on optimal dosing, non-intravenous alternatives, and long-term risks. Standardised protocols were deemed essential to ensure safety and effectiveness[7]. A meta-analysis by Silvinato et al. concluded that multiple intravenous lidocaine infusions are associated with a short-term reduction in neuropathic pain[8].

At usual doses, intravenous lidocaine is generally well tolerated. Overdose may affect cardiac sodium channels and impair electrical conduction, with potential adverse effects such as hypotension and arrhythmias. Early signs of toxicity, including dizziness and paraesthesias, may precede more serious complications such as seizures, underscoring the need for close monitoring during administration .

Intravenous ketamine and lidocaine are potential options for the management of refractory chronic pain. Their effectiveness, alone or in combination, is supported by several studies, particularly in perioperative settings to reduce pain and opioid consumption. However, adverse effects, psychotropic for ketamine and cardiovascular for lidocaine, require careful monitoring. Variability in protocols and the absence of consensus on optimal dosing emphasise the need for further studies to inform safe and standardised use.

Over the past seven years, several intravenous protocols have been implemented at the Erasme Hospital Pain Clinic. This work retrospectively analyses data from patients who received these treatments. This study aims to characterise the impact of intravenous ketamine infusions, with or without lidocaine, in patients treated at the Erasme Pain Clinic, and to assess their effectiveness and potential adverse effects.

Materials and methods

Design

This was retrospective descriptive study academic monocentric over 14 years.

Population

The inclusion criteria were Adults (≥18 years) followed at the Erasme Pain Clinic who received an intravenous ketamine infusion or a combined ketamine–lidocaine infusion for chronic pain management between.

The exclusion criteria was (i) Records too incomplete for analysis; (ii) patients who refused use of their data for research.

Objectives

The primary objective was to provide a descriptive analysis of the patient population treated between 2010 and 2024 at Erasme Hospital, including a descriptive account of the treatments administered and adverse effects observed in this cohort.
The secondary objectives were :

1. To analyse the impact of the first ketamine infusion cycle on pain and opioid consumption.
2. To analyse the impact of the first ketamine infusion cycle on overall medication use.
3. To determine whether establishing a prospective registry of patients undergoing ketamine cycles would be useful to enable future studies.
4. To determine whether a standardised follow-up form should be implemented for eligible patients to improve clinical practice.

Outcomes

The primary outcome was a characterisation of the treated population, treatments administered, and adverse effects observed.

The secondary outcomes were (1) Change in pain intensity after the first ketamine infusion cycle and change in opioid consumption; (2) change in overall medication burden after the first cycle; (3) feasibility and usefulness of establishing a prospective registry for future studies; (4) feasibility and usefulness of a standardised follow-up form to support clinical practice.

Data collection

Data were abstracted from the Erasme Hospital electronic database, and the Brussels Health Network, and comprised demographics, pain history, pre-cycle pharmacotherapy, infusion composition, clinical outcomes (VAS, DN4), adverse effects, and post-cycle maintenance treatments.

Ethics

The protocol was approved by the ULB–Erasme hospital–faculty ethics committee (P2024/362) on 13 February 2024. The study adhered to the

Declaration of Helsinki and applicable regulations for retrospective chart reviews.

Statistics

Continuous variables were summarised by first quartile, median, and third quartile; categorical variables by counts and percentages. Pearson correlations were calculated between DN4 or post-treatment VAS and lidocaine or ketamine. Paired t-tests and/or Wilcoxon signed-rank tests compared pre- and post-cycle variables (details reported in the Results). Analyses were conducted in R (R Core Team, 2021), version 4.2.0.

Results

Study population and baseline characteristics

Eighty-nine patients were included, of whom 65 were women (74%) and 23 men (26%). The mean age was 50 years (range, 20–86). Mean body mass index (BMI) was 26.19 ± 6.50 $kg \cdot m^{-2}$; mean weight and height were 73 kg and 167 cm, respectively. Among the available medical records, 72 patients had received multidisciplinary follow-up prior to the ketamine infusion. This fellow-up was not mandatory in our center.

Access times to ketamine infusions varied widely. The median interval from first consultation at the Erasme Pain Clinic to first infusion was 92 weeks (~1 year 9 months), while the mean was 150 weeks owing to a small number of very prolonged delays. One half of patients were infused within 92 weeks; one quarter waited more than 4 years. The overall range was 1 week to 16 years (842 weeks).

The distribution of indications for infusion was heterogeneous: fibromyalgia 25%, cervicobrachialgia 17%, lumbosciatalgia 16%, failed back surgery syndrome 10%, complex regional pain syndrome (CRPS) 9%, postoperative pain 8%, and other aetiologies 15% (Table I).

Daily oral morphine–equivalent dose decreased from a median of 28.7 mg [10–75] pre-cycle to 20 mg [0–60] post-cycle (median change −8.7 mg; p = 0.063) (Table II).

The duration per session was1 h 30 in 30 patients (35%) and 4 h in 56 patients (65%). The number of infusions in the first cycle was 3 infusions in 43% of prescriptions, 5 infusions in 34%, 4 infusions in 15%, and 2 infusions in 8%. The interval between infusions was 4 weeks in 39% of prescriptions, 2 weeks in 32%, 3 weeks in 19%, 1 week in 6%, and 5 or 6 weeks in 2% each.

Table I.

Characteristic	Overall (N=89)
N	89
Sex, n (%)	
Female	65 (74%)
Male	23 (26%)
Age, years - mean (min–max)	50 (20–86)
Height, cm - mean	167
Weight, kg - mean	73
BMI, kg/m² - mean ± SD	26.19 ± 6.50
Pain aetiology, n (%)	
Fibromyalgia	25%
Cervicobrachialgia	17%
Lumbosciatalgia	16%
Failed back surgery syndrome	10%
Complex regional pain syndrome (CRPS)	9%
Postoperative pain	8%
Other	15%
Baseline measures	
VAS at rest - median [Q1- Q3]	7 [6–8]
DN4 - median [Q1- Q3]	6 [6–7]
Number of daily medications - median [Q1-Q3]	4 [3–5]
Oral morphine equivalents, mg/day - median [Q1-Q3]	28.7 [10–75]
Pathway metric	
Time from first consultation to first infusion, weeks - median (range)	92 (1–842)

Table II.

Variable	Pre-cycle median [Q1–Q3]	Post-cycle median [Q1–Q3]	p-value
Number of daily medications	4 [3–5]	3 [2–4]	0.01361
Resting VAS	7 [6–8]	6 [5–7]	<0.001
DN4,	6 [6–7]	—	—
Median pre-cycle (mg)	28.7 [10 – 75]	20 [0 – 60]	0.063

Infusion characteristics

Among the 89 patients included, 15 (17%) received ketamine alone, while 74 (83%) were administered the ketamine–lidocaine combination; no lidocaine-only infusions were performed. The median ketamine dose was 0.3 $mg \cdot kg^{-1} \cdot h^{-1}$ (range 0.1–1.0), delivered either over 1.5 hours (35%) or 4 hours (65%). When combined with ketamine, lidocaine was infused at 2 $mg \cdot kg^{-1} \cdot h^{-1}$ (range 1–3). Each treatment cycle comprised a median of three infusions [IQR 2–5], with an inter-infusion interval of two to four weeks. Adjuvant medications were frequently administered to mitigate psychotomimetic or cardiovascular effects, including benzodiazepines (midazolam) in 62 patients (70%), clonidine in 18 (20%), and haloperidol in nine (10%), reflecting the heterogeneity of clinical practice.

Clinical outcomes

After the first cycle, 75% continued treatment and 25% discontinued. The patient-reported improvement was very good in 38%, moderate in 32%, minimal in 12%, and none in 18%. Regarding the pain intensity and medication burden, resting VAS decreased from a median of 7 [6–8] pre-cycle to 6 [5–7] post-cycle ($p < 0.001$). The number of concomitant daily medications decreased from a median of 4 [3–5] to 3 [2–4] ($p = 0.01361$). Regargind the neuropathic pain score, DN4 was 6 [6–7] at baseline; post-cycle data were insufficient to compute a median (Table II).

Adverse events

Within hours to days after infusions, the most frequently reported adverse effects were intense fatigue (33%), dizziness (19%), pain exacerbation (18%), and nausea (13%); hallucinations and tachycardia occurred in 4% each.

Discussion

This study provides a longitudinal overview of intravenous ketamine infusions, alone or combined with lidocaine, in a tertiary pain clinic over fourteen years. Beyond its descriptive value, it illustrates the gradual emergence of a structured but still heterogeneous practice in the management of refractory chronic pain.

Ketamine was administered at moderate doses (median 0.3 $mg \cdot kg^{-1} \cdot h^{-1}$), most often combined with lidocaine (2 $mg \cdot kg^{-1} \cdot h^{-1}$) and adjuvants such as midazolam or clonidine to enhance tolerability. Treatment cycles typically included three to four infusions spaced two to four weeks apart. The regimen proved feasible and well tolerated, with mainly transient adverse effects—fatigue, dizziness, and mild nausea—and no serious psychotropic or cardiovascular events. Pain intensity decreased modestly but significantly (median VAS 7 → 6), accompanied by a reduction in overall medication burden, and three quarters of patients elected to continue treatment.

When placed in the context of international recommendations, these findings support both the feasibility and acceptability of intravenous ketamine in specialised settings. The use of low-to-moderate doses, adjuvant sedation, and continuous monitoring aligns with current consensus statements. However, the diversity of infusion schedules, indications, and monitoring tools underscores the absence of a unified institutional protocol and the need for standardisation. Outcome evaluation in our cohort relied primarily on pain intensity, whereas IMMPACT guidelines advocate broader multidimensional assessment encompassing function, well-being, and patient satisfaction.

Delays between initial consultation and initiation of infusion (median 92 weeks) likely reflect the complexity of multidisciplinary care pathways. While this approach is consistent with the biopsychosocial model of chronic pain, earlier pharmacological escalation in selected profiles might improve responsiveness without compromising comprehensive management.

The main limitation of this work lies in its retrospective design and incomplete documentation, particularly of neuropathic pain scores. Yet, as an audit of real-world practice, it highlights a promising therapeutic niche and a clear need for methodological refinement. Prospective implementation of a standardised protocol, with fixed inclusion criteria, predefined

dosing schedules, and structured data collection, should enable more reliable assessment of efficacy, facilitate identification of responders, and ensure safer, evidence-based integration of ketamine and lidocaine into chronic pain management.

Conclusion

In this retrospective study of 89 patients, intravenous ketamine and/or lidocaine infusions for refractory chronic pain were associated with several signals of clinical benefit: a significant reduction in resting VAS, a decrease in the number of prescribed medications, and a high rate of treatment continuation. These findings suggest potential utility in selected patients but warrant cautious interpretation. In some cases, treatment appeal may extend beyond analgesia. Future work should incorporate structured psychobehavioural monitoring to better delineate benefit–risk profiles.

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