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Early use of beta blockers in patients with cocaine associated chest pain

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ABSTRACT

Background: The most common symptom of cocaine abuse is chest pain. Cocaine induced chest pain (CICP) shares patho-physiological pathways with the acute coronary syndromes (ACS). A key event is the increase of activity of the adrenergic system. Beta blockers (BBs), a cornerstone in the treatment of ACS, are felt to be contraindicated in the patient with CICP due to a potential of an "unopposed alpha adrenergic effect (UAE)".
Objectives: Identify signs of UAE and in-hospital complications in patients who received BB while having cocaine induced chest pain.
Methods: We performed a retrospective review of 378 patients admitted to a medical unit because of CICP. Twenty six of these were given a BB at the time of admission while having CICP. We compared these patients to a control group paired by age, sex, race and history of hypertension who did not received a BB while having CICP. Blood pressure, heart rate, length of stay and in-hospital cardiovascular complications were compared.
Results: No statistically significant differences were found between the two groups except for a longer length of stay in the case group. This was felt to be due to unrelated causes.
Conclusions: This study does not support the presence of an UAE in patients with continuing CICP and treated early with BB. There were no in-hospital cardiovascular complications in the group of patients who had an early dose of BB while having CICP.
Implications: BB appeared safe when given early on admission to patients with CICP.

1. Introduction

Cocaine is one of the most common drugs found in patients who seek EHC. In 2006, six million Americans aged 12 and older had abused cocaine in some form [1]. Cocaine is a potent vasoconstrictor ([2–4], Blaho, Merigian et al. 1996, Chang, Walsh et al. 2011). Some of its effects include hypertension, coronary vasospasm, accelerated atherosclerosis and myocardial infarction ([5], Chang, Walsh et al. 2011).

The most common symptom of cocaine abuse is chest pain [6]. CICP shares many of the common patho-physiologic pathways with acute coronary syndromes ([2,7], Freeman and Feldman 2008). The use of BB, a cornerstone of the treatment of acute coronary syndromes has been thought to be contraindicated in patients using cocaine [8]. This is mainly because of theoretical UAE that can lead to hypertensive complications in patients intoxicated with the drug [6]. There are some reports of death associated with the use of beta blockers in patients using cocaine [9]. Coronary vasoconstriction was induced in one study when volunteers inhaled cocaine while intra-coronary propranolol was being infused [10]. Also, there have been reports of increased levels of cardiac biomarkers in patients who were given beta blockers while having cocaine induced chest pain [11].

Recent studies have been published showing that BB can be safely used in patients admitted for cocaine induced chest pain. ([5,12,13], Ibrahim, Maselli et al. 2013).

Continuing chest pain in patients who test positive for cocaine may be a marker for the continuing presence of the drug's systemic effects. We tried to observe the effects of the administration of BB early on admission which theoretically should have resulted in unopposed alpha stimulation. As a secondary endpoint we followed troponin levels during the admission and the patient's length of stay.

2. Methods

We performed a retrospective review of all the medical records of patients admitted to a medical unit for cocaine induced chest pain to rule out acute coronary syndrome from June 2006 to June 2009. All patients had a final diagnosis of cocaine induced chest pain and a positive urine test for cocaine metabolites.

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Table 1
Comparison of the basic compared characteristic of the patients groups.

Patient characteristics	B-blockers used (n = 26)	B-blockers not used (n = 32)	P value
Age (in years)	50	48.3	0.4216
Sex (male)	23 (88.5%)	30 (93.8%)	0.8078
Race			0.6181
Black	14 (53.8%)	15 (46.9%)	
Hispanic	10 (38.5%)	16 (50.0%)	
White	2 (7.7%)	1 (3.1%)	
History of hypertension	18 (69.2%)	18 (56.3%)	0.4163

Of the patients who received a beta blocker while having chest pain, the baseline blood pressure (BP) and heart rate (HR) were reviewed. Values were obtained 1 to 3 h after administration of the beta blocker and 3 to 6 h later. We also recorded the troponin I values on admission, 6 h after admission and 12 h later. We compared the results to a control group of patients (paired by age, sex, history of hypertension and race) also diagnosed with cocaine induced chest pain who did not receive beta blockers. Statistical comparison of the BP and the HR was done using the Mann–Whitney test. The troponin values were compared using the Fisher's exact test. The use of beta blockers was at the discretion of the Emergency Department Physicians.

The data was evaluated using Graph-pad software.

3. Results

We found a total 378 patients who were diagnosed with CICP and admitted to rule out an acute coronary syndrome. From this group we identified 26 that while having chest pain received a dose of BB in the Emergency Department. The type and route of the BB were: oral metoprolol 13 patients (50%), intravenous metoprolol 5 patients (19%), intravenous labetalol 2 patients (8%), oral carvedilol 2 patients (8%), oral atenolol 2 patients (8%), and oral propranolol 2 patients (8%).

No statistically significant differences were noted in the demographics of the patients who received and who did not receive beta blockers. This is outlined in Table 1.

The group with higher BP and HR was more likely to receive BB. However, there was no statistically significant difference between the two groups. At 6 and 12 h after admission the heart rate and the blood pressure were lower in the BB group. The results are in Table 2.

There was no statistically significant difference in the troponin levels between the two groups studied (Table 3).

The length of stay was significantly different (4.6 days in the case group and 2.65 days in the control group, P: 0.04). However, this might be affected by the presence of patients who stayed in the hospital because of unrelated issues in both groups.

No cardiac complications were found, and no in-hospital mortality occurred in either group.

4. Discussion

In our study, the use of BB did not appear to harm patients with continuing CICP.

We did not observe any documented adverse effects in the cocaine positive group that received a beta blocker when compared to a similar group of patients who did not receive the beta blocker. There were no statistically significant differences between systolic, diastolic and mean arterial BP as well as HR. However, the BP and HR in the beta blocker group at 6 and 12 h were lower than the ones in the control group. This finding is not consistent with the presence of an "unopposed alpha effect" in patients using cocaine treated with beta blockers.

There were no differences between the troponin trend in both groups at any time. The length of stay was increased in the group of patients that received the BB. This might be secondary to unrelated co-morbidities and social problems that prevented discharge.

In 2013 in the United States, 24.6 million Americans aged 12 and older were current illicit drug users. There were 1.5 million cocaine users aged 12 or older. [14]. Cocaine is the most common drug associated to visits to the Emergency Department [15]. The most common reason for obtaining a consult in the Emergency Department in cocaine users is chest pain [6].

Cocaine is a potent sympathomimetic. It becomes bioavailable when absorbed through a mucosal membrane, when inhaled, ingested, injected or smoked (as in its "crack" form). It acts by blocking the re-uptake of norepinephrine in the presynaptic membrane. This is associated with a significant increase of the nor-adrenergic tone leading to vasoconstriction, hypertension, increased myocardial contractility and tachycardia. Cocaine is also associated with early atherosclerosis and thrombus formation including thrombotic myocardial infarctions [16]. Despite the proven benefit of BB in ischemic heart disease this therapy is contraindicated in patients with chest pain secondary to cocaine [8]. There have been other studies that have found no harm of the use of BB in patients with cocaine induced chest pain ([17–19], Self, Rogers et al. 2011, Fanari, Kennedy et al. 2014). In one study the use of beta blockers was associated with decreased long term mortality in patients with cocaine induced chest pain [12].

This study was designed to find evidence of the presence of an unopposed nor-adrenergic state in patients who had evidence of continuing cocaine induced chest pain when treated with beta blockers.

It is important to note that all the patients included in our study had continuing chest pain at the moment the BBs were administered in the

Table 2
Comparison of the blood pressure and heart rate in patients with CICP who received and did not received beta blockers early on admission.

Time	Blood pressure and heart rate in patients that received beta blockers		Blood pressure in patients that did not receive beta blockers		P value
	Average (95% CI)		Average (95% CI)		
0 to 1 h	Systolic	147.8 (136.5 to 159.1)	Systolic	135.5 (127.9 to 143.1)	0.0647
	Diastolic	88.5 (80.9 to 96.0)	Diastolic	82.5 (77.7 to 87.3)	0.1730
	Mean	108.2 (99.9 to 116.4)	Mean	100.17 (94.8 to 105.6)	0.0966
	Heart rate	86.4 (80.7 to 92.1)	Heart rate	87.6 (81.8 to 93.4)	0.7786
1–3 h	Systolic	135.1 (126.1 to 143.9)	Systolic	133.3 (124.2 to 142.4)	0.8053
	Diastolic	80.01 (72.9 to 87.3)	Diastolic	77.5 (72.4 to 82.8)	0.5951
	Mean	98.42 (91.0 to 105.8)	Mean	96.1 (89.9 to 102.3)	0.6662
	Heart rate	79.63 (75.3 to 83.9)	Heart rate	79.1 (74.3 to 83.9)	0.8911
3 to 6 h	Systolic	126.7 (118.3 to 135.2)	Systolic	130.1 (123.9 to 136.4)	0.5177
	Diastolic	75.57 (69.7 to 81.5)	Diastolic	76.9 (72.3 to 81.6)	0.7150
	Mean	92.62 (86.4 to 98.9)	Mean	94.7 (90.2 to 99.1)	0.5893
	Heart rate	73.11 (68.7 to 77.6)	Heart rate	75.8 (71.1 to 80.5)	0.4222

Table 3
Comparison of the troponin trend in between patients with CICP who received and did not received beta blockers early on admission.

Time	Number of patients with Troponins (+) among those that received B-blockers (mean value)	Number of patients with Troponins (+) among those that did not receive B-blockers (mean value)	P value
0–3 h	7/26 (0.1631)	7/32 (0.5406)	0.8900
3–6 h	4/26 (0.0923)	5/32 (0.0372)	0.7612
6–12 h	3/26 (0.0130)	5/32 (0.0597)	1.000

Emergency Department. Because of this we can theorize that these patients were at increased risk of suffering from acute cocaine toxicity and therefore at increased risk of having adverse effects from the beta blocker [20], this was not observed in our study. Interestingly the patients in our study who received beta blockers were more hypertensive and tachycardic on admission than the control group however in the group that received a BB both heart rate and blood pressure were lower at 6 and 12 h blockers compared to the group that did not receive a beta blocker.

Our study has several limitations. Because this is a retrospective review of medical records, the patients did not have a standardized protocol for follow-up after therapy with beta blockers was started. Different beta blockers were used, and administration was both intravenous and oral. Also it is important to state that the beta blockers were given to patients with acute cocaine induced chest pain and were discontinued after determining the presence of cocaine metabolites in the urine. The test for the presence of cocaine metabolites in the urine is a qualitative analysis and we cannot estimate the amount of cocaine ingested by the patients in either group.

Our study does not support the theory of an UAE in patients who received BB while having CICP in the Emergency Department. Our conclusions are supported by not finding a statistical difference in troponin levels or cocaine associated complications either group.

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