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Rosuvastatin Lowers Systemic Inflammatory Response in Coronary Artery Bypass Graft Accompanied by Cardiopulmonary Bypass Surgery: A Randomized Controlled Study

Abstract

Purpose: Cardiopulmonary bypass (CPB) is commonly associated with a systemic inflammatory response that may lead to severe complications. Classic signs of systemic inflammatory response syndrome are complement activation and changes in cytokine and acute phase reactant levels. The effects of rosuvastatin after CPB on interleukin-6 (IL-6), interleukin-10 (IL-10), interleukin-18 (IL-18) and High Sensitivity C-Reactive Protein (hs-CRP) levels were investigated.

Methods: Thirty-seven male and thirteen female patients (total=50) aged 42 to 78 years, who had coronary bypass surgery due to coronary artery disease were randomly divided into two groups. The 25 patients in the control group were administered placebos. The 25 in the treatment group were administered 20 mg rosuvastatin tablets daily between preoperative day 7 and postoperative day 28. Blood samples were taken at six time points; before induction of anesthesia (T₁), during CPB (T₂), five minutes after removal of cross clamp (T₃), after protamine infusion (T₄), postoperative day three (T₅) and postoperative day 28 (T₆). Data points were expressed as mean $\pm$ standard deviation (SD).

Results: Rosuvastatin lowered IL-6 levels at T₄, T₅ and T₆ time points (T₄, T₅, T₆ $p < 0.05$), and elevated IL-10 levels at T₃ and T₄ (T₃, T₄ $p < 0.05$). IL-18 levels were also elevated at multiple time points. Rosuvastatin also lowered hs-CRP levels and cholesterol levels at T₆ ($p < 0.05$).

Conclusion: Administering 20 mg/day of rosuvastatin between preoperative day 7 and postoperative day 28 may result in fewer complications in certain (especially intraoperative) cases of systemic inflammatory response caused by the CPB technique used in coronary bypass surgery.

Manuscript submitted 23rd January, 2015
Manuscript accepted 30th May, 2015

Clin Invest Med 2015; 38 (4): E154-E163.

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During coronary artery bypass graft (CABG) surgery, either off-pump or cardiopulmonary bypass (CPB) procedures can be used. The off-pump technique can be used only for a limited number of patients, whereas CPB is more versatile and thus more commonly used. CPB, implemented for the first time in 1953 by J. H. Gibbon, can lead to a condition called systemic inflammatory response syndrome (SIRS). SIRS arises due to leukocyte activation and the formation of substances such as oxygen free radicals, arachidonic acid metabolites, platelet-activating factor (PAF), nitric oxide (NO) and endothelin-1 (ET-1), which are caused by contact of blood with non-physiological surfaces, surgical trauma, ischemia-reperfusion of organs, body temperature changes, complement activation, release of endotoxin-cytokines and adhesion molecules. SIRS can lead to various pathological events such as pulmonary, renal, gastrointestinal and central nervous system complications, myocardial dysfunction, coagulopathy, vasoconstriction, increase in interstitial fluid, hemolysis, fever, predisposition to infection, leukocytosis and multiorgan failure [1]. The immune system generates proinflammatory cytokines, such as IL-6, IL-18, and anti-inflammatory cytokines, such as IL-10, as an inflammatory response [2].

IL-18 is a proinflammatory cytokine from the IL-1 family and has been described as an IFN- γ -inducing factor. Pro-IL-18 uses IL-1 β as a biologically-active protein in the caspase-1 pathway. With activation of caspase-1, the TLR pathway-mediated mechanism returns pro-IL-18 to a mature form, which can be released from macrophages, Kupffer cells, ceratinocytes, osteoblasts, astrocytes and dendritic cells [3,4].

A number of pathophysiological events, such as the delayed improvement of pulmonary function, fluid accumulation in extravascular areas, multiple organ failure and vasoconstriction, have been observed during cardiac surgery [5-7]. Hemodynamic performance disorders, which can be seen even after successful heart surgery, have also been observed. Systemic inflammatory response is believed to be the main cause of all these events, or to at least contribute to the sequence of reactions leading to these events.

The effects of rosuvastatin in cardiac surgery have already been investigated [8-10]. The aim of this study was to provide a comprehensive evaluation of the inflammatory response and the effects of rosuvastatin on the levels of proinflammatory cytokines, such as hs-CRP, IL-6 and IL-18, and anti-inflammatory cytokines, such as IL-10. The hypothesis of this study was that the well known inflammatory effects of CPB technique could be reduced or limited by rosuvastatin, which could result in improved mortality and morbidity after coronary bypass surgery.

In our study, we aimed to measure proinflammatory and anti-inflammatory cytokine levels to determine whether there were correlations between cytokine levels and clinical biochemical tests. Since SIRS is very commonly associated with CPB, assessment of cytokines may prove to be useful for prognostic estimations with high predictive values.

Methods

Having received the approval of Firat University Faculty of Medicine Ethics Committee (Date 17.02.2011, Committee No: 4, Acceptance No: 4), 50 patients aged between 42-78 years, who were hospitalized due to coronary heart disease and scheduled for CABG, were included in the study. Authorization was obtained after patients were provided with verbal and written information about the study. Patients were randomly divided into two groups: the control (Group C, n=25); and the rosuvastatin-treated group (Group R, n = 25). Patients in the treatment group received 20 mg/day of rosuvastatin (20 mg Stage. Abdi Ibrahim Pharmaceuticals Bar Code: 8699514090502) starting at preoperative day 7, through post-operative day 28. The placebo was administered as one pill per day to the control group during the preoperative day 7 to post-operative day 28. Patients using corticosteroids, salicylates, dipyridamole or anticoagulant and receiving thrombolytic therapy within five days, or who had platelet or coagulation disorders were excluded from the study. Patients with hypoxemia, hypercapnia, congestive heart failure, diabetes, chronic renal failure, chronic obstructive pulmonary disease and hepatic insufficiency, heart rate less than 60/min and ejection fraction (EF) less than 30% or active infections, or with a history of previous heart surgery, myocardial infarction in the last month, thyroid disease or surgery, or who were using chronic antiarrhythmic drugs, who had undergone emergency operations, who were to have additional surgical procedures, were also excluded from the study.

Anesthesia

Before anesthesia induction, an arterial catheter was inserted through the femoral artery and central venous catheter through the jugular vein (8F introducer, St. Jude Medical Company, USA), and a Swan-Ganz catheter (7F, Abbott Laboratories, USA) inserted. Induction and maintenance of anesthesia in all patients was provided with fentanyl (20-40 μ g/kg induction, 0.3-1 μ g/kg/min maintenance, fentanyl citrate, Abbott Laboratories), midazolam (0.1 mg/kg induction, 0.8 μ g/kg/min maintenance, Dormicum, Roche) and vecuronium (0.1 mg/kg induction, Norcuron, Organon) as a standard. A rectal probe for

the determination of rectal temperature and a Foley catheter for urine follow-up were inserted.

Surgical Technique

In all patients, the median sternotomy technique was used. The left internal thoracic artery and great saphenous vein were prepared for use as a graft. Following heparinization (3 mg/kg of Nevparin, Mustafa Nevzat Ilac San.), an arterial cannula in the ascending aorta, two-stage venous cannula and antegrade cardioplegia catheter to the right atrium were inserted. When Activated Clotting Time (ACT) reached 450 seconds, partial CPB was begun. CPB was performed with roller pump (Stockert Instrumente, Germany) and membrane oxygenator (D 708 simplex Dideco III, Italy). As prime solution, 2000 ml lactated Ringer's was used and the pump hematocrit was kept at 20%. In all patients, moderate systemic hypothermia (28-30°C) was created. Following cardiac arrest, an aortic cross-clamp was placed (full CPB). Cold (4°C) 15ml/kgcrystalloid cardioplegic solution was given through an antegrade cardioplegia catheter using high pressure (Plegisol, Abbott, USA). Maintenance of cardioplegia was performed by preparing cold blood cardioplegia (200 ml Plegisol + 800 ml of blood, hemoglobin 8 g/dl.) via antegrade catheter using high pressure every 20 minutes: 400 ml for patients under 80 kg and 500 ml for patients over 80 kg. Pump flow and mean arterial pressure were maintained at 2.0-2.4 l./m² and 50-80 mm Hg, respectively.

According to coronary artery involvement, first the right coronary artery, then the circumflex artery and its branches and the last left internal thoracic artery were anastomosed to the left anterior descending artery. After completion of all anastomoses, hot (36°C) blood cardioplegia (hot shot, 3-4 min. 500 ml) was given with antegrade 80 mmHg pressure then the cross-clamp was removed and the CPB was concluded. After weaning off CPB, arterial and venous cannulas were taken by neutralization with the heparin protamine sulfate (protamine, Roche).

After chest tubes and epicardial pacing wires were placed, the sternal incision was closed and the patients were taken to the intensive care unit.

Biochemical Analysis

After completion of the preoperative preparation of patients, 10 ml blood was collected in dry glass tubes for IL-6, IL-10 and IL-18 levels for in a total of six time periods: prior to induction of anesthesia (T₁), during CPB (T₂), 5 minutes after the cross-clamp removal (T₃), after protamine infusion (T₄), on postoperative day 3 (T₅) and postoperative day 28 (T₆). Blood (10 ml)

was taken into dry glass tubes for measurement of hs-CRP, low-density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), total cholesterol (TC), and triglyceride (TG) levels prior to induction of anesthesia (T₁) and on postoperative day 28 (T₂).

Serum was immediately separated by centrifugation (250 rpm), placed into two polypropylene plastic tubes (Eppendorf tubes) and stored in a freezer at -70°C. The levels of IL-6, IL-10, IL-18, hs-CRP and cholesterol were analyzed in the collected blood samples.

Serum IL-6, IL-10 and IL-18 levels were measured with the enzyme-linked immunosorbent assay method (ELISA) by using standard ELISA kits (BOSTER, Wuhan, CHINA), BIOTEK washer (ELX 50TM Microplate, 40710000, Winooski, USA) and BIOTEK readers (ELX 733 310 000 800T, Winooski, USA).

Serum h-CRP levels were measured with a Nephelometer device (SIEMENS BN II MODEL, 282951, Germany) by using SIEMENS commercial kits (Muenchen, Germany).

Serum LDL, HDL, VLDL, TC and TG levels were studied in a Beckman Coulter 2700 device with the kits which were compatible with the device.

Statistical Analysis

Statistical analysis was performed using SPSS v.12.0 software. The resultant data was given as the mean ± standard deviation. Student's t-test was used for comparisons between groups and variance test for repeating measures in order to reveal the time-dependent differences between the measurements within groups. $p < 0.05$ was considered significant.

Results

The demographic data of the patients are shown in Table 1. There were no differences in investigated parameters between the two groups (Table 1).

When hs-CRP levels were evaluated; there were no statistically significant differences in hs-CRP levels between the groups prior to induction of anesthesia. At T₆, there was a significant increase in the control group (Group C) compared to initial values, as well as a statistically significant reduction in the rosuvastatin-treated group (Group R) compared with the control group ($p < 0.05$) (Table 2, Figure 1).

The IL-6 levels of patients in Group R and Group C were compared: while a significant increase was observed in Group R at T₃ ($p < 0.05$), a significant reduction was observed at T₄, T₅, T₆ ($p < 0.05$). In intra-group analysis of variance of the repeated measurements performed for the evaluation of IL-6 levels of

TABLE 1. Patient Demographic Data

Data	Group C (n=25)	Group R (n=25)
Male	19 (% 76)	18 (% 72)
Age (years)	62.8 ± 9.53	61.3 ± 10.20
Weight (kg)	72.26 ± 6.56	70.55 ± 7.35
Height (cm)	164.4 ± 10.47	166.23 ± 8.43
Number of distal anastomoses	3.2 ± 0.86	3.07 ± 0.8
CPB time (minute)	78.3 ± 11.48	81.22 ± 9.23
Cross clamp time (minute)	49.60 ± 3.34	49.90 ± 3.80

TABLE 2. hs-CRP levels of the patients

Time Group	T ₁	T ₂
Control (Group C)	17.90 ± 3.27	26.15 ± 3.83*
Statine (Group R)	21.97 ± 4.13	10.21 ± 1.82*

Hs-CRP (mg/dL). (Mean ± SD)

*p<0.05 Group R compared with Group K at T₂ time

Group C, the situation prior to the induction was compared with the other five cases; a statistically significant increase was observed in blood samples taken at T₃, T₄, T₅, T₆ (p<0.05). In intra-group analysis of variance of the repeated measurements performed for the evaluation of IL-6 levels of Group R, the situation prior to the induction was compared with the other five cases; a statistically significant increase was observed at T₃ and T₄ (p < 0.05) (Table 3, Figure 2).

The IL-10 levels of patients in Group R and Group C were compared: although a significant reduction was observed in Group R at T₃, T₅ and T₆ (p<0.05), a statistically significant increase was observed at T₃ and T₄ (p<0.05). In intra-group analysis of variance of the repeated measurements performed for the evaluation of IL-10 levels of Group C, the situation prior to the induction was compared with the other five cases; a statistically significant increase was observed in blood samples, except for the samples taken at T₆ (p<0.05). In intra-group analysis of variance of the repeated measurements performed for the evaluation of IL-10 levels of Group R, the situation prior to the induction was compared with the other five cases; a statistically significant increase was observed in the blood samples taken at T₃ and T₄ (p < 0.05) (Table 3, Figure 3).

FIGURE 1. hs-CRP levels at T₁ and T₆ (mean ± SD).*p<0.05 vs control groups at T₆.

TABLE 3. IL-6, IL-10 vs.IL-18 levels

Cytokine	Time Group	T ₁	T ₂	T ₃	T ₄	T ₅	T ₆
IL-6	Group C	0.50±0.04	0.93±0.12	2.99±0.17 ^a	3.37±0.09 ^a	2.34±0.21 ^a	1.25±0.15 ^a
	Group R	1.00±0.14	1.53±0.15 ^{†*}	3.02±0.06 [†]	2.93±0.06 ^{†*}	1.34±0.13 [*]	0.71±0.06 [*]
IL-10	Group C	0.37±0.06	0.67±0.15 [†]	2.08±0.20 [†]	2.77±0.17 [†]	1.25±0.15 [†]	0.60±0.07
	Group R	0.36±0.04	0.34±0.04 [*]	3.43±0.13 ^{†*}	3.41±0.18 ^{†*}	0.52±0.06 [*]	0.42±0.04 [*]
IL-18	Group C	1.36±0.10	1.86±0.15	2.04±0.15 [†]	1.96±0.12 [†]	1.86±0.13	1.54±0.09
	Group R	2.28±0.16	1.90±0.17	2.32±0.15	2.15±0.15	2.71±0.15	2.07±0.19

IL-6, IL-10 and IL-18 levels (pg/ml) (mean ± SD)

*p<0.05 Group C compared with group R at the same time

†p<0.05 Compared with T₁ time at the same group

TABLE 4. LDL, HDL, TC, TG ve VLDL levels of the patients (mg/dL) (Mean ± SD).

Lipoprotein	Time Group	T ₁	T ₂
LDL	Group C	134.56±4.36	132.88±3.77
	Group R	135.12±3.45	101.92±3.23 [*]
HDL	Group C	38.84±2.14	39.6±2.19 [*]
	Group R	38.04±0.88	54±0.79 [*]
TC	Group C	251.92±7.88	243.08±7.36
	Group R	253.44±11.59	175.44±3.13 [*]
TG	Group C	256.08±12.87	250.72±12.38
	Group R	250.96±12.46	189.12±5.54 [*]
VLDL	Group C	51.68±1.42	49.92±1.39
	Group R	49.2±1.89	39.2±0.99 [*]

*p<0.05 Group R compared with Group C at T₂ time.

The IL-18 levels of patients in Group R and Group C were compared:in intra-group variance analysis of the repeated measurements performed for the evaluation of IL-18 levels of Group C. The situation prior to the induction was compared with the other five cases:a statistically significant increase was observed in the blood samples taken at T₃ and T₄ (p < 0.05) (Table 3, Figure 4).

It was proposed that administering 20 mg/day of rosuvastatin between preoperative day 7 and postoperative day 28 would result in fewer complications in certain (especially intraoperative) cases of systemic inflammatory response caused by the CPB technique used in coronary bypass surgery. When

the cholesterol levels of the patients included in the study were analyzed, patients in Group R showed a statistically significant decrease in LDL, TC, TG, VLDL values at time T₂ compared with T₁ (p <0.05), and a statistically significant increase in HDL levels at time T₂ compared with T₁ (p <0.05) (Table 4).The cholesterol levels were analysed in this study because of rosuvastatin's lipid lowering effects on blood samples in hypercholesterolemic patients.

FIGURE 2. IL-6 levels at each time point (mean±SD). * $p<0.05$ vs control group, a $p<0.05$ vs T₁

FIGURE 4. IL-18 levels at each time point (mean±SD). a $p<0.05$ vs T₁

FIGURE 3. IL-10 levels at each time point (mean±SD). * $p<0.05$ vs control group, a $p<0.05$ vs T₁

Discussion

It is known that, CPB, which is an indispensable technique in modern heart surgery, causes systemic inflammatory response [11]. Many factors contribute to this response; some are dependent on the materials used in the process and some are independent of these materials. Among the factors in the former group, contact between blood and non-physiological surfaces and environments seems to be the most important.

Factors that are independent of the material used include surgical trauma, ischemia-reperfusion status of organs, changes in body temperature and endotoxin release. During CPB, leu-

kocyte activation occurs as a result of C activation, release of cytokines, increase in adhesion molecules and production of a number of substances such as oxygen free radicals, arachidonic acid metabolites, PAF, NO and ET, and leads to SIRS [12]. In this clinical situation, there is a hyperdynamic circulatory state due to the reduction in systemic vascular resistance and the increased cardiac output. This chain of events in the inflammatory response may contribute to the development of postoperative complications, such as respiratory failure, renal dysfunction, bleeding disorders, neurological dysfunction, liver function impairment and, ultimately, multiorgan failure. Thus, approaches aimed at reducing this inflammatory response to CPB are of great importance. Lactic acidosis was seen in the medical history in a significant proportion of patients with SIRS, and these patients are at greater risk for multiorgan failure. The incidence of infectious complications in these patients was also high [12,13].

This inflammatory system response leads to the production of proinflammatory cytokines, such as IL-6, IL-18, and anti-inflammatory cytokines, such as IL-10. As well, there are inhibitory mechanisms that prevent organ damage and suppress the inflammatory response following cardiac surgery. Thus, the balance between inflammatory and anti-inflammatory response is important for the clinical outcome of a patient.

In recent years, the release of proinflammatory cytokines, such as hs-CRP, tumor necrosis factor- α (TNF- α), IL-6 and IL-18, has been reported to play an important role in modifying cardiac function. If cytokine production can be reduced during and after CPB, post-surgical problems such as cardiac dysfunction and respiratory distress syndrome can potentially

FIGURE 5. Consort flow diagram of randomized patients

be prevented. Pharmacological agents to minimize the cytokine responses, the use of heparin-coated lines and hemofiltration after CPB are being investigated [14]. Mannacio *et al.* in 2008 reported postoperative assessments of troponin I, myoglobin, creatine kinase-MB and hs-CRP; however, in our study, both proinflammatory cytokines (IL-6 and IL-18) and anti-inflammatory cytokine (IL-10) were measured [15].

Cytokine secretion begins to increase immediately after CPB, and reaches its highest level in the postoperative 12-24th

hours. CPB and aortic cross-clamp time are the most important parameters affecting the secretion of cytokines. In this study, when the results of the control group were evaluated, increase of inflammatory cytokines was observed during and after CABG.

Rosuvastatin is a drug used in treatment of primary hypercholesterolemia and combined dyslipidaemia. Rosuvastatin exerts its effect by selectively and competitively inhibiting HMG-CoA reductase, the rate-limiting enzyme of the meva-

lonate pathway; the metabolic pathway that ultimately produces cholesterol. HMG-CoA reductase catalyses the conversion of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA), to mevalonate [16-19]. It has been demonstrated that statistically significant reductions were provided in terms of the levels of CK-MB and troponin-I, which are myocardial ischemia markers, in the early period after CABG operation with the use of HMG-CoA reductase inhibitors prior to surgery [20]. It has also been reported that the safe and effective use of statins before and after CABG operations may act as anti-inflammatories that are independent of cholesterol levels [21]. Useful effects can also be obtained by suppressing the inflammatory response by administering higher than standard doses of statins before CABG [22]. In this study, when the results of Group R were evaluated it was concluded that levels of hs-CRP and IL-6, an inflammatory cytokine, could be reduced compared with Group C, and the levels of IL-10, an anti-inflammatory cytokine, could be increased at certain times following surgery.

IL-6 is the principal contributor to the acute phase response and it provides this by activating hepatocytes to synthesize acute phase proteins such as CRP, C components, orosomucoid, haptoglobin, fibrinogen and protease inhibitors. CRP is an acute phase protein and serum levels rise in response to infection, inflammation, autoimmune diseases and malignant diseases. It is synthesized in the liver under the control of IL-6 [23].

In a study on pigs, a statistically significant postoperative decrease in the levels of IL-6 was obtained with the administration of 20 mg of rosuvastatin 7 days prior to CABG [24]. In another study, IL-6 levels during the postoperative period were significantly lower in the statin-treated group of patients undergoing CABG [25]. In our study, determination of a significant increase in the blood levels of IL-6 in the control (non-rosuvastatin) group 5 min after cross-clamp removal, after the completion of protamine infusion, on the 3rd and 28th postoperative days compared with the postoperative period, using an intra-group analysis of variance confirmed the previously published data on this inflammatory process. A statistically significant reduction in the levels of IL-6 with the use of rosuvastatin, in the blood samples taken after completion of protamine infusion, on the 3rd and 28th postoperative days, confirmed that the anti-inflammatory activity could be obtained at the end of CPB and during postoperative period when the inflammatory consequences of CPB are observed. Thus, the suppression of CPB-induced inflammatory response, may reduce postoperative complications.

IL-10 is a key regulator of the inflammatory response. The immunosuppressive effects of IL-10 protect against conditions such as over-stimulated inflammatory responses, microbial infection and autoimmune diseases [26]. In a study performed on rats, a statistically significant increase was seen in serum IL-10 levels over a 14 day period of myocardial ischemia by using statins, compared with control group [27]. Blood samples were taken to measure IL-10 levels. A statistically significant increase in the control group, according to intra-group variance analysis, was found at all times except postoperative day 28 ($p < 0.05$). This should be considered as a result of the anti-inflammatory fight of the body against this inflammatory event during the CPB and immediate postoperative period. A significant increase in IL-10 levels was seen with rosuvastatin at 5 min post-operative. After cross-clamp removal and after completion of protamine infusion, comparison with the control group shows the contribution of the use of rosuvastatin to the fight of the body against this inflammatory event during the intraoperative period, when the most severe inflammation occurs. This observation reinforces our belief that benefits can be achieved in CABG patients during the postoperative period by reducing the complications that can occur due to inflammation.

IL-18 also plays a significant role in the body's defense. *In vitro* neutralization of IL-18 has been shown to inhibit secretion of TNF- α , IL-6 and interferon- γ (INF- γ) by macrophages. The importance of IL-18 in patients with rheumatoid arthritis (RA) was first demonstrated by Gracie *et al.* in 1999 [28]. IL-18 messenger ribonucleic acid (mRNA) and protein levels were higher in the joints of RA patients than in patients with osteoarthritis. Blood samples were used for IL-18 measurements [28]. A statistically significant increase in the control group, 5 min after cross-clamp removal and after completion of protamine infusion, and the observation of a slight (though not statistically significant) increase at all time periods with the use of rosuvastatin created the impression that rosuvastatin was not effective enough on IL-18 levels and more studies should be performed regarding the effects of this cytokine. Elevation in IL-18 concentrations after CPB operation was found to have predictive value both for type I cerebral injury and also the extent of kidney injuries [29,30].

CRP is a well characterized acute phase reactant. In recent years, many studies have been published investigating the relationship between the increase in CRP and the presence of atherosclerotic coronary artery disease, which is considered an inflammatory disease. Ridker *et al.* reported in a study published in 1997 that higher baseline CRP levels in otherwise healthy men may be a biomarker for myocardial infarction (MI) and stroke [31]. When inflammation develops for any

reason, the acute phase proteins, including CRP, are synthesized by the liver under the influence of proinflammatory cytokines. CRP is one of the indicators of inflammation, and has been used as a diagnostic tool in clinical practice [32].

hs-CRP was the other protein whose level was monitored in this study. Clinical trials have reported that rosuvastatin reduces the levels of hs-CRP. hs-CRP is a marker which is closely associated with cardiovascular risk (33-39). Despite normal or low LDL cholesterol levels, rosuvastatin was shown to reduce hs-CRP and to reduce the production of other inflammatory markers, such as von Willebrand factor, fibrinogen, serum amyloid A and platelet activating acetylhydrolase [37,40,41]. This was confirmed by the statistically significant increase in hs-CRP levels in the control group on the postoperative 28th day seen in this study. A statistically significant decrease in hs-CRP levels in the rosuvastatin group obtained on the 28th postoperative day was considered as indicative that anti-inflammatory activity could be achieved with the use of rosuvastatin.

Due to the common use of statins in the treatment of cholesterol, the blood lipid and cholesterol levels were also checked in the preoperative and postoperative periods in our study. It has been determined that rosuvastatin provided a statistically significant decrease in LDL, TC, TG and VLDL levels compared with the control group on the 28th postoperative day and a statistically significant increase in HDL levels compared with the control group on the 28th postoperative day. These results confirm previous data regarding the effectiveness of rosuvastatin on lipid levels.

Conclusion

Although complement activation was thought to be the reason for adverse events seen during and after CPB, this event is highly complex and influenced by many factors. If complement activation and/or cytokine production causing systemic inflammatory response can be completely or partially inhibited, the adverse events seen after heart surgery, which contribute to patient morbidity and mortality, can be prevented.

The use of rosuvastatin during the perioperative period may be able to contribute to positive post-CABG surgery outcomes by providing both anti-inflammatory and antihyperlipidemic effects for the cardiovascular system.

Financial Support

This study was supported by FUBAP (Firat University Scientific Research and Design Center). Project Number: TF: 1110 – 2012 Firat University Elazig, Turkey.

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