Pharmacy Friday

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Esmolol in refractory Ventricular fibrillation Cardiac Arrest

Introduction

1. Refractory ventricular fibrillation (RVF) is a severe form of electrical storm in which rapidly clustering episodes of ventricular fibrillation (VF) recur or persist after multiple defibrillation attempts, precluding any period of sustained return of spontaneous circulation (ROSC
2. In RVF, there are recommendations outlined in the American Heart Association Advanced Cardiac Life Sup-port (ACLS) guidelines, however mortality remains high in this condition.
3. While the activation of alpha-1 receptors by adrenaline (epinephrine) causes vasoconstriction and increased coronary perfusion pressure, the activation of B-1and B-2 receptors has deleterious effects by increasing myocardial oxygen requirements, worsening ischemic injury, lowering the VF threshold, and worsening post-resuscitation myocardial function.
4. Blocking B-adrenergic receptors has shown promise in terminating electrical storm in recent animal and human trials

Pharmacology	
	Esmolol (Brevibloc)
Dose	• **Loading dose**: 500 mcg/kG • IV Infusion: 0-100 mcg/kg/min
Administration	• IV infusion with bolus from bag or vial
Formulation	• **IV premix bag**: 2500 mg/250 ml or 2000 mg/100 ml • **IV Vial**: 100 mg/10 ml
PK/PD	• **Onset:** 2-10 minutes (quickest when loading dose used) • **Peak:** ~ 5 minutes • **Duration:** 10-30 minutes • **Metabolism:** primarily by esterase in blood • **Elimination:** 1-2% eliminating in the urine
Adverse Effects	• Bradyarrhythmias • Hypotension • Infusion site reaction • Nausea + vomiting
Drug Interactions and warnings	• Drug interaction: Rivastigmine, calcium channel blockers, beta blockers • Warning: Extravasation can lead to skin necrosis and sloughing
Compatibility	• Antibiotics: acyclovir, ciprofloxacin • Dexamethasone, barbituates, • Diazepam, furosemide, milrinone

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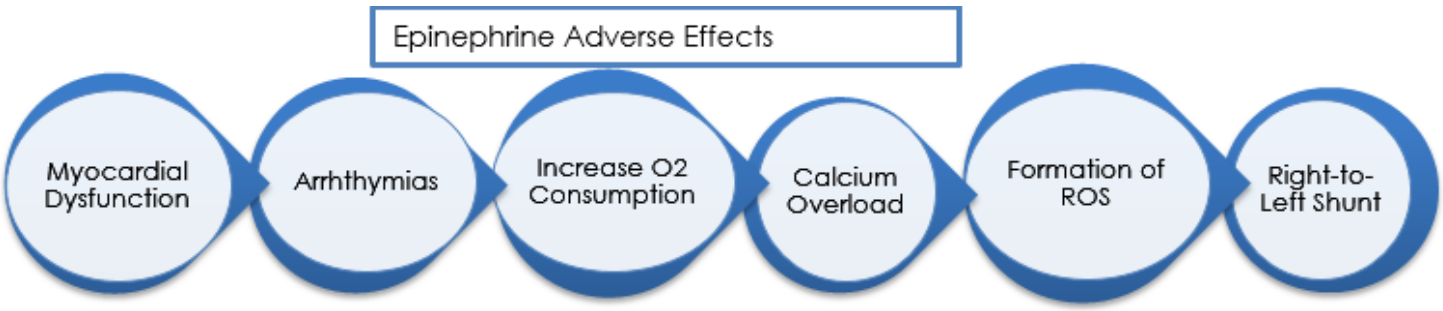

Overview of Evidence			
Author, year	Design & Sample size	Intervention & Comparison	Outcome
Lee, 2016	Single center observation n= 41	Loading dose 500 mcg/kg ↓ 0-100 mcg/kg/min infusion	↑ **(ROSC)** with esmolol **(56% vs16%)** ↑ **Survival and good neurological** outcomes with esmolol
Boehm, 2016	Case report/ n=1	80 mg IVP→100 mcg/kg/min infusion	ROSC and discharge with **good neurological** outcome
Driver, 2014	Retrospective analysis n=25	Loading dose 500 mcg/kg ↓ 0-100 mcg/kg/min infusion	↑ **Temorary ROSC (67% vs 42%)** ↑ **sustained ROSC (66% vs 32%)** ↑ **ICU admission (66% vs 32%)** **Survival to hospital D/c (50% vs 16%)** **Favorable neuro outcome (50% vs 11%)**
Bassiakou, 2008	Animal study n=20	Epinephrine 0.02 mg/kg Vs Epinephrine + atenolol (0.02 mg/kg) (0.05 mg/kg)	↑ **ROSC with epi+ atenolol (90% vs 40%)** ↑ **Aortic SBP, DBP, CPP with Epi+atentolol** ↓ **Post-resuscitation HR with Epi+atentolol**
Killingsworth, 2004	Animal study n=16	Epinephrine 0.01 mg/kg + placebo vs Epinephrine 0.01 mg/kg + Esmolol 1 mg/kg IV	Esmolol improved **ROSC** and 4-hour survival
Ditchey, 1994	Animal Study (dog) n=22	Epinephrine (0.015 mg/kg) vs Epinephrine + propranolol (0.015 mg/kg) (2 mg/kg)	↑ Coronary perfusion pressure in Epi + propanol ↑ successful defibrillation in epi + propranolol

Conclusions

Esmolol represents a possible adjunct treatment for patients with refractory VF. Studies to date do not demonstrate a clear improvement in patient centered outcomes but, this study does show a promising increase in ROSC. The results of the studies above need to be validated in larger, prospective trials with good neurologic function as primary endpoint.

References

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