# Critical Review Form
## Therapy

**Potentiation of Cocaine-Induced Coronary Vasoconstriction by Beta-Adrenergic Blockade,** *Annals of Internal Medicine* **1990; 112: 897-903**

**Objective: "To assess the effects of beta-adrenergic blockade on cocaine-induced coronary vasoconstriction in humans." (p. 897)**

**Methods: Thirty consenting cath lab patients at the University of Texas-Southwestern were randomized into two groups. Group 1 (N= 15) received intranasal saline. Group 2 (N= 15) received 2mg/kg of intranasal 10% cocaine hydrochloride of cocaine followed 15-minutes later by 2mg (0.4mg/min) intracoronary propranolol (N=10) or intracoronary saline (N=5). Treating clinicians were blinded to group allocation and pacing occurred during the study to mask the expected bradycardic response to propranolol. Measures included heart rate, blood pressure, coronary sinus blood flow, coronary vascular resistance and coronary artery diameters using hemodynamic, angiographic and thermodilation techniques. Exclusion criteria included hypertension, recent MI, or a history of pseudocholinesterase deficiency. All subjects received 5 – 10 mg oral diazepam before the catheterization.**

| Guide | | Comments |
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| **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? | Yes, but the authors don't detail the method of group allocation. |
| 2. | Was randomization concealed (blinded)? | Yes, "neither the investigator nor the subject knew which agent was infused." (p.898) |
| 3. | Were patients analyzed in the groups to which they were randomized? | No intention to treatment analysis was declared, but by design no subject could switch treatment group. |
| 4. | Were patients in the treatment and control groups similar with respect to known prognostic factors? | Unknown. No baseline demographic or prognostic variables are provided, however all 3 three-vessel CAP patients were in the cocaine group suggesting an imbalance in baseline risk. (p.898) |

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| **B.** | **Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?** | |

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| 1. | Were patients aware of group allocation? | No. "Neither the investigator nor the subject knew which agent was infused." |
| 2. | Were clinicians aware of group allocation? | No – see above. |
| 3. | Were outcome assessors aware of group allocation? | Presumably yes, but not clearly stated. |
| 4. | Was follow-up complete? | No loss to follow up was reported. |
| **II.** | **What are the results (answer the questions posed below)?** | |

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| 1. | How large was the treatment effect? | • Among the 30 subjects, 23% had normal coronary anatomy, 37% had one-vessel CAD, 30% had two-vessel CAD, and 10% had three-vessel CAD (all in cocaine group).<br><br>• In the control group, no variables were altered by the intranasal administration of saline. (p.898)<br><br>• In the cocaine group, myocardial oxygen demand (rate-pressure product and transcardiac oxygen content) increased while coronary sinus blood decreased (10%), coronary vascular resistance increased (22%) and mild diffuse constriction of the LAD and circumflex coronary arteries occurred.<br><br>• While intracoronary administration of saline following cocaine did not alter any parameter measured, intracoronary administration of propranolol decreased mean SBP without effecting MAP or myocardial oxygen demand. However, coronary sinus blood flow decreased 15% and coronary vascular resistance increased 19%.<br><br>• In 5/10 cocaine-propranolol subjects, epicardial vessels constricted > 10% after propranolol validating the hypothesis of unopposed α effect in some subjects. |

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| | | • One subject (Fig 1, p.902) had complete occlusion of one coronary after propranolol. |

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| 2. | How precise was the estimate of the treatment effect? | Wide CI consistent with the small number of subjects. |
| **III.** | **How can I apply the results to patient care (answer the questions posed below)?** | |
| 1. | Were the study patients similar to my patient? | No – these are patients at high enough risk to merit cardiac cath for some reason. Scant demographic details are provided to permit further comparison between ED patients and these cardiac cath patients. |
| 2. | Were all clinically important outcomes considered? | No – I would opine that no clinically important outcomes were evaluated. Clinicians don't work in cath labs measuring coronary vascular resistance or transcardiac oxygen content. We measure symptom response, ECG changes, biomarker elevation, and short-/long-term mortality. Although this cath lab data provides biological plausibility for concern about β-blocker use in the immediate post-cocaine period, it does not address patient or clinician important outcomes. |
| 3. | Are the likely treatment benefits worth the potential harm and costs? | Unknown based on current study. |

## Limitations

1. **Selection bias – high risk patients in cath lab are not typical ED chest pain patients.**

2. **External validity limited to cocaine patients presenting and treated with β-blockers within 15-minutes of cocaine use which probably never occurs.**

3. **Pre-treatment with benzodiazepines (as they did in this study) may attenuate cardiovascular effects of cocaine.**

4. **Impact of pacing on cocaine-toxicity or propranolol efficacy is uncertain.**

5. **Unequal prognostic distribution of patients (all 3 three-vessel CAD in cocaine group). The authors did not allocate patients by known risk factors equally, so this is not a "controlled" study. Furthermore, the authors did not specify any specific methods of randomization.**

## Bottom Line

**Cardiac cath blinded study demonstrating *in vivo* evidence of intracoronary deleterious effects following intranasal cocaine then intra-coronary propranolol, demonstrated hemodynamically, metabolically, and arteriographically. More clinically representative cocaine-abusing populations ought to be evaluated using β-antagonists of variable route and receptors specificity measuring patient and clinician important outcomes before generally condemning β-antagonist in cocaine-related ACS.**