Preoperative statin treatment reduces systemic inflammatory response and myocardial damage in cardiac surgery

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Abstract

Objective: To determine if preoperative statin treatment is associated with a reduction in systemic inflammatory response (SIR) and myocardial damage markers following cardiac surgery with cardiopulmonary bypass (CPB). Methods: We study a prospective cohort of 138 patients who underwent coronary and valvular surgery with CPB. We differentiate two study groups: patients with (group A, n = 72) or without (group B, n = 66) statins. Plasma levels of pro-inflammatory interleukins (tumour necrosis factor-alpha (TNF-α), interleukin (IL)-6, IL-8 and IL-2R), creatine phosphokinase (CPK), CPK-MB and troponin I were measured before and 1, 6, 24 and >72 h after surgery. Results: The baseline, operative and postoperative morbidity and mortality characteristics were similar for both the groups. Group A had significantly lower postoperative levels of IL-6 than group B at 6 h (68.8 ± 5 pg ml⁻¹ vs 108.9 ± 108 pg ml⁻¹, p = 0.01), 24 h (71.7 ± 7 pg ml⁻¹ vs 110.4 ± 106 pg ml⁻¹, p = 0.01) and before hospital discharge (21.6 ± 12 pg ml⁻¹ vs 32.8 ± 27 pg ml⁻¹, p = 0.005), as well as significantly lower average IL-6 levels in the first 24 h following surgery (71.8 ± 5 pg ml⁻¹ vs 112.8 ± 82 pg ml⁻¹, p = 0.002). The postoperative CPK-MB at 24 h (19.7 ± 23 ng ml⁻¹ vs 33.1 ± 32 ng ml⁻¹, p = 0.02) and troponin I levels at the end of the intervention (2.2 ± 2.2 ng ml⁻¹ vs 3.3 ± 3.1 ng ml⁻¹, p = 0.03) and at 24 h (4.1 ± 3.5 ng ml⁻¹ vs 6.6 ± 8 ng ml⁻¹, p = 0.04) were also significantly lower in the group treated with statins prior to surgery. Conclusions: Preoperative treatment with statins is associated with a lower biochemical parameters of SIR and myocardial damage following cardiac surgery with CPB, regardless of it being coronary bypass grafting (CABG) or valvular surgery.

Keywords: Extracorporeal circulation; Inflammation; Statins

1. Introduction

Despite improvements in perioperative care and optimisation of surgical techniques in the last decade, postoperative morbidity and mortality following cardiac surgery with cardiopulmonary bypass (CPB) can still be improved [1]. A large part of postoperative complications appear to be related to an excessive systemic inflammatory response (SIR) unleashed by CPB and surgical trauma [2].

Some interleukins (ILs), such as the tumour necrosis factor (TNF-α), IL-6 and IL-8, show elevated plasma levels in patients undergoing cardiac interventions as a result of SIR [3]. Additionally, a correlation between these findings and some postoperative complications has been observed [4,5].

Currently, no convincing drugs or techniques exist to reduce the severity and incidence of SIR.

The 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase inhibitors, known simply as statins, are used effectively as hypolipidaemic agents and have demonstrated their efficacy in the reduction of cardiovascular events in primary and secondary prevention for a variety of populations [6–9]. Some theories about the anti-inflammatory action of statins have arisen in recent years, which may, in part, explain those clinical benefits that cannot be attributed to a hypolipidaemic effect [10]. In addition, statins seem to improve bypass graft patency and long-term mortality rates in patients undergoing coronary bypass grafting (CABG) [11]. Based on these pleiotropic effects, some studies, but not all, appear to have shown benefits on perioperative morbidity and mortality in patients undergoing cardiovascular surgery [11–14].

Statins have been demonstrated to reduce inflammatory markers. However, it is not known if this effect is extensible to the postoperative period. The available data suggest that could be the case. The preoperative administration of statins

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decrease pro-inflammatory cytokines, mainly IL-6, in the first hours following CABG [15–18]. In addition, troponin I, a marker of myocardial damage, that increases following cardiac surgery has been correlated with the postoperative increase in inflammatory parameters [19].

Currently, no prospective study exists that shows a reduction in pro-inflammatory ILs and troponin I as a consequence of preoperative statins in cardiac surgery involving valvular and coronary surgery, nor have significant differences in morbidity been found. In this study, we prospectively analyse, based on preoperative statin treatment, the SIR, the effect on myocardial damage and complications following cardiac surgery with CPB.

2. Materials and methods

2.1. Study protocol

We performed a prospective study with a cohort of patients included between November 2006 and April 2007 in the Hospital Clínico Universitario of Santiago de Compostela. The cohort to be studied was composed of 138 consecutive patients who underwent cardiac surgery with CPB. We included all those patients who underwent coronary surgery (isolated coronary surgery or coronary surgery + valve surgery) and non-coronary surgery (isolated valvular surgery) within this time period. We excluded those patients who had undergone any type of transplant, those receiving corticosteroid or immunosuppressant treatments, those with infections, active tumours, autoimmune diseases and acute renal failure; patients who underwent surgery on an emergency basis were not included in the study either.

Of the 138 patients included in this study, we differentiated two groups of patients based on whether they were treated with statins prior to surgery (group A: 72 patients) or did not receive this treatment (group B: 66 patients). All of the patients in group A suffered from dyslipidaemia and were under statin treatment for a minimum of 3 weeks before surgery. Statins were administered in the usual manner, including the night before surgery, and they were again administered the evening following surgery, continuing with the same regimen throughout the entire duration of hospitalisation. In both the groups, anti-platelet agents were discontinued 10 days before surgery. Other medications were discontinued on the same morning of surgery.

The study protocol was approved by the local ethics committee. Informed consent was obtained from each of the patients included in our study.

3. Surgical procedure and postoperative care

Anaesthesia induction and maintenance were similar for all patients and consisted of doses of Midazolam, vecuronium bromide, Remifentanil and sevoflurane, adjusted for weight. During the intervention, systemic and pulmonary blood pressure, central venous pressure, pulse oximetry, five-lead electrocardiogram, oesophageal and urethral temperature and ventilatory parameters were monitored, all using a standard anaesthesia device (Datex-Ohmeda Aestiva 3000°; AS/3 monitor®, Datex-Ohmeda Instrumentarium Corp., Helsinki, Finland).

All patients underwent valvular surgery or coronary bypass surgery with CPB, mild hypothermia between 32 and 33 °C and electromechanical arrest of the heart by aortic clamping and administration of intermittent cold blood cardioplegia every 20 min.

An extracorporeal circulation machine (Stockert SIII®, Germany) equipped with a centrifugal pump (Stockert SCP Revolution®, Germany) was used, to which a heat exchanger was attached (Stockert SIII®, Germany). Before connecting to extracorporeal circulation, the patients were heparinised with 3 mg·kg⁻¹ of sodium heparin (Heparina Rovi®, S.A., Spain), keeping an activated coagulation time above 300 s (Hemotec ACT III®, Medtronic Inc., USA) during the entire procedure, adding additional doses of heparin when necessary. A membrane oxygenator was used (Dideco Avant 903 D®, Italy) priming the circuit with a base of 1000 ml of lactated Ringer’s crystalloid solution (Ringer Lactato Braun®, Braun, Spain), 0.5 mg·kg⁻¹ of mannitol (Manitol Braun 20%, Braun, Spain); 100 ml of 1 M sodium bicarbonate (Venofusin®, Fresenius Kabi, Spain) and 0.5 mg·kg⁻¹ of sodium heparin (Heparina Robi®, Rovi S.A., Spain).

The approach was performed through conventional median sternotomy. Venous and/or arterial grafts were used in patients with ischaemic heart disease in order to perform the coronary re-vascularisation.

The ascending aorta and the right atrium were cannulated in the usual manner. Two cannulae were used in the right atrium for mitral and tricuspid valve disease interventions, as well as a single cavo-atrial cannula in coronary and aortic patients.

At the end of the surgical procedure, the patients were transferred to the Resuscitation Unit where they remained sedated with propofol, morphine and Midazolam administered as needed. The patients remained intubated and connected to a mechanical ventilator in synchronised SIMV mode between 6 and 10 ml·kg⁻¹ at a respiratory rate of 12 bpm, PEEP between 5 and 7 cm H₂O with a trigger between −1 and 1 cm H₂O and with an FIO₂ adjusted according to arterial blood gas analysis. The minimum mechanical ventilation time was 6 h; after which all those patients in whom haemodynamic, ventilation, oxygenation and temperature stability conditions permitted were extubated. Haemodynamic monitoring was maintained for at least the first 12 h of the postoperative period.

4. Blood sample collection, stocking and analysis

The following biochemical parameters were measured: erythrocyte sedimentation rate (ESR), iron, transferrin, ferritin, thyroid-stimulating hormone (TSH), total bilirubin, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), gamma-glutamyl transferase (GGT), alkaline phosphatase, haematocrit, creatinine and BUN, at baseline prior to the surgical intervention and after surgery once the patients were stabilised in the Hospitalization Unit.

Venous samples were collected to measure levels of TNF-α, IL-6, IL-8, IL-2 receptor (IL-2R), CH50, C3, C4 and C-reactive
protein in serum as shown: before anaesthesia induction; at the end of the intervention with CPB; at 6 and 24 h after surgery and before discharge from the hospital, with the patient in stable condition. Levels of creatine phosphokinase (CPK), CPK-MB, troponin I, BUN, creatinine and haematocrit were also measured immediately after surgery and at 6 and 24 h.

4.1. Myocardial necrosis markers

CPK-MB levels were measured using commercially available enzyme immunoassay (Behring Laboratories Inc.) Dimension® system with the heterogeneous immunoassay module; the minimum detectable levels are below 0.5 ng ml⁻¹ (μg l⁻¹). Cardiac troponin I levels were measured with the same commercially available colorimetric immunoassay.

4.2. Interleukins

The samples were collected through venipuncture in tubes with ethylenediaminetetraacetic acid (EDTA) and immediately centrifuged at 4 °C and stored at −20°C prior to analysis. TNF-α, IL-6, IL-8 and IL-2R were measured using the IMMULITE® (DCP®) system, which is an enzyme immuno- metric assay using solid-phase chemiluminescence for use in the IMMULITE® (DCP®) automatic analyser and is designed for the quantitative measurement of these interleukins.

5. Statistical analysis

The qualitative data are expressed in absolute numbers (percentage). The quantitative data are presented as the average ± standard deviation, adding or substituting them with the median (interquartile range) when the distribution of the values of this variable is markedly outside of the normal distribution; this last value was calculated using Kolmogorov–Smirnov and Shapiro–Wilk tests.

Univariate analyses were performed, comparing the different variables obtained between the groups defined as having received or not received preoperative statins. For comparison of quantitative data, the Student’s t (parametric) or Mann–Whitney’s U (non-parametric) tests were used depending on the case. Comparison of the qualitative data was performed using the χ² (chi-square) test, applying Yates’ correction to obtain the most conservative results.

In order to establish the role of preoperative statins as a possible independent predictor of postoperative IL-6 levels, a multivariate multiple linear regression analysis was performed, including the average postoperative IL-6 values as a dependent variable. To avoid forcing the model excessively, it was decided to include, as a maximum, an independent variable for every 10 patients. The independent variables included in the analysis were the treatment with statins before surgery (the variable around which the entire analysis revolves) and those whose possible association with IL-6 values was established based on prior scientific evidence, the common sense of the researchers and the statistical significance obtained in the univariate analysis. In order to avoid collinearity phenomena, the level of tolerance for each independent variable regarding all others of their type (qualitative or quantitative) was determined; if two variables demonstrated a tolerance <0.01, only one of them was included in the multivariate model based on clinical judgement analysing the theoretical justification for each of the variables involved and the quality with which they had been measured. The data were analysed with the SPSS statistical package for Windows, version 13.0 (SPSS Inc., Chicago, IL, USA). Values of p < 0.05 were considered statistically significant.

6. Results

6.1. Baseline characteristics of the patients

Both the groups had very similar clinical and operative characteristics (Table 1).

The type of statin used most was atorvastatin (63.9%), followed by simvastatin (22.2%), pravastatin (12.5%) and lovastatin (1.4%).

The most common dose of atorvastatin, simvastatin and lovastatin was 20 mg per day and for pravastatin it was 40 mg per day.

None of the patients showed side effects attributable to statins.

Table 2 shows the distribution of the different types of surgery in both the groups.

6.2. Patient analytical evolution

Upon analysis of the baseline characteristics, similar values were shown in the majority of the parameters measured in the two study groups. Differences were not seen either when comparing the postoperative analyses of both the groups.

Only the preoperative levels of total cholesterol and low-density lipid (LDL) were significantly lower in the group under treatment with statins (total cholesterol 160.43 ± 39.5 mg dl⁻¹ vs 183.69 ± 50.5 mg dl⁻¹, p = 0.004, and LDL 91.64 ± 31.3 mg dl⁻¹ vs 119.69 ± 47 mg dl⁻¹, p = 0.001). The levels of preoperative high-density lipid (HDL) and triglycerides were very similar in both the groups. However, the postoperative total cholesterol, LDL, HDL and triglyceride levels did not differ significantly between the two study groups.

6.3. Evolution of postoperative myocardial damage markers

The CPK, CPK-MB and troponin I levels were elevated in all measurements in both the study groups.

A progressive increase in the levels of CPK at 6 and 24 h was observed, without significant differences between the untreated group and the group treated with statins.

The levels of CPK-MB reached a maximum peak at 6 h in both groups. As can be seen in the curve in Fig. 1, the levels observed in the statin treatment group were always lower than those in the group that did not receive treatment, this difference only being significant in the measurement at 24 h (19.7 ± 23 ng ml⁻¹ vs 33.1 ± 32.6 ng ml⁻¹, p = 0.02).

Levels of troponin I were also elevated in both treatment groups once the patients arrived to the Post-Surgery Unit.
The lower levels of troponin I at the three measurements performed on the group that was receiving statins can be seen in the curve in Fig. 1, with this difference being significant in the sample collected at the end of the intervention (2.25 ± 0.6 ng ml\(^{-1}\) vs 3.32 ± 0.3 ng ml\(^{-1}\), \(p = 0.03\)) and at 24 h (4.15 ± 0.54 ng ml\(^{-1}\) vs 6.64 ± 0.80 ng ml\(^{-1}\), \(p = 0.04\)).

### 6.4. Chronological interleukin profile

The TNF-\(\alpha\) and IL-8 values increased following surgery, but significant differences between the study groups were not seen (Fig. 2).

The chronological evolution of IL-6 levels is also seen in Fig. 2.

### Table 2

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Treatment with statins ((n = 72))</th>
<th>Treatment without statins, (n = 66)</th>
<th>(p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolated coronary surgery</td>
<td>21 (29%)</td>
<td>9 (14%)</td>
<td>0.027*</td>
</tr>
<tr>
<td>Coronary + aortic valve surgery</td>
<td>10 (14%)</td>
<td>10 (15%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Coronary + mitral valve surgery</td>
<td>1 (1%)</td>
<td>3 (5%)</td>
<td>0.3</td>
</tr>
<tr>
<td>Non-coronary or valvular surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic valvular surgery</td>
<td>30 (42%)</td>
<td>30 (45%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Mitral valvular surgery</td>
<td>10 (14%)</td>
<td>14 (21%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Coronary–non-coronary surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary surgery</td>
<td>32 (44%)</td>
<td>22 (33%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Non-coronary surgery</td>
<td>40 (56%)</td>
<td>44 (67%)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

* Statistical significance \(p < 0.05\).
The levels observed in each of the measurements in group A were always lower than those measured in group B, being statistically significant at 6 h (68.85 ± 49.41 pg ml⁻¹ vs 108.91 ± 108.8 pg ml⁻¹, p = 0.012), at 24 h (71.7 ± 73.1 pg ml⁻¹ vs 110.4 ± 106.5 pg ml⁻¹, p = 0.015) and before discharge from the hospital (21.61 ± 12.03 pg ml⁻¹ vs 32.84 ± 27.9 pg ml⁻¹, p = 0.005).

We also obtained the average postoperative levels of IL-6 in the first 24 h (weighted according to the number of 6-h periods included between each pair of measurements), as seen in Fig. 3, showing that the levels are significantly lower in the group under treatment with statins as compared to the untreated group (71.82 ± 50.3 pg ml⁻¹ vs 112.88 ± 82.86 pg ml⁻¹, p = 0.002). The average postoperative IL-6 levels before discharge (Fig. 3) also showed a statistically significant reduction in group A as compared to group B (52.3 ± 42.27 pg ml⁻¹ vs 80.3 ± 59.9 pg ml⁻¹, p = 0.007).

The increase in IL-2R levels is fundamentally delayed, as is seen in Fig. 2. The IL-2 levels following intervention are always lower in the group receiving statins, with this difference only being significant in the levels measured before discharge from the hospital (909.54 ± 532.7 μg ml⁻¹ vs 1265.6 ± 935.2 μg ml⁻¹, p = 0.014).

Levels of CH50, C3c and C4 showed a clear reduction following cardiac intervention with CPB, and levels of C-reactive protein were progressively elevated from the first measurement until the last measurement prior to discharge. There were no statistically significant differences between the two study groups.

6.5. Postoperative clinical evolution

Table 3 shows the different results over the postoperative period. In general, significant differences were not seen over the postoperative period between the two study groups.

6.6. Variables related to the average postoperative IL-6 levels

In an attempt to ascertain which factors may potentially influence the relation between statins and IL-6 levels, those variables related to IL-6 were also analysed.

Among all the variables studied, the only ones related to average postoperative IL-6 levels within the first 24 h that held a significant direct correlation were CPK at 24 h (p = 0.007), CPK-MB at 24 h (p = 0.001) and troponin I at 24 h (p = 0.005).
6.7. Multivariate analysis

Upon performing the multivariate analysis (multiple linear regression), it was shown that preoperative statins treatment independently reduced the average postoperative IL-6 levels in the first 24 h with statistical significance ($p = 0.008$); therefore, statins are independent predictors of a reduction in IL-6. The IL-6 value in those who are under statins preoperatively is, on average, $36.4 \text{ pg m}^{-1}$ lower than in those who did not take statins. The multivariate analysis also shows that the effect of statins is similar regardless of the type of surgery performed (coronary or non-coronary).

7. Discussion

IL-6 is responsible for coordinating of the acute phase of inflammation, among other functions. It increases later than TNF and IL-1 following cardiac surgery. The increase in IL-6 values has been demonstrated within the context of cardiac interventions, though not invariably [20]. In addition, IL-6 is considered to be a cardiac depressant. Serum concentrations may correlate to mortality following paediatric cardiac surgery [4]. In some studies, it has been found to be a predictor of infection following cardiac surgery in patients with abnormal ventricular function [5]. Thus, IL-6 appears to be partly responsible for the morbidity associated with the inflammatory response related to CPB.

In our study, we find elevated postoperative IL-6 levels in both the study groups, with significantly lower levels in the group treated with statins. Our results are strengthened by the method of assessing IL-6 (five measurements per patient) and a novel concept of average postoperative IL-6 levels. The kinetic behaviour of postoperative IL-6 in our study is similar to prior observations [15—18] in coronary patients. This is the

**Table 3**

Postoperative course. Details (average ± standard deviation).

<table>
<thead>
<tr>
<th></th>
<th>Treatment with statins ($n = 72$)</th>
<th>Treatment without statins ($n = 66$)</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for electrical shock (n)</td>
<td>21 (30%)</td>
<td>26 (41%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Postoperative bleeding (ml/3 h)</td>
<td>186 ± 168</td>
<td>174 ± 148</td>
<td>0.7</td>
</tr>
<tr>
<td>Postoperative bleeding (ml/24 h)</td>
<td>652 ± 452</td>
<td>620 ± 501</td>
<td>0.7</td>
</tr>
<tr>
<td>Average transfusions of packed red blood cells in the first 48 h</td>
<td>2.3 ± 2</td>
<td>2.3 ± 2.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Reoperation due to bleeding</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Postoperative AF$^*$ (n)</td>
<td>24 (34%)</td>
<td>28 (42%)</td>
<td>0.3</td>
</tr>
<tr>
<td>AF$^*$ at discharge (n)</td>
<td>14 (20%)</td>
<td>18 (27%)</td>
<td>0.3</td>
</tr>
<tr>
<td>Perioperative myocardial infarction</td>
<td>3 (4%)</td>
<td>4 (6%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Mechanical ventilation time (h)</td>
<td>28.2 ± 60</td>
<td>39.6 ± 105</td>
<td>0.5</td>
</tr>
<tr>
<td>Acute renal failure (n)</td>
<td>9 (13%)</td>
<td>8 (12%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Need for haemofilter (n)</td>
<td>8 (11%)</td>
<td>5 (8%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Low output (n)</td>
<td>5 (7%)</td>
<td>6 (9%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Temperature in the first 12 h ($^\circ$C)</td>
<td>36.4 ± 1.4</td>
<td>36.7 ± 0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Infections (n)</td>
<td>16 (22%)</td>
<td>18 (27%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Respiratory infection</td>
<td>14 (20%)</td>
<td>16 (24%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Mediastinitis</td>
<td>2 (3%)</td>
<td>3 (4%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>6 (8%)</td>
<td>2 (3%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Prosthetic endocarditis</td>
<td>1 (1%)</td>
<td>0</td>
<td>0.3</td>
</tr>
<tr>
<td>Stroke (n)</td>
<td>1 (1.4%)</td>
<td>2 (3%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Average days in ICU (\textdegree)</td>
<td>6.3 ± 7.8</td>
<td>7.2 ± 9.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Average days following surgery</td>
<td>13.8 ± 8</td>
<td>14.8 ± 8.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Deaths (n)</td>
<td>4 (5%)</td>
<td>2 (3%)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

$^*$ AF: atrial fibrillation.
$^\text{ICU}$: intensive care unit.
first study that demonstrates that patients with preoperative statin treatment before cardiac surgery with CPB show a significant reduction in postoperative IL-6 levels, regardless of the type of surgery performed (coronary or valvular).

On the other hand, in none of the scarce studies assessing the effect of statins on the profile of certain interleukins after myocardial revascularisation surgery was IL-2R studied. We demonstrate a dampening of IL-2R levels following cardiac surgery with CPB in patients under preoperative statin treatment. Its delayed increase following cardiac surgery and the dampening of this increase in levels in patients under statin treatment may have prognostic implications or a role in the morbidity and mortality, which is currently unknown.

The increase in postoperative CPK may indicate damage to other tissues apart from such as thoracic skeletal muscle or the calves. However, CPK-MB is specific to the myocardium and its release is possible due to ischaemia during CPB, as well as from myocardial or aortic incisions during the operation (e.g., from the right atrium for cannulation of the vena cavae). Due to the almost universal release of CPK-MB, the diagnosis of myocardial infarction (MI) should not be made unless the CPK-MB is significantly increased (i.e., >30 ng ml\(^{-1}\)), and if a series of diagnostic variables are also met.

Troponin I specific to the heart is elevated after surgery in practically all patients undergoing cardiac surgery with CPB [21]. Patients with preoperative MI release greater amounts of troponin, because the serum level may remain between 10 and 20 times above the upper limit of the reference interval for at least 4 or 5 days after surgery.

Among all the variables in the study, the only parameters showing a direct correlation with the average postoperative IL-6 levels up to 24 h were: CPK, CPK-MB and troponin I at 24 h. This suggest that the higher the inflammation (measured by IL-6 levels), the higher the levels of CPK-MB and troponin I. On the other hand, we find a significant reduction in postoperative CPK-MB and troponin I levels in the group under treatment with statins, as well as in the IL-6 levels.

Since, that the baseline patient characteristics were similar and the ischaemia times during aortic cross-clamp, CPB times and the cardiopulmonary technique were also almost the same, the only differentiating factor that remains to justify these findings would be statin treatment. Probably statins offer myocardial protection and, consequently, less myocardial damage due to their widely demonstrated anti-inflammatory effects.

The majority of studies in which a correlation is suggested between poorer clinical progress with elevated troponin levels [22,23] are based on patient populations that only undergo myocardial revascularisation surgery and few are based on non-coronary open heart surgery patients [24]; therefore, it still remains to be seen if troponin levels have prognostic implications in non-coronary cardiac surgery with CPB.

7.1. Limitations of the study

This is not a randomised single-centre study, based on a low number of patients who underwent the administration of multiple statin drugs at different dosage and duration.

8. Conclusion

This is the first study to report that preoperative treatment with statins reduces biochemical parameters of systemic inflammatory response and myocardial damage in cardiac surgery with cardiopulmonary bypass, regardless of being CABG or valvular surgery. Future randomised studies are needed, and with larger patient populations, in order to clarify the true prognostic repercussions of these findings.

References


