β-Blocker treatment and prognosis in acute coronary syndrome associated with cocaine consumption: The RUTI-Cocaine Study

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A R T I C L E   I N F O
Article history:
Received 12 November 2017
Received in revised form 7 December 2017
Accepted 2 February 2018

Keywords:
β-Blocker
Prognosis
Acute coronary syndrome
Cocaine

A B S T R A C T

Background: The use of β-blocker therapy in the setting of acute coronary syndrome (ACS) associated with cocaine consumption (ACS-ACC) is discouraged due to the risk of coronary vasoconstriction. We examined the prognostic value of β-blocker therapy during hospital admission and after discharge. During a median follow-up of 4.0 (IQR: 2.4–6.5) years after the index event, 2 (6.1%) patients treated with β-blocker therapy died and 6 (18.2%) experienced hospital re-admission for myocardial infarction (MI); in contrast, there were 5 (20.8%) deaths and 5 (20.8%) readmissions due to MI in patients without β-blocker therapy. Lower rates of MACE were observed in patients treated with β-blocker therapy (30.3%) than those without β-blocker therapy (41.7%). The 90-day survival was higher in patients treated with β-blocker therapy (87.5% vs. 100%; Log rank test p = 0.035).

Conclusions: In patients with ACS-ACC, β-blocker treatment was associated with a significantly better clinical outcome, with lower rates of death and MI. Our findings support the evidence for long-term β-blocker administration in high-risk patients and highlight the need for large prospective multicenter studies of β-blocker treatment in ACS-ACC.

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1. Introduction

Cocaine use has increased in recent years, being the second most frequently consumed drug in Europe after cannabis. Its growing consumption has generated an increase in the number of admissions in emergency departments due to clinical conditions resulting from its toxicity [1]. The vast majority of these patients are admitted for chest pain, and the incidence of cocaine-induced myocardial infarction is reported to be around 6% [2]. Current recommendations for management of these patients are largely based on expert consensus [3].

The use of β-blocker therapy in the setting of acute coronary syndrome (ACS) associated with cocaine consumption (ACS-ACC) is discouraged due to the risk of coronary vasoconstriction secondary to unopposed α-receptor stimulation [4,5]. However, the management of ACS has evolved substantially over the past two decades, and the value of β-blockade in this setting has not been re-evaluated. Accordingly, we examined the prognostic value of β-blocker therapy in a contemporary ACS cohort.

2. Methods

The RUTI-Cocaine Study was a prospective study conducted between January 2001 and December 2014 that examined cocaine use among young (<50-year-old) consecutive patients admitted with an ACS. During the study period, 1002 patients were admitted; of these, 57 (5.7%) had a positive cocaine urine test. We collected data on clinical characteristics and major adverse cardiovascular events (MACE) during follow-up. Among ACS-ACC patients, 33 (57.9%) received β-blocker therapy during hospital admission and after discharge. During a median follow-up of 4.0 (IQR: 2.4–6.5) years after the index event, 2 (6.1%) patients treated with β-blocker therapy died and 6 (18.2%) experienced hospital re-admission for myocardial infarction (MI); in contrast, there were 5 (20.8%) deaths and 5 (20.8%) readmissions due to MI in patients without β-blocker therapy. Lower rates of MACE were observed in patients treated with β-blocker therapy (30.3%) than those without β-blocker therapy (41.7%). The 90-day survival was higher in patients treated with β-blocker therapy (87.5% vs. 100%; Log rank test p = 0.035).

Conclusions: In patients with ACS-ACC, β-blocker treatment was associated with a significantly better clinical outcome, with lower rates of death and MI. Our findings support the evidence for long-term β-blocker administration in high-risk patients and highlight the need for large prospective multicenter studies of β-blocker treatment in ACS-ACC.

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* All above authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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mortality was also analyzed. The follow-up events were obtained from patients’ electronic clinical records and from death registers.

2.1. Statistical analysis

Data are presented as medians and IQRs for continuous variables and as counts with percentages for categorical variables. The baseline characteristics of patients were compared using the Wilcoxon rank-sum test for continuous variables and Pearson’s χ² test for categorical variables or Fisher’s exact test when needed. Kaplan–Meier survival curves and the Log rank test were used to assess differences in 90-days survival. Differences were considered statistically significant at p < 0.05. STATA V.13.0 (College Station, Texas, USA) was used for all analyses (Tables 1 and 2).

3. Results

During the study period, 1002 patients were admitted; of these, 864 (86.2%) underwent cocaine urine testing. The study included the 57 (5.7%) patients with a positive cocaine urine test. Of these, 33 (86.2%) underwent cocaine urine testing. The study included

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographics</th>
<th>Overall (n = 57)</th>
<th>Without β-blocker treatment (n = 24)</th>
<th>With β-blocker treatment (n = 33)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>Age, years</td>
<td>44 (38–47)</td>
<td>45 (37–48)</td>
<td>45 (42–48)</td>
<td>0.296</td>
</tr>
<tr>
<td></td>
<td>Male sex</td>
<td>52 (91.2)</td>
<td>21 (87.5)</td>
<td>31 (93.9)</td>
<td>0.640</td>
</tr>
<tr>
<td>Clinical history</td>
<td>Prior MI</td>
<td>6 (10.5)</td>
<td>2 (8.3)</td>
<td>4 (12.1)</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>Previous PCI</td>
<td>5 (8.8)</td>
<td>1 (4.2)</td>
<td>4 (10.1)</td>
<td>0.385</td>
</tr>
<tr>
<td></td>
<td>Dyslipidemia</td>
<td>22 (38.6)</td>
<td>7 (29.2)</td>
<td>15 (45.5)</td>
<td>0.212</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
<td>6 (10.5)</td>
<td>2 (8.3)</td>
<td>4 (12.1)</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>Arterial hypertension</td>
<td>12 (21.1)</td>
<td>2 (8.3)</td>
<td>10 (30.3)</td>
<td>0.045</td>
</tr>
<tr>
<td></td>
<td>Periperal arterial disease</td>
<td>2 (3.5)</td>
<td>1 (4.2)</td>
<td>1 (3.0)</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>Current or previous smoker</td>
<td>55 (96.5)</td>
<td>23 (95.8)</td>
<td>32 (96.9)</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>Familiar history of ischemic cardiomyopathy</td>
<td>13 (22.8)</td>
<td>4 (16.7)</td>
<td>9 (27.3)</td>
<td>0.346</td>
</tr>
<tr>
<td>Physical examination</td>
<td>Killip I</td>
<td>44 (77.2)</td>
<td>18 (75.0)</td>
<td>26 (78.8)</td>
<td>0.736</td>
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<tr>
<td></td>
<td>Killip II</td>
<td>4 (7.0)</td>
<td>1 (4.2)</td>
<td>3 (9.1)</td>
<td>0.631</td>
</tr>
<tr>
<td></td>
<td>Killip III–IV</td>
<td>5 (8.8)</td>
<td>2 (8.3)</td>
<td>3 (9.1)</td>
<td>1.000</td>
</tr>
<tr>
<td>Characteristics of ACS</td>
<td>STEMI</td>
<td>48 (84.2)</td>
<td>18 (75.0)</td>
<td>30 (90.9)</td>
<td>0.146</td>
</tr>
<tr>
<td></td>
<td>Anterior location</td>
<td>24 (42.1)</td>
<td>9 (37.5)</td>
<td>15 (45.5)</td>
<td>0.548</td>
</tr>
<tr>
<td></td>
<td>Troponin I, peak, ng/L</td>
<td>30.7 (10.3–68.3)</td>
<td>12.4 (4.3–45.7)</td>
<td>37.3 (15.9–72.0)</td>
<td>0.055</td>
</tr>
<tr>
<td></td>
<td>LEVF at discharge, %</td>
<td>53 (45–60)</td>
<td>55 (45–61)</td>
<td>52 (39–60)</td>
<td>0.571</td>
</tr>
<tr>
<td>ST elevation myocardial infarction (n = 50)</td>
<td>Main epicardial coronary arteries &gt;70% stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>6 (12.0)</td>
<td>6 (30.0)</td>
<td>0</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>31 (62.0)</td>
<td>10 (50.0)</td>
<td>21 (70.0)</td>
<td>0.153</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>8 (16.0)</td>
<td>2 (10.0)</td>
<td>6 (20.0)</td>
<td>0.450</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>5 (10.0)</td>
<td>2 (10.0)</td>
<td>3 (10.0)</td>
<td>1.000</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td></td>
<td>40 (70.2)</td>
<td>16 (66.6)</td>
<td>24 (72.7)</td>
<td>0.653</td>
</tr>
</tbody>
</table>

Data are presented as no. (%) or median (IQR). MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST elevation myocardial infarction; LEVF, left ventricular ejection fraction.

4. Discussion

This study reveals that in patients with ACS-ACC, β-blocker treatment was associated with a significantly better clinical outcome, with lower rates of death, revascularization and myocardial infarction. These findings suggest that β-blocker therapy is safe and effective in the management of patients with ACS-ACC.

The link between cocaine use and myocardial ischemia is well known and may involve catecholamine accumulation [6], thrombosis [7–9], premature atherosclerosis [10], and coronary spasm [11,12]. Physicians became alarmed about β-blocker use in patients with ACS-
ACC in the 1980s after case reports showed that β-blockers elicited adverse events in the setting of cocaine toxicity. Since then and for over 30 years, the paradigm of “unopposed α-stimulation” endures in medical literature. In fact, clinical practice guidelines do not recommend β-blocker therapy in this population [4–13]. However, the use of β-blockers in ACS-ACC remains controversial due to a lack of prospective contemporary clinical studies evaluating its safety and/or efficacy in this clinical setting. Endorsing the controversy, a recent study has shown that in a considerable percentage of patients with ACS-ACC, β-blocker treatment is used in the in-hospital setting [14] and our study reveals that in a high percentage of patients with ACS-ACC, β-blocker use was introduced upon discretion by the physician in charge. These findings suggest that many clinicians appear to be disregarding the paradigm.

Regarding the use of β-blocker therapy in different clinical settings related to cocaine consumption, a recent systematic review found that β-blockers more reliably mitigated cocaine-induced concomitant tachycardia and hypertension than other classes of medication [15]. Several retrospective analyses examining the safety and efficacy of β-blocker use in patients with cocaine chest pain did not find any harm. Dattilo et al. [16] reported that β-blocker therapy was associated with a reduction in the incidence of MI after cocaine use. Rangel et al. [17] found that the mortality rate in chest pain patients with cocaine-positive urine tests was significantly reduced during follow-up when they were discharged with β-blocker therapy. Fanari et al. [18], found that no differences in outcomes were observed between patients treated or not treated with β-blocker therapy in the setting of cocaine-related chest pain and Espana Schmidt et al. [19] did not find any in-hospital cardiovascular complication in patients with cocaine associated chest pain who had an early dose of β-blocker.

Our data are consistent with the studies mentioned above suggesting not only that β-blocker therapy is a safe treatment option, but also, that is associated with a significantly better clinical outcome. These findings seem to have a pathobiological basis: first, the enormous adrenergic overload from acute cocaine use can desensitize cellular adrenoreceptors via uncoupling or actual receptor loss; thus, the hyperadrenergic state produced by cocaine probably decreases α-adrenergic responses [20], and second, the use of β-blockers as an essential therapy in the setting of myocardial infarction, is due to their ability to decrease myocardial work, oxygen consumption, and provide protection for myocardial muscle in times of decreased flow and increased demand [21]. Consequently, the myocardial protective benefits of β-blockers may offset cocaine-derived concerns and may provide important long-term prognostic benefits as we observe in our study. This new evidence supports routine β-blocker use in young patients with ACS-ACC, which is growing alarmingly in Western countries [22].

Our study has several limitations. This is a single center study with a limited number of patients. Due to the small sample size, it was not possible to perform a complete analysis on the impact of β-blockers on in-hospital outcomes. Different types of β-blockers were used. We were not able to distinguish precise timing of cocaine consumption. The test for the presence of cocaine metabolites in the urine is a qualitative analysis not being possible to estimate the amount of cocaine ingested by the patients.

In conclusion, the RUTI-Cocaine Study generates new evidence about the use of β-blocker therapy in patients with ACS-ACC, which is associated with a better clinical outcome. This study underscores the evidence for long-term β-blocker administration in high-risk patients with ACS-ACC, and highlights the need for large prospective multicenter studies assessing the relative benefits and risks of β-blocker treatment in this population.

Funding

AB-G was supported by grants from the Ministerio de Educación y Ciencia (SAF2014-59892), Fundació La MARATÓ de TV3 (201502, 201516), CIBER Cardiovascular (CB16/11/00403), and AdvanceCat 2014–2020 (COMRDI15-1-0013-10).

Conflict of interest

None of the authors have any disclosures relevant to the content of the manuscript.

References


