Comparison of In-Hospital Outcomes for Beta-Blocker Use Versus Non−Beta Blocker Use in Patients Presenting With Cocaine-Associated Chest Pain

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Beta blockers are indicated for management of acute coronary syndromes, but they generally are withheld in patients with cocaine-associated chest pain because of concerns for adverse outcomes related to the unique physiological effects of cocaine. Because few clinical studies have evaluated this interaction, we identified patients with toxicology screen results positive for cocaine treated for chest pain at 2 academic hospitals. Clinical characteristics and in-hospital outcomes were compared between patients with and without β-blocker therapy. We then constructed propensity scores to evaluate the independent relation between β-blocker use and the composite primary end point of myocardial infarction, stroke, ventricular arrhythmia, or all-cause mortality after adjusting for clinical characteristics. Of 376 consecutive patients with cocaine-related chest pain, β blockers were used in 164 (44%). Compared with no β blockers, patients treated with β blockers were more likely to describe anginal chest pain, to have known cardiovascular risk factors, and to receive other antiatherosclerotic therapies. Despite these higher risk clinical characteristics, patients treated with β blockers experienced similar peak troponin levels, individual adverse events, and rates of the composite primary end point (15.9% vs 12.3%, p = 0.32). The primary end point also was similar after propensity score analysis (odds ratio 1.37, 95% confidence interval 0.64 to 2.93, p = 0.42), including specific comparisons of beta-1 selective (odds ratio 1.83, 95% confidence interval 0.79 to 4.24) and nonselective (odds ratio 0.90, 95% confidence interval 0.33 to 2.42) β blockers, when compared with patients not receiving β blockers. In conclusion, no differences in outcomes were observed between patients treated versus not treated with β-blocker therapy in the setting of cocaine-related chest pain. **(Am J Cardiol 2014;113:1802−1806)**

Several clinical studies, including a retrospective analysis by Rangel et al,[1] have demonstrated the safety of β-blocker (BB) use in patients with cocaine-associated chest pain, including similar or lower rates of in-hospital complications and mortality.[1−3] However, current guidelines recommend using other medications instead of BB therapy for patients with acute coronary syndrome (ACS) and recent cocaine ingestion, largely based on mechanistic studies reporting unopposed α-adrenergic stimulation with concurrent BB administration.[4−6] To better characterize contemporary practice patterns in patients with ACS and cocaine intoxication, we evaluated the rates and types of BB therapy used in 2 urban hospitals, and we studied the interaction between BB use and adverse in-hospital outcomes in this population.

Methods

We studied patients presenting to the 2 major hospitals affiliated with an academic teaching university from January 2000 to December 2007 with urine toxicology screen results positive for cocaine (immunoassay urine drug test; Ortho-Clinical Diagnostics, Rochester, New York) and reported cocaine use within the previous 24 hours. Of these cocaine-positive patients, we then identified those subjects with International Classification of Diseases, ninth revision, codes for chest pain, angina, or chest discomfort. All charts were reviewed manually by physician members of the research team to exclude patients with chest pain diagnosed as pulmonary in etiology while in the emergency department (ED), such as pneumonia or pulmonary embolus. We collected all cardiac medications administered within the first 24 hours of presentation, electrocardiographic (ECG) findings, telemetry strips, and notes in the hospital chart. Records were analyzed for information about clinical presentations, previously prescribed medications, clinical course in the ED, medications prescribed during the hospitalization, timing of BB therapy, and important in-hospital outcomes including death, myocardial infarction (MI), stroke, or ventricular arrhythmia.

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Chest pain was defined as typical versus atypical according to standard definitions.[7] Typical chest pain was reported as a pressure-like sensation (heavy or squeezing feeling), particularly if associated with exertion. Atypical chest pain was either sharp or defined in a specific area. Hypertension, dyslipidemia, and diabetes were considered to be present if previously established in the patient's medical history or if taking an antihypertensive, lipid-lowering, or antihyperglycemic medication, respectively. Coronary artery disease was present if the patient had a previous coronary revascularization procedure, documented MI, or known coronary stenosis ≥50% in severity. Vital signs, laboratory studies, and electrocardiograms were those obtained clinically on presentation to the ED. Stress test and echocardiographic data were collected from studies obtained clinically, and diagnoses were those determined clinically (e.g., left ventricular hypertrophy and wall motion abnormality on echocardiogram). Risk scores from the Thrombolysis In Myocardial Infarction (TIMI) studies were calculated after collecting the TIMI risk factors during chart review.[8] Acute MI during the index hospitalization was defined by a troponin-T level greater than the upper limit of normal (>0.1 ng/dl at our hospital laboratory), or by significant ST-segment elevations in 2 contiguous leads by electrocardiography, associated with chest pain or anginal equivalent.[5] Acute MI associated with BB use was defined as a documented increase in angina, troponin, or ECG changes after BB administration. Stroke and ventricular arrhythmias were identified clinically by treating physicians during the chest pain hospitalization.

The primary end point for this study was the composite clinical outcome of MI, stroke, ventricular arrhythmia, or all-cause mortality. Characteristics of patients with and without in-hospital BB use within the first 24 hours were compared using chi-square for categorical, *t* test for continuous, and Wilcoxon rank sum and other appropriate nonparametric tests for variables without normal distribution. Given the significant differences in baseline characteristics between the groups of patients with and without BB use, we constructed propensity scores to evaluate the independent relation between BB use and the composite primary end point.[9–11] The propensity score for an individual is defined as the conditional probability of being treated (in this case, getting BBs) given the individual's covariates or characteristics, and it is designed to balance a large number of potential confounders equally across 2 observational cohorts of patients.[10] Because quintile stratification removes ≥90% of the bias due to unbalanced factors,[11] we stratified patients in our cohort by propensity score quintile and constructed a logistic regression model adjusted for propensity score to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for experiencing the composite primary end point. With many clinicians choosing nonselective BBs in these patients, as a secondary analysis we reran the regression models to compare rates of the primary end point between patients receiving beta-1 selective BBs (atenolol and metoprolol) and those with no BB therapy, and again for nonselective BBs (carvedilol and labetalol) versus no BB therapy. Statistical significance was defined as $p \leq 0.05$. All analyses were performed using SAS, version 9.2 (SAS Institute, Cary, North Carolina). The study protocol was reviewed and approved by the university's Institutional Review Board.

Table 1
Baseline characteristics, treatments, and disposition of patients with and without β-blocker (BB) therapy

Variable	BB Therapy		p Value
	Yes (n = 164)	No (n = 212)	
Patient characteristics			
Age (yrs)	46 ± 9	42 ± 11	<0.001
Women	32%	26%	0.18
White	10%	13%	0.36
Black	81%	76%	0.23
Chest pain typical for angina pectoris	17%	8%	0.012
TIMI risk score			<0.001
0	44%	69%	
1	32%	23%	
2	18%	5%	
≥3	6%	3%	
History of hyperlipidemia	23%	11%	<0.001
History of hypertension	80%	38%	<0.001
Diabetes mellitus	25%	14%	0.005
Known coronary artery disease	33%	13%	<0.001
Lung disease	9%	8%	0.58
Heart rate (beats/min)	91 ± 22	94 ± 25	0.29
Respiratory rate (breaths per minute)	21 ± 5	21 ± 7	0.50
Systolic blood pressure (mm Hg)	152 ± 36	138 ± 32	<0.001
Diastolic blood pressure (mm Hg)	89 ± 26	80 ± 22	<0.001
Hemoglobin (g/dl)	13 ± 3	14 ± 2	0.16
Creatinine (mg/dl)	2.1 ± 2.4	1.7 ± 2.3	0.20
Total cholesterol (mg/dl)	155 ± 46	163 ± 47	0.26
Low-density lipoprotein cholesterol (mg/dl)	96 ± 34	100 ± 43	0.54
High-density lipoprotein cholesterol (mg/dl)	41 ± 14	44 ± 18	0.22
Triglycerides (mg/dl)	107 ± 94	113 ± 83	0.67
Other medications ordered			
Aspirin	84%	57%	<0.001
Clopidogrel	23%	8%	<0.001
Systemic anticoagulation	23%	9%	<0.001
Nitrates	50%	36%	0.007
Angiotensin-converting enzyme inhibitors	72%	24%	<0.001
Disposition			
Cardiac intensive care unit	22%	8%	<0.001
Medical intensive care unit	19%	11%	0.038
Telemetry floor	58%	77%	<0.001
Home from ED	1%	4%	0.20

Data are expressed as proportion (%) or mean ± SD.

Results

A total of 376 patients with positive urine toxicology screen results for cocaine were admitted with chest pain, of whom 164 (44%) received a BB in the first 24 hours. The type of BB given was metoprolol in 74, carvedilol in 43, labetalol in 44, and atenolol in 3 patients. As listed in Table 1, patients who received BBs were older and had more cardiovascular risk factors, more established coronary