Title: Efficacy and safety of prehospital diltiazem to treat rapid ventricular response associated with atrial fibrillation and atrial flutter.

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Clinical Scenario: You respond to a patient complaining of heart palpitations generalized weakness and dizziness. Upon completion of your assessment you have determined that your patient has a history of cardiac risk factors and appears to have developed atrial fibrillation with an uncontrolled rapid ventricular response. The patient currently has no associated chest pain or signs of cardiac failure and their vitals include a tachycardia and a stable blood pressure. Following current protocols treatment for this patient would be supportive in nature until they began to become unstable at which point you would move to electrical cardioversion. Another treatment, however, could be the use of diltiazem in order to reduce rapid ventricular response before the patient began destabilizing and therefore avoid complication of cardiogenic shock as well as any adverse effects of electrical cardioversion.

PICO (Population-Intervention-Comparison-Outcome) Question:

Should patients presenting to Advanced Care Paramedics with stable atrial fibrillation/flutter with rapid ventricular response (Heart Rate > 150) and in the absence of contraindications receive 0.25mg/kg to a maximum 20mg of Diltiazem as opposed to supportive care in order to decrease likelihood of clinical deterioration?

Search Strategy: "prehospital and atrial fibrillation or atrial flutter and diltiazem and safety"

Search Outcome: 81 hits

Relevant Papers:

Author, Date	Population Characteristics	Design	Outcomes	Results	Strengths/ Weaknesses
Rodriguez A, 2019	197 patients total who were given Diltiazem by Orange Country EMS over 2 years. Protocol aimed to treat patients with no signs of shock, a-fib and RVR with HR > 150 and SBP > 90mmHg. 131 administrations were within this protocol and 66 were not.	A Retrospective Cohort Study.	To measure rates of clinical improvement, defined as a drop in HR of 20% or rates of HR lowered below 100, and rates of adverse events across protocol compliant (PC) and non-compliant (NC) administrations.	<u>Averse events:</u> PC – 8% NC – 18% Total – 11% P Value .033 <u>Final HR < 100:</u> PC – 31% NC – 35% Total – 32% P Value .628 <u>HR Decreased 20%:</u> PC – 47% NC – 19% Total – 38% P Value .002	<u>Strengths:</u> - Pertinent Definitions of appropriate administration and clinical improvement - Follow up interpretation of EKGs by physicians showed 92% agreement with a P Value < .001 - Breakdowns of protocol compliance helps show effectiveness and safety of the protocols criteria in a prehospital setting <u>Weaknesses:</u> - No control group or comparison treatment to Diltiazem

				Clinical Improvement: PC – 63% NC – 46% Total – 58% P Value .031	- Observational retrospective study of one service and cannot be generalized.
Fromm C, 2015	Patients were >18 years old with atrial fibrillation or atrial flutter and a ventricular rate of 120bpm or greater and systolic BP 90 mm Hg or greater. 54 patients recruited 25 randomized to Diltiazem 29 Randomized to Metoprolol One of each group Excluded post administration due to a lack of cooperation and an unblinding of the study respectively.	A Prospective, Randomized, Double-Blind study to compare the effectiveness of intravenous metoprolol 0.15 mg/kg to a max of 10mg vs. diltiazem 0.25mg/kg to a max of 30mg	Efficacy was measured by HR < 100 within 30 min of drug administration and patients were monitored at 0, 5, 10, 15, 20, 25, and 30 min after administration. Safety was measured as HR < 60bpm and SBP <90 mm Hg.	At five minutes: 50.0% of diltiazem and 10.7% of metoprolol patients had reached <100bpm, P Value < 0.005 At thirty minutes: 95.8% of diltiazem and 53.6% of metoprolol patients had reached <100bpm, P Value < 0.0001 The was no conclusive difference in the safety between the two medications Bradycardia occurred in 1 diltiazem patient P value 0.462 and Hypotension occurred in 5 metoprolol patients and 1 diltiazem patient P value 0.199.	Strengths: -Double Blind study help show the effectiveness of one medication over another in a setting where options for both would not be accessible to the provider to consider based on assessments. - Randomization produced no significant difference between to two groups regarding previous medical history that may have effected results. Weaknesses: -The dosage of metoprolol used in this study followed the ACLS guidelines and was less than some studies state would be safe whereas the diltiazem dosage was based on current manufacturer recommendations. - Convenience sampling of participants may have introduced bias based on time of day and local EMS prehospital administration of diltiazem.
Salerno DM, 1989	Patients were >18 years old with atrial fibrillation or flutter and a RVR >119 bpm and were without exclusion criteria of advanced CHF hypotension or 2nd and 3rd degree heart blocks 113 patients enrolled 57 randomized to placebo 56 randomized to diltiazem	A Randomized Double-blind placebo trial. Patients were evaluated at baseline, then randomized to receive either first doses of a placebo or of 0.25mg/kg of diltiazem. If the had	The patients were monitored at the 2, 7, 12, and 17-minute marks post administration and results were measured in percentage of HR reduction after	First Dose: Diltiazem caused 75% of patients respond The placebo caused 7% of patients to respond P Value < 0.001 Second Dose: The total of patients who responded to diltiazem rose to 93%	Strengths: -Appropriate randomization allowed no significant differences in patients history or current medical conditions. -effective monitoring of various vital signs over several points outlines a profile of expected patient responses to diltiazem

		no response the were then given either a second dose of the placebo or 0.35 mg/kg of diltiazem. Following the second dose if without effect the placebo group was allowed to unblind and crossover.	each of the dosages. A patient was considered to have responded if it was determined they needed no more intervention to stabilize their RVR. Patients who developed adverse events like hypotension were classified as non-responders	The total of patients who responded to the placebo rose to 12% P Value < 0.001 <u>Open Label Diltiazem:</u> Of the 50 patients in the placebo group who did not respond, 49 received the open label diltiazem in two doses like the blinded diltiazem with 38 responding to the first dose and 9 more to the second dose. This totals 94% of the patients were effectively treated with diltiazem	-Includes a break down of adverse events to determine safety and found no statistical difference between placebo and diltiazem <u>Weaknesses:</u> -Concomitant administration of other medication may have altered results. -Effects after the unblinding and administration of open label diltiazem unable to be quantified. - patient exclusion criteria included CHF which is a significant condition to not have inclusive data on.

Comments: Use of diltiazem in the pre-hospital setting is rare and studies of its effectiveness in safely preventing deterioration are more so, however, by combining retrospective studies of its safety in regards to adverse events with the more valid conclusions of properly randomized hospital studies of its efficacy conclusions of its possible effect in other regions might be. Several more relevant articles exist but due to the similarity of their results were not included here.

Consider:

Occurrence rate of stable atrial fibrillation and atrial flutter prehospitally in the target region

Occurrence rate of stable atrial fibrillation and flutter deteriorating to be unstable prehospitally in the target region

Rate of agreement between prehospital providers and physicians in the interpretation of EKG findings of atrial fibrillation and flutter in target region

Ability of prehospital providers to administer an antidote to diltiazem over dosage, either calcium chloride or calcium gluconate

Rate of protocol adherence in target region

Clinical Bottom Line: Salerno et al. have shown that the administration of diltiazem is a safe and effective way to treat stable RVR as a result of atrial fibrillation and flutter and that patients receiving placebo and supportive care would eventually need to be treated to avoid deterioration. Avoiding this deterioration limits risk and if safe to do so there seems no indication to wait for patients to become unstable and treated with cardioversion. Fromm et al. shows, that without the option to choose between interventions, diltiazem would have equally safe and more effective results over a 30 minutes time frame then metoprolol. This shows its potential to be used more acutely in the prehospital setting. Rodriguez et al. and other retrospective studies like it show that, with adherence to protocols, diltiazem has been safely and effectively used in the prehospital setting and that even with a portion of administrations outside of protocol it presents with a low rate of adverse events.

References:

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