Case Report

Blood Purification

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DOI: 10.1159/000506176

Received: November 28, 2019
Accepted: January 27, 2020
Published online: February 28, 2020

A Promising Innovative Treatment for ST-Elevation Myocardial Infarction: The Use of C-Reactive Protein Selective Apheresis: Case Report

Darko Boljevic[a] Aleksandra Nikolic[a, b] Sinisa Rusovic[a] Jovana Lakcevic[a] Milovan Bojic[a, b] Bela Balint[a, c]

[a]"Dedinje" Cardiovascular Institute, Belgrade, Serbia; [b]Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [c]Department of Medical Sciences, Serbian Academy of Sciences and Arts, Belgrade, Serbia

Keywords
Myocardial infarction · C-reactive protein apheresis · Selective plasma exchange

Abstract
Background: In patients with ST-elevation myocardial infarction (STEMI), C-reactive protein (CRP) levels are associated with larger infarct size, transmural extent, and poor function of left ventricle and independently predict 30-day mortality. CRP-apheresis following STEMI showed to be feasible, safe, and has significant beneficial effect both on myocardial infarction size and wall motion. To the best of our knowledge, this is only the second published clinical evaluation of the efficacy and safety of selective CRP-apheresis in the STEMI treatment using Spectra-Optia and Pentrasorb CRP-adsorber systems. ***Case Report:*** A 53-year-old female was referred with anterior STEMI. After percutaneous coronary intervention, patient received standard post-STEMI therapy according to current guidelines. Selective therapeutic plasma exchange (TPE) was performed using Spectra-Optia (Terumo BCT; USA) and Pentrasorb CRP-adsorber (Pentracor GmbH; Germany) systems. Antecubital veins were used for vascular access and acid-citrate-dextrose solution (ACD formula A; total volume = 1,026 mL) was utilized as anticoagulant. The volume of processed blood was 15,600 mL. The removed "natural" plasma (total volume = 8,329 mL) was replaced with CRP-depleted autologous plasma (total volume = 8,085 mL). This intensive TPE-treatment was well tolerated, without adverse effects, or complications. The CRP plasma levels were: initial = 4.2 mg/L 6 h after acute myocardial infarction (AMI), pre-apheresis = 16.4 mg/L, and post-apheresis = 4.59 mg/L (CRP-depletion = 72%). There were neither significant changes observed in biochemistry nor any alterations in plasma hemostatic activity investigated before and after CRP-adsorption performed. ***Conclusion:*** Early performed CRP-apheresis is a promising innovative therapeutic approach for STEMI treatment that could provide a reduced size of infarction zone – with inferior occurrence of heart failure after AMI. However, precise and complete evaluation of the efficacy and safety of this treatment requires further multicenter randomized and larger clinical studies.

Introduction

C-reactive protein (CRP) is a sensitive marker of inflammation and important mediator of tissue damage in acute myocardial infarction (AMI) [1]. Association between CRP levels and adverse outcomes in patients pre-

D.B and B.B. contributed equally to this article.

E-Mail karger@karger.com
www.karger.com/bpu

Darko Boljevic, MD
"Dedinje" Cardiovascular Institute
Heroja Milana Tepica 1
Belgrade 11000 (Serbia)
E-Mail darkoboljevic@gmail.com

senting with ST-elevation myocardial infarction (STEMI) is well known. In patients with STEMI treated with primary percutaneous coronary intervention (PCI), higher baseline CRP levels are associated with larger infarct size, transmural extent, and poor systolic and diastolic function of left ventricle (LV) and independently predicted 30-day mortality [2–4]. CRP-apheresis following STEMI is feasible, safe, and results presented from a small cohort showed significant beneficial effects of CRP both on myocardial infarction size and wall motion [4]. Therefore, CRP reduction from plasma brings selective CRP-apheresis as innovative therapeutic approach in the treatment of AMI [3, 4].

The aim of this report was to evaluate CRP-reductive efficacy of Spectra-Optia and Pentrasorb CRP-adsorber systems (based upon the in vivo CRP-depletion), using our modification of the original protocol from Ries et al. [5, 6]. Exactly, CRP-apheresis in our center was performed earlier than in mentioned studies: 12 vs. 27.5 ± 4.6 h after chest pain onset due to AIM. To the best of our knowledge, this is only the second published clinical evaluation of the efficacy and safety of selective CRP-apheresis in the STEMI treatment using Spectra-Optia and Pentrasorb CRP-adsorber systems.

Case Report

A 53-year-old woman was admitted to "Dedinje" Cardiovascular Institute, Belgrade, Serbia, from regional non-PCI medical center where she presented with acute onset of chest pain during physical activity followed by nausea and vomiting. She was diagnosed with anterior STEMI and transferred to our cardiac catheterization laboratory for primary PCI. Time from chest pain onset to door was around 4 h and 30 min, and time from door to balloon was around 30 min.

The patient's medical history was significant only for hypertension, which was her only risk factor for coronary artery disease. A physical examination of the hemodynamically stable patient showed a regular heart rhythm with no murmurs. Blood pressure was 180/100 mm Hg and pulse rate 85 bpm. Chest and neurological examinations were normal, respiratory sounds in both lungs as well, without edema in the lower extremities. As in Figure 1a presented, a 12-lead electrocardiogram demonstrated normal sinus rhythm, pulse rate 85 bpm, and ST elevation of 3 mm in V1 – V5 leads with 1–2 mm ST depression in standard inferior leads (Fig. 1a, b).

Transthoracic echocardiography showed normal dimensions of LV, moderately reduced LV ejection fraction (= 45%) with hypokinesis of anterior wall and septum and akinesis of apex.

Emergency coronary angiography was performed via right radial artery approach with a use of 6 Fr sheath. It revealed thrombotic 90% stenosis of the medial segment of the left anterior descending artery (LAD) with large thrombus burden and thrombolysis in myocardial infarction 2–3 flow and no significant stenosis in other coronary arteries were noticed. Primary PCI included aspiration of thrombus from LAD with Aspiron (Meril Life Sciences, India). After thromboaspiration 1 drug-eluting stent Xience Xpedition 3.5 × 28 mm (Abbott Vascular, Abbott Park, IL, USA) was implanted. Final cineangiographic shoot reveled LAD with no residual stenosis and with thrombolysis in myocardial infarction 3 flow (Fig. 1b). The hemodynamically stable patient was monitored at the coronary care unit.

Selective therapeutic plasma exchange (TPE) procedure was performed by Spectra-Optia (Terumo BCT; USA), using secondary plasma device protocol and Pentrasorb CRP-adsorber system (Pentracor GmbH; Germany). Antecubital veins were used for vascular access and acid-citrate-dextrose solution (ACD formula A; total volume = 1,026 mL) was utilized as anticoagulant (ACD: whole blood ratio was 1:10) [7, 8]. The volume of processed blood was 15,600 mL. The removed patient's "natural" plasma (total volume = 8,329 mL) was replaced with CRP-depleted (ex vivo purification) autologous plasma (total volume = 8,085 mL). The intensive selective TPE-treatment performed was generally well-tolerated procedure, without adverse effects or complications.

As presented in Figure 2a, the CRP plasma levels were: initial = 4.2 mg/L (6 h after AMI), pre-apheresis = 16.4 mg/L, and post-apheresis = 4.59 mg/L. CRP maximal elevation (16.4 mg/L) was at 12 h from chest pain onset. Cardiac enzymes were enlarged with maximal elevation of hs-Troponin I 25,003 pg/mL, creatine kinase 1,224 IU/L, and creatine kinase MB isoenzyme 139 IU/L at 24 h from chest pain onset (Fig. 2a, b).

Laboratory assessment showed normal hemogramm, no significant changes in biochemistry and hemostatic activity (levels were practically the same in the plasma samples prior and following CRP-apheresis) with normal renal and liver function.

Following PCI, patient received standard post-AMI therapy according to current guidelines. During hospitalization patient had no complication, no signs of heart failure, no chest pain or arrhythmias. She was discharged in good condition, hemodynamically stabile.

Discussion

CRP is an acute phase reactant, biomarker of inflammation but also a mediator of myocardial damage in setting of AMI together with activated system of complement [9]. Studies demonstrated that CRP independently predicts adverse cardiovascular events [10]. In their paper, Stumpf et al. [9] presented a statistically significant negative correlation between LV ejection fraction and peak CRP levels and they demonstrated a clear relationship between in-hospital CRP plasma concentrations and the development of post-infarction heart failure in patients with first STEMI treated with PCI. Animal models showed that administration of human CRP after ligation of the coronary artery reproducibly enhanced increased infarct zone size by up to 40% [11]. CRP-apheresis in animal model significantly reduces CRP levels and the volume of the infarction zone after myocardial infarction [12].

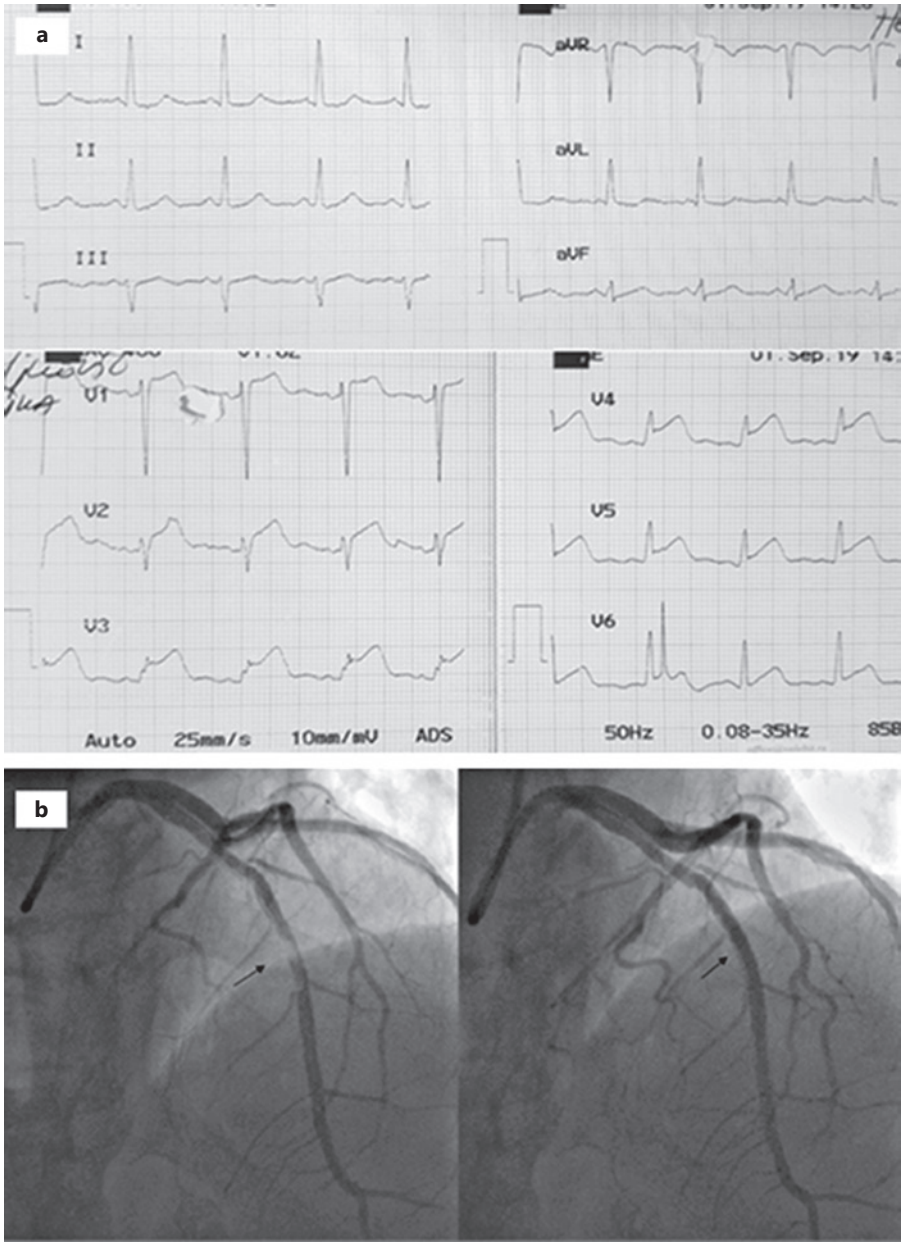

Fig. 1. a ECG changes at admission. **b** LAD before and after successful primary PCI.

As mentioned, the first case in man was described by Ries et al. [5]. They reported selective CRP-apheresis in 69-year-old male who was referred due to STEMI of anterior wall. After successful PCI patient underwent CRP-apheresis using Spectra-Optia with Pentrasorb CRP-adsorber system. However, the CRP-apheresis in these studies [5, 12] was performed later, that is, 27.5 ± 4.6 h after AMI onset. Ongoing human multicenter matched-control pilot CRP-apheresis in Acute Myocardial Infarction 1 (CAMI-1) study will determine the further direction of research, clinical implication, and development of procedure. The first result of 67 out of 80 patients and control showed that CRP-apheresis in STEMI is safe and feasible and CRP-depletion has significant beneficial effect both on myocardial infarction size reduction and recovery of wall motion as well [4]. We are waiting for result from cardiac magnetic resonance imaging to quantify myocardial zone "saved" due to this apheresis and CRP-depletion procedure.

We presented a case of 53-year-old woman who referred with anterior STEMI. She was treated with primary PCI after which she received standard post-STE-

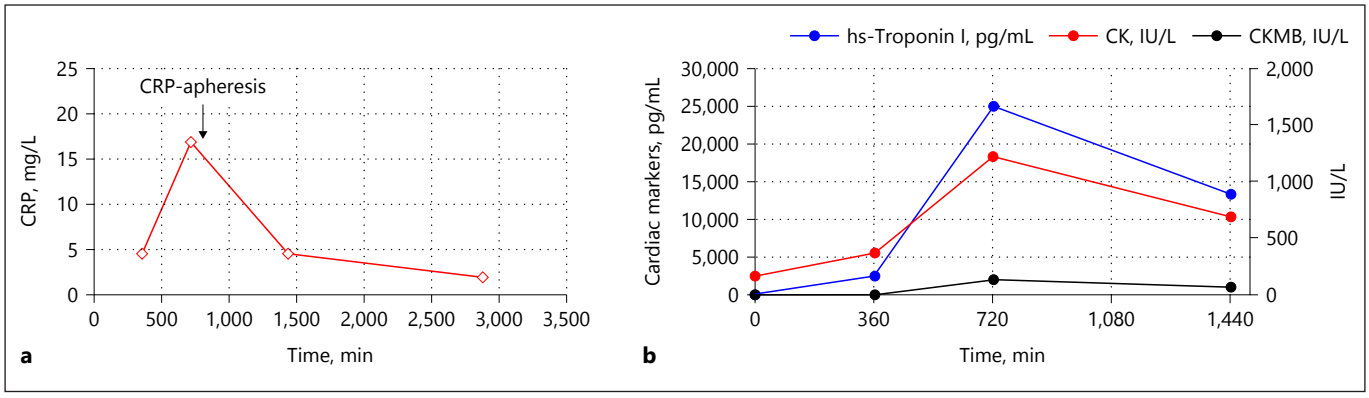

Fig. 2. a, **b** CRP levels before and after CRP-apheresis and cardiac enzyme progress following AMI. CRP, C-reactive protein; CK, creatine kinase; CKMB, creatine kinase MB isoenzyme.

MI therapy according to current ESC guidelines. Hemodynamically stable patient was monitored at the coronary care unit where selective and intensive CRP-apheresis was performed. As mentioned, the pre-apheresis CRP level was 16.4 mg/L, and the post-apheresis concentration was 4.59 mg/L (CRP-depletion = 72%). There were neither significant changes observed in plasma biochemistry nor any alterations in investigated hemostatic activity before versus after CRP-apheresis performed. Finally, patient tolerated well this intensive selective TPE without adverse effects or complications.

Early performed CRP-apheresis is undoubtedly a promising innovative therapeutic approach for STEMI treatment that could provide a reduced size of infarction zone – with inferior occurrence of heart failure after AMI. Precise and complete evaluation of the efficacy and safety of this treatment requires further multicenter randomized and larger clinical studies.

Acknowledgment

None.

Statement of Ethics

Therapeutic method was reviewed and approved by Ethics Committee at the Dedinje Cardiovascular Institute. Written informed consent was obtained from patients, including consent for intervention and to publish the findings.

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contributions

D.B. and A.N. conceptualized this paper and wrote the manuscript, S.R. and J.L. collected the data, M.B. and B.B. revised the final revision of article. All authors provided critical feedback and contributed to the manuscript and approved the final version of the manuscript.

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