Case Report

Unconventional Use of Continuous Ketofol with Therapeutic Hypermagnesemia for Spasm-Free Conscious Sedation in Refractory Tetanus: First Reported Case

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Abstract

Background: Prolonged neuromuscular blockade in severe tetanus remains a major clinical challenge, often complicating ventilator weaning and exposing patients to secondary complications. We report, to our knowledge, the first PubMed-indexed use of continuous ketamine-propofol (ketofol) in tetanus and its sequential use after sustained therapeutic hypermagnesemia. A 48-year-old man with refractory generalized tetanus and dysautonomia required continuous cisatracurium for 18 days despite repeated weaning attempts. Therapeutic hypermagnesemia (serum magnesium 2-4 mmol/L) was established from day 15, followed by ketofol on day 18. Within 24 hours, cisatracurium was discontinued and spasm-free conscious sedation with hemodynamic stability was achieved. Ketofol was continued for five days, with progression to CPAP, T-piece trials, and decannulation on day 26. By facilitating earlier withdrawal of paralysis, this sequential strategy may reduce exposure to ICU-acquired weakness and pulmonary complications associated with prolonged ventilation, although causality cannot be established from a single case.

Keywords: Generalized tetanus; dysautonomia; therapeutic hypermagnesemia; ketamine-propofol; ketofol; cisatracurium; tracheostomy.

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Introduction

Tetanus is a toxin-mediated neurological disease characterized by trismus, rigidity, stimulus-induced generalized spasms, and, in severe disease, autonomic dysfunction. Management is multimodal and includes toxin neutralization, active immunization, source control, antimicrobial therapy, control of spasms and dysautonomia, airway protection, and prolonged supportive care until the effect of internalized tetanospasmin resolves.[1,2]

Benzodiazepines are commonly used for sedation and spasm control; magnesium sulfate is frequently used to attenuate autonomic overactivity and can reduce the requirement for additional antispasmodic drugs. Refractory cases may nevertheless require prolonged mechanical ventilation and continuous nondepolarizing neuromuscular blockade, making subsequent withdrawal difficult.[2,3]

Published experience supports propofol-based sedation and reports ketamine as an adjunct in tetanus, but evidence regarding their combined use specifically to facilitate withdrawal of prolonged neuromuscular blockade remains sparse. We report a case in which sustained therapeutic hypermagnesemia was established first, followed by addition of ketamine-propofol (ketofol), after which an 18-day cisatracurium infusion could be discontinued rapidly.[3]

Case Report

A 48-year-old man presented with trismus and jaw tightness after a penetrating injury to the left foot sustained approximately one week earlier while gardening. A wooden splinter had entered the foot, producing an approximately 3 × 3 cm wound, and he also reported fever. He had not received a tetanus booster during the preceding five years. At initial presentation, heart rate and blood pressure were within normal limits. The clinical picture subsequently progressed to severe generalized tetanus with recurrent painful spasms and autonomic instability.

Human tetanus immunoglobulin 500 IU was administered intramuscularly, and tetanus toxoid vaccination was initiated with a plan to complete the active immunization series at 0, 1, and 6 months. Piperacillin-tazobactam (Tazact) and metronidazole (Metrogyl) were started at presentation in recommended doses, together with wound care and debridement. Antibiotic therapy was subsequently modified according to culture and antimicrobial-susceptibility results.

Because of frequent spasms with respiratory compromise, he required endotracheal intubation and assist-control volume-

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controlled ventilation. Sedation and analgesia were provided with midazolam and fentanyl, while persistent stimulus-induced generalized spasms required continuous cisatracurium. In view of difficult weaning and anticipated prolonged ventilator dependence, tracheostomy was performed on ICU day 8.

Repeated attempts to reduce or discontinue cisatracurium were made daily or on alternate days, but each attempt precipitated recurrence of generalized spasms and autonomic instability, requiring reinstitution of the infusion. This pattern persisted for 18 days. From day 15, magnesium sulfate therapy was titrated to maintain sustained therapeutic hypermagnesemia, with a serum magnesium target of 2–4 mmol/L, under clinical and biochemical monitoring.

The prolonged ICU course was complicated by Gram-negative infections. A wound-swab culture collected on 21 May 2025 grew Escherichia coli and Enterobacter cloacae. A paired blood culture collected on 30 May 2025 grew Klebsiella pneumoniae with a carbapenem-resistant susceptibility pattern. GeneXpert Carba-R testing of the Klebsiella isolate on 2 June 2025 detected the New Delhi metallo-beta-lactamase (NDM) gene; IMP, VIM, KPC and OXA-48 were not detected. Antimicrobials were modified in accordance with culture-sensitivity findings and clinical assessment.

A body-fluid report labelled as bronchoalveolar lavage fluid documented a total leucocyte count of 1300/µL with 90% lymphocytes, 10% neutrophils and occasional red blood cells; reported glucose was 20 mg/dL, protein 2.0 mg/dL, albumin 1.0 g/dL, lactate dehydrogenase 513 U/L and adenosine deaminase 2.52 U/L. Echocardiography on 30 May 2025 showed a left ventricular ejection fraction of 55%, no regional wall-motion abnormality, trace mitral and tricuspid regurgitation, grade I diastolic relaxation abnormality, right ventricular systolic pressure of 26 mmHg, and no intracardiac clot, vegetation or pericardial effusion. NCCT head and cervical spine showed no significant abnormality.

On ICU day 18, after therapeutic hypermagnesemia had been established, ketofol was introduced. A 50-mL 1:1 admixture was prepared using 25 mL propofol containing 250 mg, 5 mL ketamine containing 250 mg, and 20 mL normal saline, yielding final concentrations of ketamine 5 mg/mL and propofol 5 mg/mL. The documented ketofol regimen consisted of a 0.3 mg/kg loading bolus followed by a maintenance infusion of 0.2–0.5 mg/kg/h, titrated to clinical response.

Within hours of ketofol initiation, cisatracurium was successfully discontinued without immediate recurrence of spasms. Within 24 hours, the patient had achieved a spasm-free state with conscious/light sedation while remaining hemodynamically stable, without recurrence of major autonomic fluctuations. The temporal sequence was interpreted as the complementary effect of established therapeutic hypermagnesemia followed by additional ketamine-propofol sedation, rather than an effect of ketofol alone.

By day 20, the patient had been successfully weaned to continuous positive airway pressure (CPAP) under mild sedation without triggering spasms or hemodynamic instability. Continuous ketofol was maintained for five days (day 18 to day 23) without clinically evident adverse effects. Over the same period, he tolerated progressive T-piece trials as sedation was gradually withdrawn. He remained free of recurrent clinically significant spasms and was decannulated on day 26.

Table 1: Clinical timeline of the ICU course

Time	Clinical course	Management/outcome
Day 0	Generalized tetanus after a 3 × 3 cm penetrating left-foot wound; trismus/jaw tightness; initial HR/BP within normal limits	TIG 500 IU IM, tetanus toxoid, wound care/debridement, piperacillin-tazobactam and metronidazole; intubation, ACVC ventilation, midazolam-fentanyl sedation and cisatracurium
Days 1–7	Persistent spasms; repeated attempts to reduce neuromuscular blockade unsuccessful	Ongoing cisatracurium and ICU support
Day 8	Difficult ventilator weaning and expected prolonged ventilator dependence	Tracheostomy performed
Day 15	Persistent refractory spasms and dysautonomia	Therapeutic hypermagnesemia established; serum Mg maintained at 2–4 mmol/L
Day 18	Ketofol added after sustained therapeutic hypermagnesemia	1:1 ketamine-propofol admixture; cisatracurium discontinued within hours without recurrent spasms
Day 20	Stable spontaneous breathing without spasm or hemodynamic deterioration	Transitioned to CPAP under mild sedation
Days 18–23	Progressive ventilator liberation	T-piece trials; ketamine gradually withdrawn over 5 days
Day 26	Sustained clinical stability	Tracheostomy decannulated
During ICU stay	Wound culture: E. coli and E. cloacae; blood culture: carbapenem-resistant K. pneumoniae; Carba-R: NDM detected	Antibiotics modified according to culture and susceptibility results

Table 2: Wound-swab culture and antimicrobial susceptibility findings

Section	Parameter	Result/interpretation	MIC (µg/mL)
Report details	Sample date	21 May 2025	Not applicable
Report details	Report date	23 May 2025	Not applicable
Report details	Sample and method	Wound swab; aerobic culture, identification and susceptibility by Vitek 2	Not applicable
Culture	Organisms isolated	Escherichia coli and Enterobacter cloacae	Not applicable
E. coli susceptibility	Amikacin	Sensitive	4
E. coli susceptibility	Gentamicin	Sensitive	<=1
E. coli susceptibility	Ciprofloxacin	Intermediate	0.5

E. coli susceptibility	Cefuroxime	Resistant	>=64
E. coli susceptibility	Ceftriaxone	Resistant	>=64
E. coli susceptibility	Cefepime	Sensitive	2
E. coli susceptibility	Ertapenem	Sensitive	<=0.12
E. coli susceptibility	Imipenem	Sensitive	<=0.25
E. coli susceptibility	Meropenem	Sensitive	<=0.25
E. coli susceptibility	Cefoperazone-sulbactam	Sensitive	<=8
E. coli susceptibility	Piperacillin-tazobactam	Sensitive	<=4
E. coli susceptibility	Amoxicillin-clavulanic acid	Sensitive	<=2
E. coli susceptibility	Co-trimoxazole	Sensitive	<=20

Note: The antimicrobial susceptibility results visible in the supplied report image pertained to Escherichia coli. Susceptibility details for Enterobacter cloacae were not visible in that image.

Table 3: Paired blood-culture and antimicrobial susceptibility findings

Section	Parameter	Result/interpretation	MIC (µg/mL)
Report details	Sample date	30 May 2025	Not applicable
Report details	Report date	2 June 2025	Not applicable
Report details	Sample and method	Paired blood; automated culture by BacT/Alert with identification and susceptibility by Vitek 2	Not applicable
Culture	Organism isolated	Klebsiella pneumoniae	Not applicable
K. pneumoniae susceptibility	Amikacin	Resistant	16
K. pneumoniae susceptibility	Gentamicin	Sensitive	<=1
K. pneumoniae susceptibility	Ciprofloxacin	Resistant	>=4
K. pneumoniae susceptibility	Levofloxacin	Sensitive	Not legible
K. pneumoniae susceptibility	Cefuroxime	Resistant	>=64
K. pneumoniae susceptibility	Ceftriaxone	Resistant	>=64
K. pneumoniae susceptibility	Cefepime	Resistant	>=32
K. pneumoniae susceptibility	Aztreonam	Intermediate	Not legible
K. pneumoniae susceptibility	Ertapenem	Resistant	>=8
K. pneumoniae susceptibility	Imipenem	Resistant	8
K. pneumoniae susceptibility	Meropenem	Resistant	>=16
K. pneumoniae susceptibility	Colistin	Intermediate	<=0.5
K. pneumoniae susceptibility	Fosfomycin	Sensitive	<=16
K. pneumoniae susceptibility	Cefoperazone-sulbactam	Resistant	>=64
K. pneumoniae susceptibility	Piperacillin-tazobactam	Resistant	>=128
K. pneumoniae susceptibility	Amoxicillin-clavulanic acid	Resistant	>=32
K. pneumoniae susceptibility	Co-trimoxazole	Sensitive	<=20

Note: MIC values for levofloxacin and aztreonam were not legible in the supplied image. The profile demonstrated carbapenem-resistant Klebsiella pneumoniae.

Table 4: GeneXpert Carba-R findings in the Klebsiella pneumoniae isolate

Report component	Test/gene	Finding
Specimen	Sample	Isolate of Klebsiella pneumoniae
Method	Assay	Cartridge-based nucleic acid amplification test (CBNAAT), real-time PCR
Carbapenemase gene	IMP	Not detected
Carbapenemase gene	VIM	Not detected
Carbapenemase gene	NDM	Detected
Carbapenemase gene	KPC	Not detected
Carbapenemase gene	OXA-48	Not detected

Interpretation: Detection of the NDM carbapenemase gene supported an NDM-producing carbapenem-resistant Klebsiella pneumoniae isolate.

Discussion

Severe generalized tetanus requires simultaneous control of toxin production and circulating toxin, suppression of spasms, management of dysautonomia, and prolonged organ support. Early airway protection and tracheostomy are often required in patients with severe spasms or prolonged ventilator dependence, and neuromuscular blocking agents remain appropriate when sedation alone cannot prevent dangerous spasms.[1,2]

A central feature of this case is the sequence of therapies. Cisatracurium could not be withdrawn during repeated daily or alternate-day trials over 18 days. Therapeutic hypermagnesemia was then established from day 15, with serum magnesium maintained at 2–4 mmol/L. This target is supported by clinical experience in tetanus: Attygalle and Rodrigo controlled spasms in most of 40 patients within a serum magnesium range of 2–4 mmol/L, and contemporary reviews continue to describe this range as a practical therapeutic target with close monitoring.[3,10]

Magnesium is mechanistically relevant because it antagonizes calcium-dependent neurotransmission, reduces catecholamine release, produces presynaptic neuromuscular effects, and may attenuate both skeletal-muscle spasm and autonomic

overactivity. Importantly, the randomized trial by Thwaites et al. did not show a reduction in the need for mechanical ventilation or mortality, but magnesium significantly reduced requirements for midazolam and pipecuronium and reduced the need for verapamil to control cardiovascular instability. These data support magnesium as an adjunct rather than a stand-alone definitive therapy.[3,11]

Propofol has previously been used during prolonged treatment of severe tetanus. Orko et al. reported long-term propofol and midazolam infusions with vecuronium, whereas Borgeat et al. demonstrated a rapid reduction in spontaneous electromyographic muscle activity after propofol boluses without impairment of evoked neuromuscular transmission, supporting a central antispasmodic effect. Peduto et al. similarly emphasized that sedation, autonomic control, and paralysis should be viewed as complementary components of treatment.[4–6]

Ketamine itself is not novel in tetanus: Obanor et al. reported ketamine as an adjunct for breakthrough spasms refractory to diazepam in generalized cephalic tetanus. Propofol has likewise been reported separately in severe tetanus. However, to our knowledge, no prior PubMed-indexed report has described continuous ketamine-propofol (ketofol) in tetanus or its sequential addition after sustained therapeutic hypermagnesemia specifically to facilitate withdrawal of prolonged neuromuscular blockade. The novelty of the present case therefore lies in this sequential regimen rather than in the use of either component alone.[4-7]

Several complementary pharmacologic properties provide a plausible explanation for the observed rapid response. Magnesium reduces neuromuscular excitability by antagonizing calcium-dependent transmitter release at the neuromuscular junction and attenuates catecholamine release, thereby addressing both spasms and dysautonomia. Propofol provides centrally mediated sedation and has demonstrated a rapid central antispasmodic effect in severe tetanus without impairing evoked neuromuscular transmission. When added to an established background of therapeutic hypermagnesemia, these effects may have acted additively to suppress residual tetanic activity. Ketamine contributes analgesic and sedative effects and, in general anesthesia studies, its cardiostimulant actions have been shown to counterbalance the cardiodepressant effects of propofol, providing a pharmacologic rationale for the observed hemodynamic stability; however, such evidence cannot be directly extrapolated to prolonged ICU sedation in tetanus.[3,5,8,10,11]

Although causality cannot be established from a single observation, the close temporal association is clinically relevant: repeated attempts to withdraw cisatracurium failed for 18 days, whereas after therapeutic hypermagnesemia had been established and ketofol was added on day 18, neuromuscular blockade was discontinued within 24 hours and spasm-free conscious sedation was achieved. The patient subsequently progressed to CPAP, T-piece trials, cessation of ketofol after five days, and decannulation on day 26. This sequential approach may represent a pragmatic option when conventional attempts to discontinue prolonged neuromuscular blockade have failed. By potentially shortening exposure to paralysis and prolonged ventilation, it may also reduce downstream risks such as ICU-acquired weakness and secondary pulmonary complications, although this potential benefit requires prospective evaluation.[12]

Several limitations must temper interpretation. This is a single case without a comparator, and improvement could have reflected the natural time course of tetanus, cumulative effects of magnesium and other sedatives, infection control, or other concurrent ICU interventions. The pharmacological interaction between therapeutic hypermagnesemia and ketofol was not formally tested; therefore, the observed response should be described as sequential and complementary rather than as proven synergy. The absence of clinically evident ketofol-related adverse effects over five days is reassuring but cannot establish safety in other patients. Further case accumulation and prospective evaluation are required before this strategy can be recommended routinely.

Conclusion

Sustained therapeutic hypermagnesemia followed by the addition of continuous ketamine-propofol (ketofol) enabled successful discontinuation of cisatracurium within 24 hours after 18 days of continuous neuromuscular blockade in refractory generalized tetanus with dysautonomia. The patient achieved a spasm-free state with conscious sedation while remaining hemodynamically stable. Ketofol was continued for five days without clinically evident adverse effects, allowing progressive ventilator liberation and decannulation on day 26. To our knowledge, this is the first PubMed-indexed report of continuous ketofol in tetanus and the first description of its sequential combination with therapeutic hypermagnesemia. By facilitating earlier withdrawal of neuromuscular blockade, this unconventional sequential approach may help reduce the risks of ICU-acquired weakness and secondary pulmonary complications associated with prolonged paralysis and ventilation. Although causality cannot be confirmed from a single case, the rapid temporal association is clinically relevant and warrants further evaluation in similarly refractory cases.

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Conflicts of interest

There are no conflicts of interest.

References

1. Sudarshan R, Sayo AR, Renner DR, et al. Tetanus: recognition and management. Lancet Infect Dis. 2025;25(11):e645-e657. doi:10.1016/S1473-3099(25)00292-0.
2. Karnad DR, Gupta V. Intensive care management of severe tetanus. Indian J Crit Care Med. 2021;25(Suppl 2):S155-S160. doi:10.5005/jp-journals-10071-23829.
3. Rodrigo C, Fernando D, Rajapakse S. Pharmacological management of tetanus: an evidence-based review. Crit Care. 2014;18(2):217. doi:10.1186/cc13797.
4. Orko R, Rosenberg PH, Himberg JJ. Intravenous infusion of midazolam, propofol and vecuronium in a patient with severe tetanus. Acta Anaesthesiol Scand. 1988;32(7):590-592. doi:10.1111/j.1399-6576.1988.tb02791.x.

5. Borgeat A, Dessibourg C, Rochani M, Suter PM. Sedation by propofol in tetanus—is it a muscular relaxant? Intensive Care Med. 1991;17(7):427-429. doi:10.1007/BF01720683.
6. Peduto VA, Pisanu GM, Piga M. Midazolam, propofol, and clonidine for sedation and control of autonomic dysfunction in severe generalized tetanus. Minerva Anestesiol. 1993;59(4):171-178.
7. Obanor O, Osazuwa HO, Amadasun JEO. Ketamine in the management of generalised cephalic tetanus. J Laryngol Otol. 2008;122(12):1389-1391. doi:10.1017/S0022215107001223.
8. Hui TW, Short TG, Hong W, Suen T, Gin T, Plummer J. Additive interactions between propofol and ketamine when used for anesthesia induction in female patients. Anesthesiology. 1995;82(3):641-648. doi:10.1097/00000542-199503000-00005.
9. Ghojazadeh M, Sanaie S, Paknezhad SP, Faghih SS, Soleimanpour H. Using ketamine and propofol for procedural sedation of adults in the emergency department: a systematic review and meta-analysis. Adv Pharm Bull. 2019;9(1):5-11. doi:10.15171/apb.2019.002.
10. Attygalle D, Rodrigo N. Magnesium as first line therapy in the management of tetanus: a prospective study of 40 patients. Anaesthesia. 2002;57(8):811-817. doi:10.1046/j.1365-2044.2002.02698_6.x.
11. Thwaites CL, Yen LM, Loan HT, et al. Magnesium sulphate for treatment of severe tetanus: a randomised controlled trial. Lancet. 2006;368(9545):1436-1443. doi:10.1016/S0140-6736(06)69444-0.
12. Vanhorebeek I, Latronico N, Van den Berghe G. ICU-acquired weakness. Intensive Care Med. 2020;46(4):637-653. doi:10.1007/s00134-020-05944-4.