Journal Club Eastern Virginia Medical School
Therapy Article

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CITATION: Miwa Y **Effects of landiolol, an ultra-short-acting beta1-selective blocker, on electrical storm refractory to class III antiarrhythmic drugs. Circ J. 2010 May;74(5):856-63**

I. **WHAT IS BEING STUDIED?**	LANDIOLOL; ULTRASHORT ACTING BETA BLOCKER
1. Study Objective	Evaluate effect of IV injection of landiolol on electrical storm resistant to Class III Antiarrhythmic drugs (Amiodarone & Nifekalant)
2. Study Design	Case Series: 42 consecutive patients (31men 11 women age 65 +/- 16)
3. Inclusion Criteria	Patients presenting to Center of Kyorin University Hospital (Tokyo, Jopan) between Oct 2006 and September 2009 in whom ES occurred and was difficult to treat following established guidelines (CPR, Electrical, Cardioversion, and antiarrhythmic drugs) ES = Electrical Storm; sustained VT/VF twice or more per hour or 3x's or more over 6 hours. QRS configuration id'd on ECG = VT QRS configuration not id'd on ECG = VF If class III Antiarrhythmic drugs (Amiodarone or Nifekalant) were administered to patients and inffective to be administered treatment
4. Exclusion Criteria	• Cardiac arrest at time of arrival • administration of antiarrhythmic drugs prior to arrival • Renal failure (Serum Cr > 2 mg/dL) • Hemodynamically stable VT
5. Interventions Compared	n/a; compared responders and non-

	responders to landiolol as well as survivors and non-survivors with factors varying between the two such as:
	• Age
	• Sex
	• Baseline Heart Disease
	  o Acute MI
	  o PCI/CABG
	  o Previous MI
	  o Idiopathic Dilated Cardiomyopathy
	  o Hypertrophic Cardiomyopathy
	  o Secondary Cardiomyopathy
	  o Idiopathic VT/VF
	• LVEF (%)
	• Killip Class III and IV
	  o Categorizes patients with an acute MI based upon the presence or absence of physical examination findings that suggest LV dysfunction and heart failure
	  i. No evidence of heart failure
	  ii. findings c/w mild to moderate heart failure (S3 gallop, lung rales less than one-half way up the posterior lung fields, or jugular venous distension)
	  iii. Overt pulmonary edema
	  iv. Cardiogenic shock
	• APACHE II score
	• ABG
	  o pH
	  o A-aDO2 (alveolar-arterial oxygen pressure difference)
	• HTN
	• Hypercholesterolemia
	• Diabetes
	• # of DC shocks
	• Class III Antiarrhythmic drugs
	  o Amiodarone
	  o Nifekalant
	• General Anesthetic
	• Assisted Circulation Device

	○ IABP (intra-aortic balloon pump) ○ PCPS (percutaneous cardiopulmonary support)
6. Outcomes Evaluated	• Survival vs non-survival
II. **Are the results of the study valid**	
1. Was the assignment of patients randomized?	No, as was case series, patients either were enrolled in the study or were excluded. Evaluated responder's vs non-responders . Study did report all those who did not respond did not survive and compared variable factors between the two groups.
2. Was randomization concealed (blinded)?	n/a
3. Were patients analyzed in the groups to which they were randomized?	n/a
4. Were patients in the treatment and control groups similar with respect to known prognostic factors?	When divided into responders and non-responders, regardless of antiarrhythmic given there was a statistical difference between age groups, with non-responders being older, as well as APACHE II scores being higher in non-responders group, lower pH in non-responders. Amongst amiodarone responder's vs non-responders there were no statistically significant differences in variables evaluated. Amongst nifekalant responder's vs non-responders there was an age difference with non-responders being older and ABG pH being lower Amongst survivors and non-survivors there were statistical differences between 1. Age, with non-survivors being older 2. Acute MI, with non-survivors having more 3. Killip Class with survivors having more in classes I and II (no evidence of heart failure to mild to moderate heart failure) being more

	in survivor group and classes III and IV (pulmonary edema/cardiogenic shock) being greater in non-survivor group 4. Lower pH in non-survivor group 5. HTN being more prevalent in non-survivor group 6. IABP being used more in non-survivor group
III. **Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1. Were patients aware of group allocation?	No. They were arrest victims.
2. Were clinicians aware of group allocation?	Yes
3. Were outcome assessors aware of group allocation?	Yes
4. Was follow-up complete?	No. They report outcomes to hospital D/C only.
IV. What were the results? Answer the questions posed below	
1. How large was the treatment effect? (Difference between treatment and control group).	Difficult to determine as no control group in this study, all received treatment. Did not report p-value for survivor's vs non-survivors, only number of each, however was greater number numerically of survivors. 25/33 (60%) who got landiolol survived to hospital D/C. 24/33 could ambulate at the time of D/C. Higher age, Apache score and level of acidosis were associated with poorer outcome.
2. What was the estimated treatment effect at a 95% confidence interval? (Precision)	Was not reported
V. **Will the results help me in caring for my patients? (Applicable?)**	
1. Were the study patients similar to my patient?	Not really. The majority of our patients are out-of-hospital cardiac arrests. Their in-patient demographic is similar, and includes many common comorbidities such as large proportion with MI, advanced LV

	dysfunction, HTN, hypercholesterolemia, and diabetes are very prominent factors amongst our patient population. Although these are also risk factors which would place many patients at higher risk for cardiac events in the future.
2. Were all clinically important outcomes considered?	Yes. Survival to hospital D/C was reported. Did not use standardized quality of life scores such as Rankin. No economic analysis was included Would additionally be good to look at the repeat events for those placed on Carvedilol vs bisprolol and further repeat events.
3. Are the likely treatment benefits worth the potential harm and costs?	Yes, if considering this population if they are refractory to standard methods of treatment having an additional agent which could help terminate a potentially fatal arrhythmia could improve overall outcomes for these patients. Harms were limited (bradycardia) However, after some research this particular agent is only approved in the US for intraoperative tachycardia.

Study Limitations

- **Single Center**
- **Case Series; no controls or similar agents such as esmolol or other beta blocking agents compared. Could also be compared to patient receiving separate class III antiarrhythmic drug other than nifekalant**
- **No reporting of confidence intervals**
- **Low Power**
- **Potential for selection bias with some of the exclusion criteria in study**

Clinical Bottom Line:

- **Presents a novel approach to a sometimes difficult to treat pathology**
- **Requires further study**
- **If have run out of traditional measures during a code situation like this may not be harmful option as alternative would be death.**