Ketamine in Status Epilepticus: How Soon Is Now?

Authors: *Giuseppe Magro MD*, Lamezia Terme Hospital, Neurology Department, Catanzaro

Introduction & background

Status epilepticus (SE) is a neurological emergency. Current evidence dictates a step-by-step approach with a first line of therapy consisting of benzodiazepines (BDZs). In many situations, the currently approved approach does not terminate a BDZ-resistant SE.

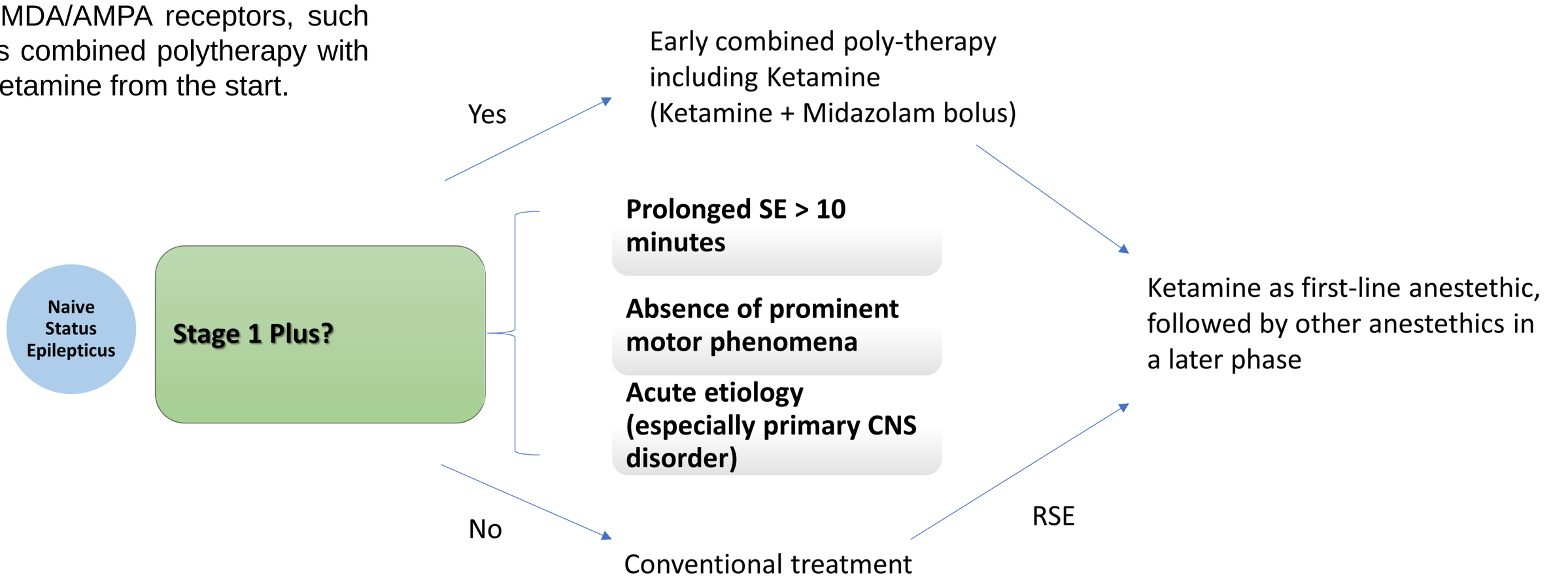
This happens in Stage 1 Plus, a framework designed by the author to recognize cases of probable benzodiazepine-resistant status epilepticus even before treatment initiation. These cases include Prolonged SE (SE lasting > 10 min), the absence of prominent motor phenomena, and acute etiology (primary central nervous system etiologies most of all). BDZ-refractory SE cases (Stage 1 Plus) might require a different approach, one targeting the unresponsive GABA signaling state mediated by NMDA/AMPA receptors, such as combined polytherapy with Ketamine from the start.

Methods

PubMed was searched with no restriction on time, including publications up to 21 April 2025. The search terms and the string used were as follows: “ketamine” AND “status epilepticus”. The research yielded 288 results. English language restriction was applied. Case reports and series with fewer than 25 patients, studies from pre-hospital settings, and super-refractory SE studies were excluded. This is due to many confounding factors and high variability of studies in out-of-hospital settings, which have substantial heterogeneity in protocols, delayed treatment documentation, and uncontrolled environments that limit interpretability. Studies on SRSE were also excluded, since Ketamine is already widely used and accepted in this context and its role is less debated. Moreover, in super-refractory cases in which Ketamine is used, many confounding factors intervene, such as numerous drugs being given before and during Ketamine infusion, making it harder to extrapolate Ketamine’s role. Consequently, only articles of Ketamine in early, established, and refractory SE were included in the analysis. Reviews and studies on animals were excluded from the primary analysis, and the output table summarizes all studies. The following variables were collected for each study: population, SE type, Ketamine timing, initial dose, infusion rate, response rate, adverse events, population group, median age, pre-existing epilepsy, and anti-seizure medication before Ketamine. Studies in which super-refractory SE and RSE patients were not differentiated were excluded and classified as having “wrong study design”. Pre-hospital works and small case series were excluded and classified as having “wrong population”. Reviews and meta-analyses were excluded and classified as being “wrong publication type”. *A total of 9 articles are included.*

Conclusions

These works of combined polytherapy bring up essential considerations: lower doses might be required to control SE with fewer adverse events. Moreover, Ketamine has the enormous advantage of preventing intubation, possibly shortening the length of stay in the intensive care unit and preventing intubation-related infections. Some conditions, such as prolonged SE (>10 min) and primary central nervous system etiologies (Stage 1 Plus), seem to require a different approach, such as combined polytherapy from the start, especially one counteracting the unbalanced networks of NMDA/GABA receptors, such as with Ketamine. This drug’s mechanism of action offers potential in restoring responsiveness to GABAergic therapies in SE. Combined polytherapy from the start, in those situations in which a loss of GABA signaling can be expected (Stage 1 Plus), might represent a better choice and possibly change the outcome and disease burden for many people. Ketamine polytherapy with first-line BDZ in the early SE stages falling in the category of Stage 1 Plus and as a first-line anesthetic infusion drug in those cases of Stage 1 Plus progressing to refractory SE might represent a more reasonable approach in cases that are probably BDZ-resistant.



DISCLOSURE & REFERENCES

The authors declare that they have no conflict of interest. The authors did not receive support from any organization for the submitted work.

(1) Magro G, Laterza V. Status epilepticus: Is there a Stage 1 plus? Epilepsia. 2024; 65: 1560–1567. https://doi.org/10.1111/epi.17953

(2) Magro G. Ketamine in Status Epilepticus: How Soon Is Now? Neurology International. 2025; 17(6):83. https://doi.org/10.3390/neurolint17060083

CONTACT INFORMATION

Giuseppe Magro, Lamezia Terme Hospital (CZ)

Correspondence: giuseppemagro.neuro@gmail.com