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Ketamine for Rapid Sequence Intubation

Introduction

Rapid sequence intubation (RSI) is the most common method for emergency airway management, involving administration of a sedative induction agent and neuromuscular blocking agent in rapid succession to facilitate endotracheal intubation.

Ketamine and etomidate are the most commonly used induction agents for RSI due to their favorable hemodynamic profiles. While etomidate has historically been preferred, ketamine has gained renewed interest as an alternative. Etomidate causes reversible adrenal suppression even after a single dose, with significantly higher rates of adrenal insufficiency compared to ketamine (OR 6.7). This is particularly concerning in septic patients where adrenal function is critical.

Recent large observational studies suggest ketamine may be associated with improved mortality outcomes compared to etomidate in critically ill patients. The RSI Trial (NCT05277896) is an ongoing multicenter RCT expected to provide definitive evidence in 2025.

PHARMACOLOGY		
	Crotalidae Polyvalent Immune Fab (Ovine) **(*Crofab*®)**	Crotalidae Immune F(ab')2 (Equine) **(*Anavip*®)**
Mechanism of Action	Fab fragment of IgG antibody isolated from sheep serum; antibody binds to venom and removes it from tissue	$F(ab')_2$ fragment of IgG antibody isolated from horse serum; antibody binds to venom and removes it from tissue

Dose	• Initial Dose
	  ○ **Progressing tissue/hematologic effects: 4 – 6 vials**
	  ○ **Systemic effects including shock: 8 – 12 vials**
	  ▪ May repeat every hour as needed until initial control of local, hematological, and systemic symptoms is achieved
	• Maintenance: 2 vials q6h x 3 after control is achieve
		• **Initial dose: 10 vials**
		  ○ May repeat every hour as needed until initial control of local, hematological, and systemic symptoms is achieved
		• Maintenance: 4 vials as needed; may administer for any re-emerging symptoms

Administration	• Inject ≥18 mL NS (or SWFI) into each vial; more volume will speed up dissolution • **Gently swirl or roll vials in hand or combine all vials in bag to roll simultaneously; DO NOT SHAKE** • Add/QS solution to 250 mL bag of NS admin over 1 hour • NOTE: Many clinicians choose a slower initial rate to allow for assessment of allergic reaction	• **Reconstitute each vial with 10 mL NS** • **Gently swirl or roll vials in hand or combine all vials in bag to roll simultaneously; DO NOT SHAKE** • Solution should be clear to yellow/green and opalescent; do not use if otherwise discolored • Add/QS solution to 250 mL bag of NS • Administer total volume over 1 hour • NOTE: Many clinicians choose a slower initial rate to allow for assessment of allergic reaction
Formulation	**IV only; each box contains 2 vials (~$5000/box)**	**IV only; each vial costs ~$1220**
PK/PD	T½: 12 – 23 hours	T½: ~5.5 days
Adverse Effects	• Hypersensitivity reactions ranging from pruritus/urticaria to anaphylaxis • Serum sickness (rare)	• Nausea (23%), arthralgia (11%), peripheral edema (8%) • Hypersensitivity reactions ranging from pruritus/urticaria to anaphylaxis • Serum sickness (rare)
Drug Interactions	No known drug interactions	No known drug interactions

Overview of Evidence			
Author, year	**Design/ sample size**	**Intervention & Comparison**	**Outcome**
Dart RC, 1997	Prospective, multicenter trial (n = 11)	Patients received 4 vials of *Crofab*® for initial control of symptoms following minimal or moderate crotalid envenomation	**Ten of 11 patients were deemed to have a clinical response and reduction in snakebite** severity score; one patient required 4 addition vials
Dart RC, 2001	Multicenter, randomized, prospective, open-label trial	Initial 6 vials of *Crofab*® patients were randomized to receive either 2 vials	**No statistical difference between groups in snakebite severity score**;

Compatibility	NS or SWFI for reconstitution; NS for infusion	NS
Comments	**Approved for treatment of any North American crotalid envenomation**	**Recently approved any North American crotalid envenomation**

	(n = 31)	PRN vs 2 vials Q6h x 18 hours	Overall severity was reduced from 4.35 to 2.39 ($p < 0.001$)
Boyer LV, 2013	Phase 2, RCT for rattlesnake bites in Tuscon, AZ (n = 12)	*Crofab*® vs *Anavip*® for reduction in serum venom levels at various pre-defined times following crotalid envenomation	Venom levels were **insignificantly lower** following initial control in the *Crofab*® group, but **significantly lower following maintenance and during follow-up** in the *Anavip*® group ($p = 0.004$); No difference between groups in safety outcomes
Bush SP, 2015	RCT at 18 sites in the US (n = 123)	*Crofab*® vs *Anavip*® for the prevention of late coagulopathy following crotalid envenomation	**More patients in the Crofab® group vs the Anavip group ® experienced late coagulopathy versus** • 29.7% vs 10.3% • $p < 0.05$, NNT = 5
Gerardo CJ, 2017	RCT in 18 ED in the US (n = 74)	*Crofab*® versus placebo to measure limb function 14 days after envenomation using Patient-Specific Functional Scale	**Crofab reduced limb disability** measured by the Patient-Specific Functional Scale 14 days after copperhead envenomation. • 8.6 in the treatment group vs 7.4 in the control group (95% CI 0.1 – 2.3; $p = 0.04$)
Gerardo CJ, 2020	Post-hoc analysis (N=21)	Group 1: Anavip 10 Vials + Anavip 4 vials q6 x 3 Group 2: Anavip 10 vials + Placebo Group 3: Crofab 5 vials + 2 vials q6h x 3	In Copperhead bites (n=21) there was no difference between Anavip® and Crofab® in o Time to achieve initials control o Patient requiring PRN or unscheduled doses

Conclusions

Ketamine and etomidate appear comparable for achieving initial intubation success during RSI, with no significant difference in first-pass success rates between agents.
Recent large observational studies (>1.6 million patients) suggest etomidate may be associated with higher in-hospital mortality compared to ketamine (adjusted OR 1.28), independent of subsequent corticosteroid use.
Etomidate causes adrenal suppression even after a single dose (OR 6.7 vs ketamine). Ketamine should be strongly considered in patients with sepsis or at risk for adrenal insufficiency.

References

1. DeMasi SC, et al. Protocol for the RSI Trial. medRxiv. 2025. doi:10.1101/2025.01.18.25320768
2. Wollenman LC, et al. Ketamine vs Etomidate and PTSD Symptoms at 12 Months. CHEST Crit Care. 2025;3(2). doi:10.1016/j.chstcc.2025.100136
3. Maia IWA, et al. Ketamine, Etomidate, and Mortality in ED Intubations. JAMA Netw Open. 2025;8(12):e2548060. doi:10.1001/jamanetworkopen.2025.48060
4. Wunsch H, et al. Etomidate vs Ketamine and Mortality in Critically Ill Patients. Am J Respir Crit Care Med. 2024;210(10):1243-1251. doi:10.1164/rccm.202404-0813OC
5. Koroki T, et al. Ketamine vs Etomidate: A Bayesian Meta-analysis. Crit Care. 2024;28(1):48. doi:10.1186/s13054-024-04831-4
6. Kim J, et al. Ketamine vs Etomidate for RSI in Trauma Patients. BMC Emerg Med. 2023;23(1):57. doi:10.1186/s12873-023-00833-7
7. Engstrom K, et al. Pharmacotherapy Optimization for RSI in the ED. Am J Emerg Med. 2023;70:19-29. doi:10.1016/j.ajem.2023.05.004

8. Sharda SC, et al. Etomidate vs Ketamine for RSI: Systematic Review. Indian J Crit Care Med. 2022;26(1):108-113. doi:10.5005/jp-journals-10071-24086
9. Stanke L, et al. Hemodynamic Effects of Ketamine vs Etomidate for Prehospital RSI. Air Med J. 2021;40(5):312-316. doi:10.1016/j.amj.2021.05.009
10. Jabre P, et al. Etomidate vs Ketamine for RSI: Multicenter RCT. Lancet. 2009;374(9686):293-300. doi:10.1016/S0140-6736(09)60949-1
11. Ketamine. Lexi-Drugs. Lexicomp. Wolters Kluwer Health. Available at: http://online.lexi.com. Accessed February 2026.
12. Etomidate. Lexi-Drugs. Lexicomp. Wolters Kluwer Health. Available at: http://online.lexi.com. Accessed February 2026.
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