

NEWS, VIEW, & REVIEWS

The Utilization of Ketamine for Patients With Challenging Pruritus: An Evidenced-Based Overview

Chapman Wei BS,^{a,c} Theodore Quan BS,^a Eric Heinz MD,^b Paul Dangerfield MD,^b Adam J. Friedman MD FAAD^c

^aGeorge Washington University School of Medicine and Health Sciences, Washington, DC

^bDepartment of Anesthesiology & Critical Care Medicine, George Washington University School of Medicine and Health Sciences, Washington, DC

^cDepartment of Dermatology, George Washington University School of Medicine and Health Sciences, Washington, DC

Pruritus can heavily impact one's quality of life, especially when conventional treatments fail to adequately provide relief.¹ Ketamine is a *N*-methyl-D-aspartate receptor inhibitor that modulates pain-fiber signaling.² This review provides a concise summary of the evidence supporting the use of ketamine for chronic or recalcitrant pruritus treatment.

Most studies investigated compounded variations of topical ketamine with other antipruritic agents. In two case reports, applying topical 0.5%-ketamine/1%-amitriptyline cream to affected areas two to four times daily for recalcitrant brachioradial pruritus provided moderate to complete pruritus relief within minutes.^{3,4} Treatment durations ranged from four weeks to four years. Tightness of topically-applied areas were observed, but no systemic adverse effects were recorded.⁴ In another case report, one patient's recalcitrant post-herpetic-associated pruritus was moderately relieved with adjunctive topical 0.5%-ketamine/2%-amitriptyline gel.⁵ Jaller and colleagues published a case report showing complete relief of inflammatory linear verrucous epidermal nevus-associated pruritus using topical 10%-ketamine/5%-amitriptyline/5%-lidocaine (TKAL) applied one to three times daily for six weeks.⁶ However, this dose should be cautiously used when applying to large areas in young and elderly patients with skin barrier dysfunction because systemic absorption may result in neurologic consequences, such as toxic encephalopathy in a case report published by Cardis and colleagues.⁷

A retrospective analysis of 16 patients using topical 0.5%-ketamine/1%-2%-amitriptyline applied one to five times daily significantly relieved patients' neuropathic and non-specified pruritus without systemic adverse effects after an average treatment of ten months.² Similarly, a retrospective analysis of 96 patients with neuropathic pruritus, atopic dermatitis, and chronic pruritus following topical 5-10%-ketamine/5%-amitriptyline/5%-lidocaine applied one to three times daily significantly relieved patients' pruritus within minutes.⁸ One patient reported dizziness and few reported topically-applied side effects.

Few studies have published on the use of intravenous ketamine for treating pruritus. One review recommended a dose of 0.5mg/kg as for treating recalcitrant neuropathic pruritus.⁹ A case series following two patients with recalcitrant erythro-

dermia-associated and chronic lymphatic leukemia-associated pruritus were treated with single doses of 7.5-8mg/day ketamine resulting in moderate pruritus relief with no adverse effects.¹⁰ Similarly, a case report published the use of intravenous ketamine for treating lichen sclerosus-associated neuropathic pain.¹¹ Ketamine was infused for 4 hours/day and titrated from 200mg to 800mg for five days, resulting in significant analgesia. Since lichen sclerosus can be pruritic, ketamine may be useful for treating the lichen neuropathic pain and pruritus associated with this inflammatory disease.

In conclusion, ketamine can be a practical option used to treat challenging types of pruritus when conventional therapies fail. Although systemic side effects are rare, one should be aware and monitor for signs of systemic ketamine toxicity.

Disclosure

Authors declare no conflicts of interest.

References

- Grundmann S, Ständer S. Chronic pruritus: clinics and treatment. *Ann Dermatol*. 2011;23(1):1–11. doi:10.5021/ad.2011.23.1.1
- Poterucha TJ, Murphy SL, Sandroni P, et al. Topical amitriptyline combined with topical ketamine for the management of recalcitrant localized pruritus: a retrospective pilot study. *J Am Acad Dermatol*. 2013;69(2):320–1. doi: 10.1016/j.jaad.2013.03.013.
- Poterucha TJ, Murphy SL, Davis MD, et al. Topical amitriptyline-ketamine for the treatment of brachioradial pruritus. *JAMA Dermatol*. 2013;149(2):148–50. doi: 10.1001/2013.jamadermatol.646.
- Magazin M, Daze RP, Okeson N. Treatment refractory brachioradial pruritus treated with topical amitriptyline and ketamine. *Cureus*. 2019;11(7):e5117. doi: 10.7759/cureus.5117.
- Griffin JR, Davis MD. Amitriptyline/ketamine as therapy for neuropathic pruritus and pain secondary to herpes zoster. *J Drugs Dermatol*. 2015;14(2):115–8.
- Jaller JA, Yosipovitch G. Successful treatment of epidermal nevus-associated pruritus with topical ketamine-amitriptyline-lidocaine. *Acta Derm Venereol*. 2018;98(1):121–122. doi: 10.2340/00015555-2811.
- Cardis MA, Pasieka HB. Safety of topical neuromodulators for the treatment of pruritus. *JAMA Dermatol*. 2016;152(12):1390–1391. doi: 10.1001/jamadermatol.2016.3118.
- Lee HG, Grossman SK, Valdes-Rodriguez R, et al. Topical ketamine-amitriptyline-lidocaine for chronic pruritus: A retrospective study assessing efficacy and tolerability. *J Am Acad Dermatol*. 2017;76(4):760–761. doi: 10.1016/j.jaad.2016.10.030.
- Mittal A, Vyas K. Drug treatment of pruritus and systemic origin. *Indian J Dermatol*. 2018;4(2):52–56. doi: 10.4103/ijdd.ijdd_39_18
- Fischer M, Steinborn A. Therapy-resistant erythrodermia-related pruritus: effective treatment with ketamine hydrochloride. *Arch Dermatol*. 1999;135(10):1274–5. doi: 10.1001/archderm.135.10.1274
- Hanna AF, Armstrong JS, Smith AJ. Effects of intravenous ketamine infusions in a neuropathic pain patient with lichen sclerosus et atrophicus. *Case Rep Dermatol*. 2016;8(2):164–170. Published 2016 Jun 6. doi:10.1159/000446528

AUTHOR CORRESPONDENCE

Adam J. Friedman MD FAAD

E-mail: ajfriedman@mfa.gwu.edu