CONTINUOUS INFUSION KETAMINE AS ANALGESIA OR SEDATION IN MECHANICALLY VENTILATED ADULTS IN THE INTENSIVE CARE UNIT: A SCOPING REVIEW

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Introduction

Mechanical ventilation (MV) is a common and often live-saving intervention on the Intensive Care Unit (ICU). Patients requiring MV experience high mortality and morbidity. In order to facilitate this intervention, the majority of patients require medical sedation. Optimising sedation is one of the fundamentals of ICU care, and inadequate sedation (predominantly too deep) has consistently been associated with worse outcomes for patients.(1)

Ketamine is an N-methyl D-aspartic acid (NMDA) receptor antagonist that has been used since the 1970s to provide cataleptic, amnesic, analgesic, and dose dependant anaesthetic effects. Owing to it's haemodynamic profile it has become increasingly popular as an anaesthetic agent for emergency surgical procedures in hypotensive patients.(2)
Although having been around for 50 years, ketamine, particularly as a continuous infusion, has not become a routine sedative option to facilitate MV in ICU.

We conducted a scoping review designed to answer the question '***What is known about the use of ketamine as a continuous infusion to provide sedation in mechanically ventilated adults in the intensive care unit, and what gaps in the evidence exist?***'

Materials and Methods

Protocol:
The protocol was designed using the Preferred Reporting Items for Systematic Reviews and Meta-analysis extension for Scoping Reviews (PRISMA-ScR) checklist and is available as a preprint online.(3)

Inclusion criteria:
- Full text reports of mechanically ventilated patients
- Published in English (or translated to English) in a peer-reviewed journal
- Any geographical location
- Adult patients (≥18 years old)
- Mechanically ventilated on ICU
- Administration of continuous ketamine infusions for the purpose of analgesia / sedation during mechanical ventilation
- Any comparator

Initial Search

"(Ketamine) AND (Intensive Care) AND ((Sedation) OR (Analgesia))"

Data were extracted from all included publications by two independent reviewers using a specifically developed data extraction tool.

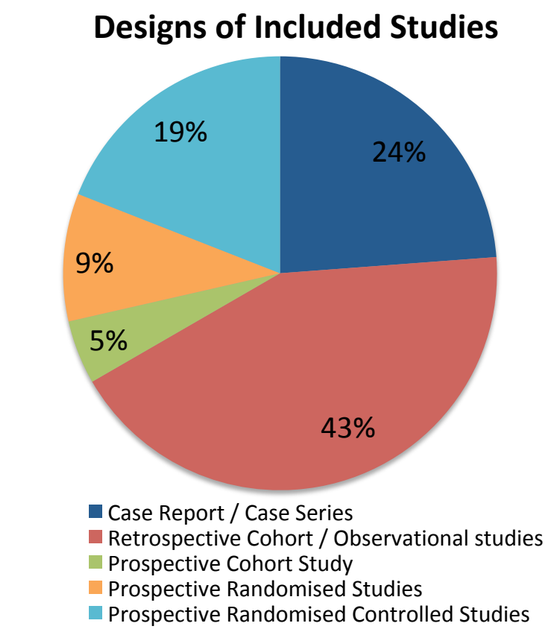

Fig. 2 – Graphical Breakdown of Methods Used in Included Studies

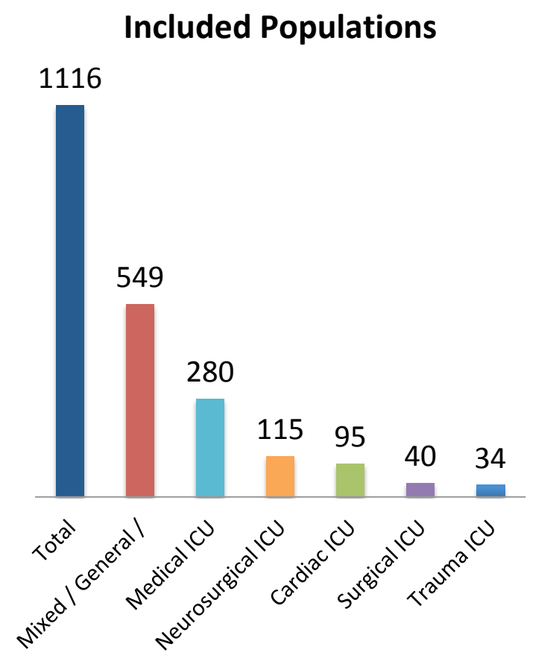

Fig. 3 – Graphical Breakdown of Included Populations

Results

- **21 articles** published between 1987 and 2021 from peer-reviewed literature were included.
- **Retrospective methods** were most common (43%) (breakdown in **Fig. 2**).
- **1116 participants** from a variety of ICU were included (breakdown in **Fig. 3**).

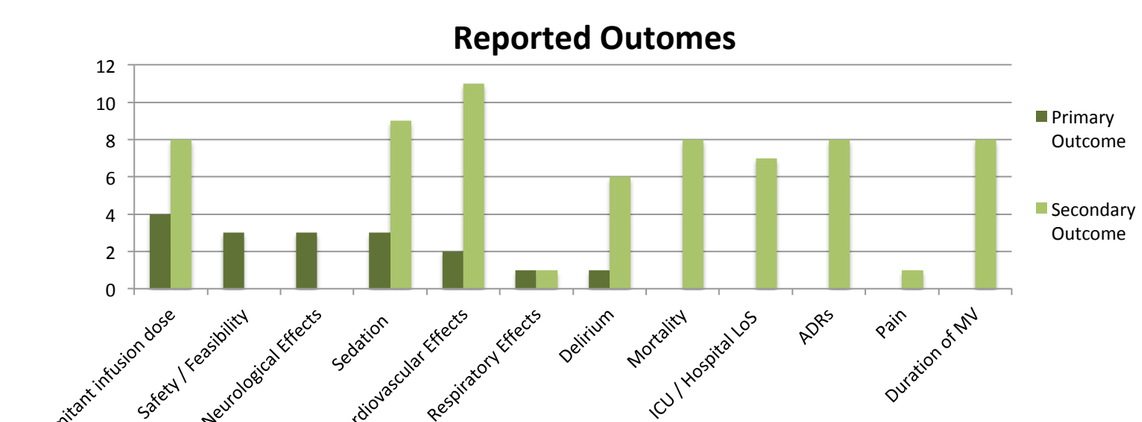

Fig. 4 – Graphical Representation of Reported Primary and Secondary Outcomes

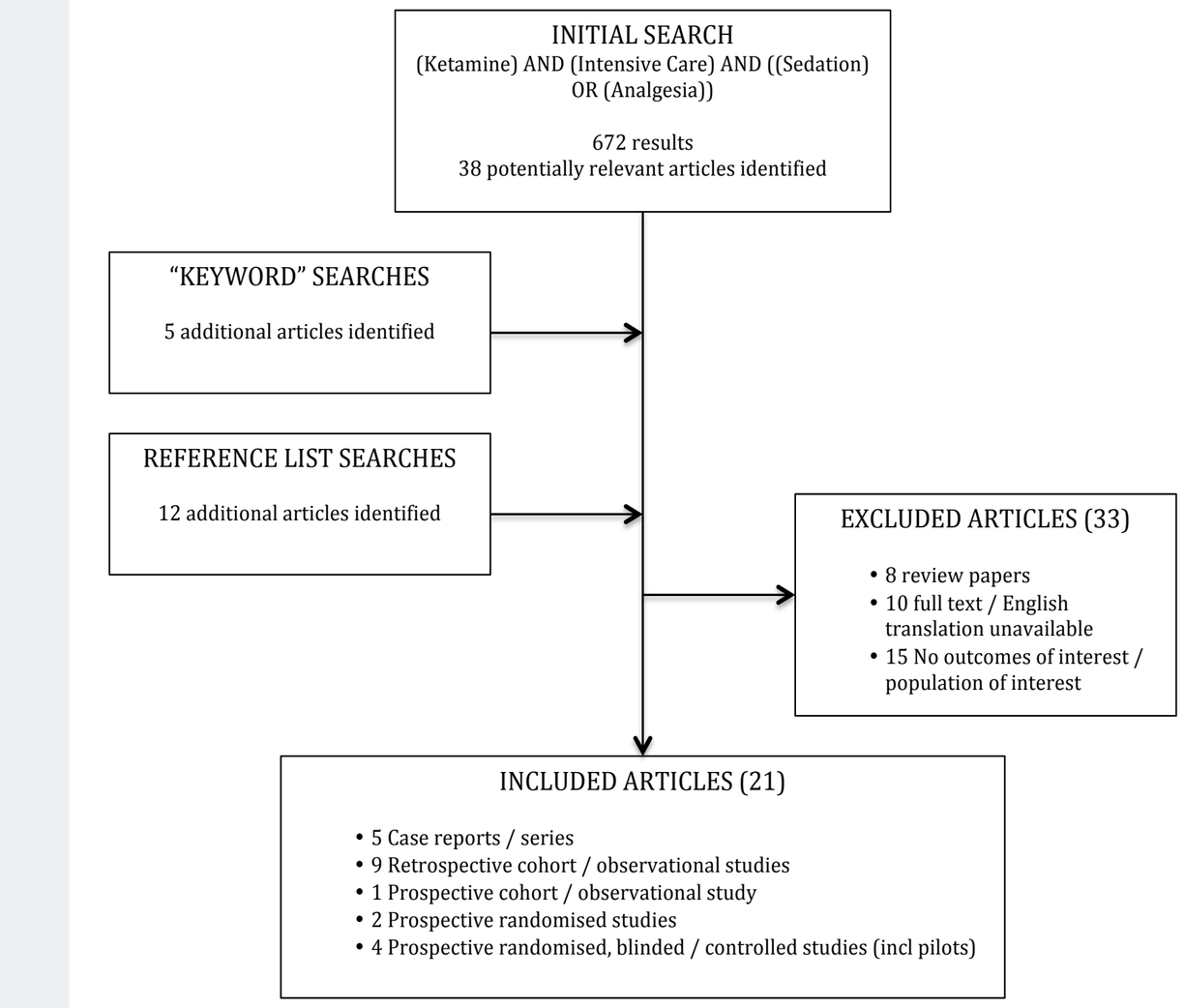

Fig. 1 – Search, Inclusion, and Exclusion Flow Diagram

- **Six studies (28.6%)** investigated ketamine as a primary sedative (71.4% using adjunctive ketamine).
- **Four studies (19%)** used a primary outcome of 'reduction in concomitant sedatives or analgesic infusions' and **three studies (14.3%)** using efficacy of sedation as the primary outcome (other reported outcomes are shown in **Fig. 4**.).
- Approximately **half of studies (52.4%)** used either a control or comparator.

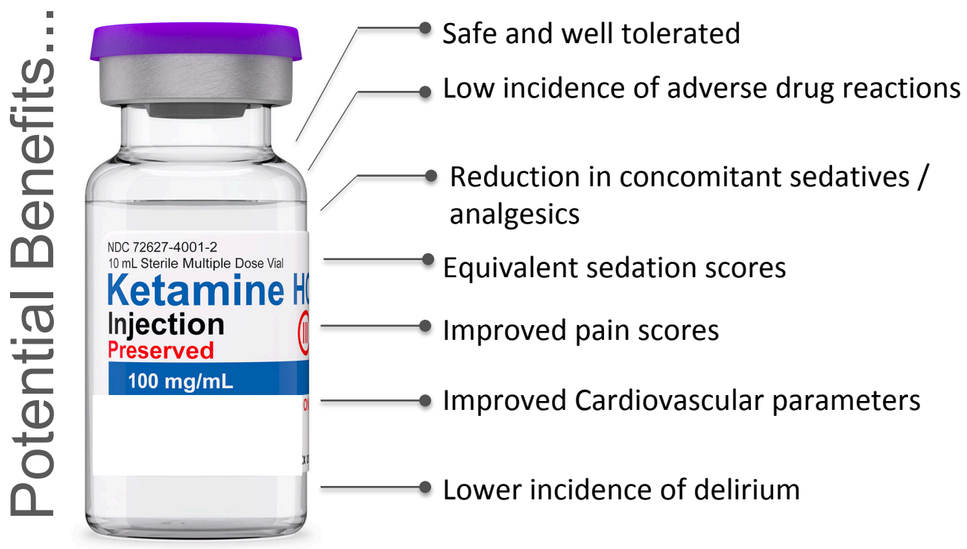

Fig. 5 – Illustration of Positive Author Findings

Discussion

We have highlighted a lack of high-quality evidence for the use of ketamine infusions as primary sedation on ICU: Of the **21 studies** included, the **majority of participants (64.4%**) were included from **retrospective cohort studies** and **only four studies (19.0%)** prospectively compared ketamine as a primary sedative to an alternative regime.

The evidence provides reassurance around the safety and use of ketamine; there were low **numbers of ADRs or SAEs recorded**, reductions in concomitant sedatives and analgesics, and reports of **improved sedation and pain scores**, as well as some reports of improved cardiovascular parameters.

Conclusion

This scoping review has identified gaps in the literature and evidence base, that could be addressed by a well-designed prospective randomised controlled trial. The next step is to design a study to address these gaps.

References

1. Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med*. 2012 Jan; 41(1):263-306. PubMed PMID: 23269131. Epub 12/28. eng.
2. Morris C, Perris A, Klein J, et al. Anaesthesia in haemodynamically compromised emergency patients: does ketamine represent the best choice of induction agent? *Anaesthesia*. 2009 May;64(5):532-9. PubMed PMID: 19413824. Epub 05/06. eng.
3. Continuous infusion ketamine as analgesia or sedation in mechanically ventilated adults in the intensive care unit: a scoping review [Preprint] https://www.researchsquare.com/article/rs-910472/v1

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