Critical Review Form
Therapy

β-Blockers Are Associated With Reduced Risk of Myocardial Infarction after Cocaine Use

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Objective: "To study the effects of β-blocker administration on the development of myocardial infarction or death after hospital admission with documented cocaine use by urine toxicology." (p. 2)

Methods: Retrospective chart review of all cocaine positive urine drug screen patients admitted to the telemetry unit or ICU of Jacobi Medical Center (Bronx, NY) between 2000 and 2005. The authors analyzed those who received β-Blockers compared with those who did not for the primary outcome of MI and the secondary outcome of in-hospital mortality. The only exclusion criteria were those not obtaining a troponin or those patients on β-Blockers prior to ED presentation. MI was defined as troponin – I > 0.10 or significant ST-elevation associated with chest pain or anginal equivalent.

To address potential selection bias of an observational cohort, the authors used propensity scores to adjust baseline risk for the outcomes and isolate β-blocker use. The authors used multiple regression equations to formulate adjusted models for MI and mortality including all potential confounding variables. Furthermore, "all regression models were assessed to ascertain that logistic regression model assumptions were met." (p.3)

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	No, this is a retrospective observational study and therefore subject to substantial bias.
2.	Was randomization concealed (blinded)?	No randomization occurred.
3.	Were patients analyzed in the groups to which they were randomized?	No randomization.

4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	No treatment and control groups, but if reviewing Table 1 (p.5), the β-blocker cohort was older with more HTN and CHF and less asthma (all significant) – all increasing the risk of MI.
B.	**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?	Patients not randomized, so presumably yes, unaware of treatment they were receiving.
2.	Were clinicians aware of group allocation?	Yes.
3.	Were outcome assessors aware of group allocation?	Yes, outcome assessors not specifically blinded to treatment allocation although they could have been. Chart review studies should closely follow established methods to minimize bias and enhance validity (http://pmid.us/8599488 and http://pmid.us/14759964)
4.	Was follow-up complete?	Fig (p.4) reports no loss to follow up.
II.	**What are the results (answer the questions posed below)?**	

1.	How large was the treatment effect?	• β-blockers were administered during 17% of admissions, including 18/60 (30%) in ED. Most β-blockers were β-selective (66%). • A total of 105 MI's occurred with MI significantly less likely for those who did (6.1%) than those who did not (26.0%) receive β-blockers. • Troponin peak higher for those not receiving β-blockers (> 1ng/mL in 33 patients) than those receiving β-blockers with subsequent MI (> 1 in no patient with an MI). Even when adjusting MI definition to troponin >0.1, β-blocker administration still had beneficial effects with difference in proportion 15.1% (95% CI 0.8% - 31%). • No patient who received β-blocker had a second MI during the hospitalization (compared with four in the no-β-blocker cohort). • Patients who died were more likely to have HIV, CHF, lower systolic BP, lower serum albumen, and higher BUN and CR-----i.e., they were sicker to begin with. • Among all patients, β-blocker use adjusted for CHF history, BP, and gender was associated with reduced MI incidence (OR=0.06, 95% CI 0.01-0.61). • Among those with the primary diagnosis of CP, adjusted OR = 0.09 (0.01-0.70), favoring β-blocker. • For in-hospital mortality, adjusted OR 0.01 (0.00-0.33) for first admission, but borderline significant for full cohort OR = 0.22 (0.02-2.41)

2.	How precise was the estimate of the treatment effect?	Reasonably narrow CI as illustrated above.
III.	**How can I apply the results to patient care (answer the questions posed below)?**	
1.	Were the study patients similar to my patient?	Yes, admitted ED patients presenting with suspected angina equivalent and urine drug screen positive for cocaine.
2.	Were all clinically important outcomes considered?	Yes, although prospective studies might assess dysrhythmia incidence to further assess biological plausibility of β-blocker benefit in these subjects.
3.	Are the likely treatment benefits worth the potential harm and costs?	Yes – this paper offers reason to have clinical equipoise about the risk/benefit of β-blocker use in cocaine – positive admitted chest pain patients. Although insufficient to drive practice change given the bulk of contradictory lab evidence and the limitations inherent to a retrospective review, this study ought to be the basis of support for a RCT to definitively answer the question in a clinical context.

Limitations

1. Chart review without explicitly stated or referenced methods opening the door to potential *selection* and *ascertainment* bias. Why were data abstractors not blinded to outcomes?

2. Results lack external validity to cocaine-positive chest pain patients not admitted or not tested. Such patients may differ in a systematic fashion from those in the current study.

3. Lacking data about cocaine time of ingestion or serum cocaine levels (or clinical evidence of sympathomimetic syndrome), the cause-effect relationship of MI, mortality, or β-blocker adverse effect cannot be elucidated.

4. Authors fail to present or adjust for other ACS treatment modalities, although only ASA has been shown to decrease mortality.

5. The authors present no NNT calculation or discussion of recent contradictory evidence about the use of β-blocker in non-cocaine related ACS populations – the COMMIT trial.

Bottom Line

β-blocker administration to admitted cocaine-positive angina patients is associated with a significant reduction in MI (adjusted OR 0.06, 95%, CI 0.01-0.61) and a strong trend towards decreased mortality (adjusted OR 0.22, 05% CI 0.02-2.41). Retrospective design limitations precludes the incorporation of β-blocker into routine clinical practice based upon this paper, but this study does present clinical equipoise sufficient to justify a future prospective RCT.