Cocaine & Beta-Blockers

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Journal Club 1/17/2008
Cocaine Chest Pain

• Common presentation.

• Human cardiac catheterization studies have shown cocaine to be a powerful coronary vasoconstrictor.

• In the case described, there was concern about ongoing tachycardia and hypertension in face of myocardial ischemia.
Cocaine

• Causes HTN and tachycardia by inhibiting the reuptake of NE and DA.

• Sympathetic activation – Running away from a dinosaur:
  – Dilated Pupils – alpha receptors activated
  – Tachycardia – beta receptors activated
  – Hypertension – alpha receptors activated
  – Diaphoresis – sympathetic cholinergic
Cocaine

- Lange et al. showed that cocaine induced coronary artery vasospasm in the cath lab.¹
- Also has type la sodium channel blocking effects, can lead to arrhythmias.
- Accelerates CAD by increasing platelet aggregation and plaque formation.
- What about MI?
Cocaine and MI

• Hollander et al. showed that patients with cocaine related CP had a low incidence of MI.\(^2\) – 5%

• On follow up of 203 patients over 408 days after visit for cocaine related CP, only 2 non-fatal MIs were reported in patients who continued to use cocaine.\(^3\)
Cocaine Chest Pain

Unlikely to have significant mortality or morbidity.
Cocaine + UDS

- Urine remains + for 3 days after use.
- Tests for benzylecognine, a metabolite.
- Exceedingly uncommon to have a false + result.
Beta- Blockers

• Used in ED to treat tachycardia associated with possible ACS.
• Do not acutely lower BP.
• Block both $\text{Beta}_1$ and $\text{Beta}_2$ receptors.
  – In asthmatics can cause bronchospasm
  – In pheochromocytoma can cause unopposed alpha
Beta Blockers & AMI

• Post-MI beta blocker vs. placebo to prevent six-month total mortality for different risk groups:
  • Low risk (no PVC’s and no clinical CHF) NNT = 242
  • Medium risk (1-10 PVC’s and no CHF) NNT = 217
  • High risk (1-10 PVC’s and CHF) NNT = 44
  • Very High risk (> 10 PVC’s and CHF) NNT = 30

• For NNH, using the high-risk subset from the COMMIT trial
  — OR = 1.42 and Control Event Rate = 15.7%
  — NNH = 19
Beta Blockers

WHAT IS UNOPPOSED ALPHA ACTIVATION?

WHY DON’T PEOPLE WHO TAKE BETA-BLOCKERS GET ORTHOSTATIC HYPOTENSION?
Beta Blockers

- Beta \textsubscript{2} receptors are located on the vasculature to the skeletal muscle.
- No orthostatic hypotension because these vessels constrict when beta-blockers are administered.
- In the presence of alpha activation, beta-blockade can exacerbate HTN.
Beta Blockers and AMI

- Proven mortality benefit in the setting of MI
- Adopted into quality of care guidelines
- However, little data on administration in the 1st 12-24 hours of symptoms.
- COMMIT trial suggests that early administration decreases arrhythmias, however benefit offset by increase in cardiogenic shock.

⁴
Cocaine and Beta Blockers

• Propanolol was routinely used in treatment of cocaine intoxication in the 1970s
• Catravas conducted a lethality study in dogs – all cocaine intoxicated dogs that got propanolol died.\(^5\)
  – All animals that got diazepam survived.
• Led to removal of beta-blockers as 1\(^{st}\) line treatment for cocaine intoxication.
Now we’re back to square 1
Article #1

- Retrospective review of 348 admissions to telemetry and ICU with + UDS for cocaine.\textsuperscript{6}
- 60 people got beta-blockers.
- Multivariate analysis showed decrease risk of MI in patients who got beta-blockers (1.7% vs. 4.5%)
• Lots of fancy stats!
• Parsimonious multivariate generalized estimating equations.
• Covariates considered for inclusion were those with a $P < 0.25$ on bivariate analysis.
• Propensity scores to address non-randomized administration of beta-blockers.
Remember with statistics…..
• < 50% of patients presented with CP (165/348).

• ~ 30% of the patients who presented with CP had an MI. (51/165)
  – “Beta-blocker use was of borderline significance in reducing the risk of a myocardial infarction (OR 0.05; 95% CI 0.00-2.08)”

• + UDS cutoff level may remain + for up to 2 weeks in chronic users.
Article #1

Look at the mortality table and tell me which of those patients should get beta-blockers
Prospective study in 15 patients undergoing cardiac catheterization. All got low dose of intranasal cocaine (1/2 of that used for intranasal anesthesia for ENT). 6 got saline. 9 got labetalol. Conclusion: Labetalol reduces MAP, but not coronary vasoconstriction.
Article #2

- Look at Table #1
- Trend to increased vasoconstriction although this is not statistically significant.
- Conclusion: Not much of a benefit if coronary artery diameter does decrease in size.
Article #3

• Prospective study of 7 patients all under 50 years of age.

• All had recent cocaine use or + UDS.

• Got 0.5 mg/kg esmolol followed by infusion of 0.05 mg/kg/min

• Outcome: 3 patients had “good” outcome, 3 patients “failed”, 1 patient “equivocal”.

• Conclusion: Cannot recommend routine use of esmolol.
Beta blockers in Cocaine users

BP Before
BP After
Article #4

• Randomized double-blind placebo controlled prospective study of 30 patients.⁹
• 15 got intranasal saline, 15 got intranasal cocaine.
• 5/15 in saline group got propanolol
• 15/15 in cocaine group got propanolol
Article #4

- Cocaine decreased coronary-sinus blood flow from 139 to 120 ml per minute.
- Propranolol further decreased coronary-sinus blood flow to 100 ml per minute.
- Coronary vascular resistance rose from a baseline value of 0.87 mm Hg/ml/min to 1.05 mm Hg/ml/min after cocaine and 1.20 mm Hg/ml/min after propranolol.
With propranolol one subject had complete coronary-artery occlusion, symptoms of myocardial ischemia, and electrocardiographic changes.
Evidence Based Medicine + Toxicology

• Very difficult, unable to conduct randomized controlled trial where half the study group is poisoned and half not.

• How to decide what is best?
  – Physiologic principles
  – Pharmacologic principles
  – Animal studies
  – Case reports
  – Human studies
Cocaine and Beta Blockers

- Physiologic principles suggest that it is contraindicated.
- Pharmacologic principles suggest that it is contraindicated.
- Animal studies suggest that it is contraindicated.
- Case reports suggest that it is contraindicated.
- Randomized trials in humans suggest that it is contraindicated.
References