Short Communication

Comparative Study of Clinical Outcomes of Methylprednisolone and Dexamethasone in Prime Solution during Cardiopulmonary Pump after Coronary Artery Bypass Grafting

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Abstract

Background: The study was performed to compare clinical outcomes of methylprednisolone and dexamethasone in prime solution during cardiopulmonary pump after coronary artery bypass grafting (CABG).

Materials and Methods: In this double-blind clinical trial, sixty-two patients who underwent CABG were divided into the control group (31 patients with dexamethasone in their prime solution) and the study group (31 patients using methylprednisolone in their prime solution). Duration of mechanical ventilation, length of intensive care unit (ICU) stays, bleeding rate (chest tube volume), arrhythmia, and need for inotropic intake were compared.

Results: The mean duration of mechanical ventilation and ICU stay in the dexamethasone group were significantly higher than the methylprednisolone group and the mean bleeding rate in the dexamethasone group was significantly lower than the methylprednisolone group ($p<0.05$).

Conclusion: The mean duration of mechanical ventilation and ICU stay in the dexamethasone group was higher than the methylprednisolone group, but the use of dexamethasone has the advantage of being associated with less bleeding.

Keywords: Cardiopulmonary bypass, Prime solution, Stay in ICU, Mechanical ventilation time, CABG, Inotrope, Bleeding

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Introduction

Nowadays, cardiovascular diseases such as coronary heart disease are one of the leading causes of death worldwide (1, 2). Death from cardiovascular disease is on the rise and will reach 23.6 million deaths annually by 2030; their leading cause is Coronary artery disease yet, with similar effects regarding death and disability in the Iranian population (3, 4).

Coronary artery bypass grafting (CABG) surgery is one of the most efficient modalities to reduce mortality and disease complications (5-7). However, using cardiopulmonary bypass and cardioplegia, cardiac surgery is never truly physiological though, leading to a considerable burden of tissue stress due to the artificial environment (8-10). Exposure of blood to extracorporeal artificial surfaces during cardiopulmonary bypass (CPB) induces alteration in

cell-mediated immune response, resulting in a state resembling whole-body inflammation and activate a pro-inflammatory response, leading to cytokine release (10-14). Though the cascade of inflammatory mediators is significantly affected due to the cardiopulmonary bypass, several remedies have been proposed to defy this phenomenon (15-17) with the ultimate goal of reducing CPB-induced mortality and morbidity (2, 3, 5, 10, 12, 14, 17-21); corticosteroids have been a mainstay in this way since they are reported to reduce the complement-mediated activation of neutrophils and inhibit the secretion of proinflammatory cytokines, including TNF-α and IL-6 and limit postoperative complications (9, 10, 13, 19, 20, 22, 23).

This study was designed and performed to compare the clinical results of applying methylprednisolone vs. dexamethasone in the prime solution during CPB in CABG patients.

Methods

In this double-blind parallel clinical trial carried out in the operating room of Chamran Hospital, Isfahan University of Medical Sciences, Isfahan, Iran in 2018-2019, using a convenient sampling method, 62 adult patients scheduled for elective CABG entered the study. After taking the informed written consent, the inclusion and exclusion criteria were checked, the patients entered the study and were randomly divided into two groups. Randomization was done based on permuted block randomization method. Each block had a capacity for 4 subjects. Then, within each block, subjects were randomly assigned to the treatment or control groups.

The control group consisted of 31 patients using dexamethasone in their prime solution and the control group consisted of 31 patients using methylprednisolone in their prime solution (Figure 1). Data entry was performed by the same physicians in the operating room and the postoperative period; however, the patients were blinded regarding the study group; so this was a single-blinded study.

The inclusion criteria were patients who were a candidate for CABG surgery, aged 40 to 60 years old with a left ventricular ejection fraction more than 40%. The exclusion criteria were patients whose cardiopulmonary bypass time would exceed 140 minutes, need the support of an intra-aortic balloon pump (IABP) in the operating room or the intensive care unit, would encounter myocardial infarction following the surgery, undergoing simultaneous CABG + valve surgery, and having one of these comorbidities: malignancies like thyroid, pituitary, or adrenal tumor, any underlying congenital coagulation disorder or any underlying inflammatory disorder.

All the patients received general anesthesia, using a standard combination of sodium thiopental, pancuronium bromide, and fentanyl for induction of anesthesia, added with Isoflurane and morphine for anesthetic maintenance before the start of cardiopulmonary bypass; while an infusion of dexmedetomidine and Isoflurane was used during the cardiopulmonary bypass.

The same cardioplegia solution was used in all patients. The cardiopulmonary bypass procedure was uniform for all the patients using a roller pump, a constant brand of the oxygenator, and a 40 µ arterial line filter. All the patients were cooled using a heat exchanger to a temperature of 30 °C.

In the control group, 8 mg of dexamethasone was used in the prime solution. Then, in the first 24 hours after surgery, each patient received 8 mg of dexamethasone every 8 hours; while in the second 24 hours after surgery, 4 mg of dexamethasone every 8 hours was given; however, dexamethasone was discontinued in the third 24 hours.

In the methylprednisolone group, 5 mg/Kg methylprednisolone was administered in the prime solution of the intervention group, added with 10 mg per kilogram of body weight during induction of anesthesia. The main study outcomes included:

- the duration of mechanical ventilation following CABG surgery
- the duration of postoperative ICU stay
- the total amount of postoperative chest tube drainage which was assumed as bleeding volume
- the incidence of postoperative benign and malignant arrhythmias
- the need for treatment with inotropes, with each inotrope dose

To analyze the data, quantitative data were

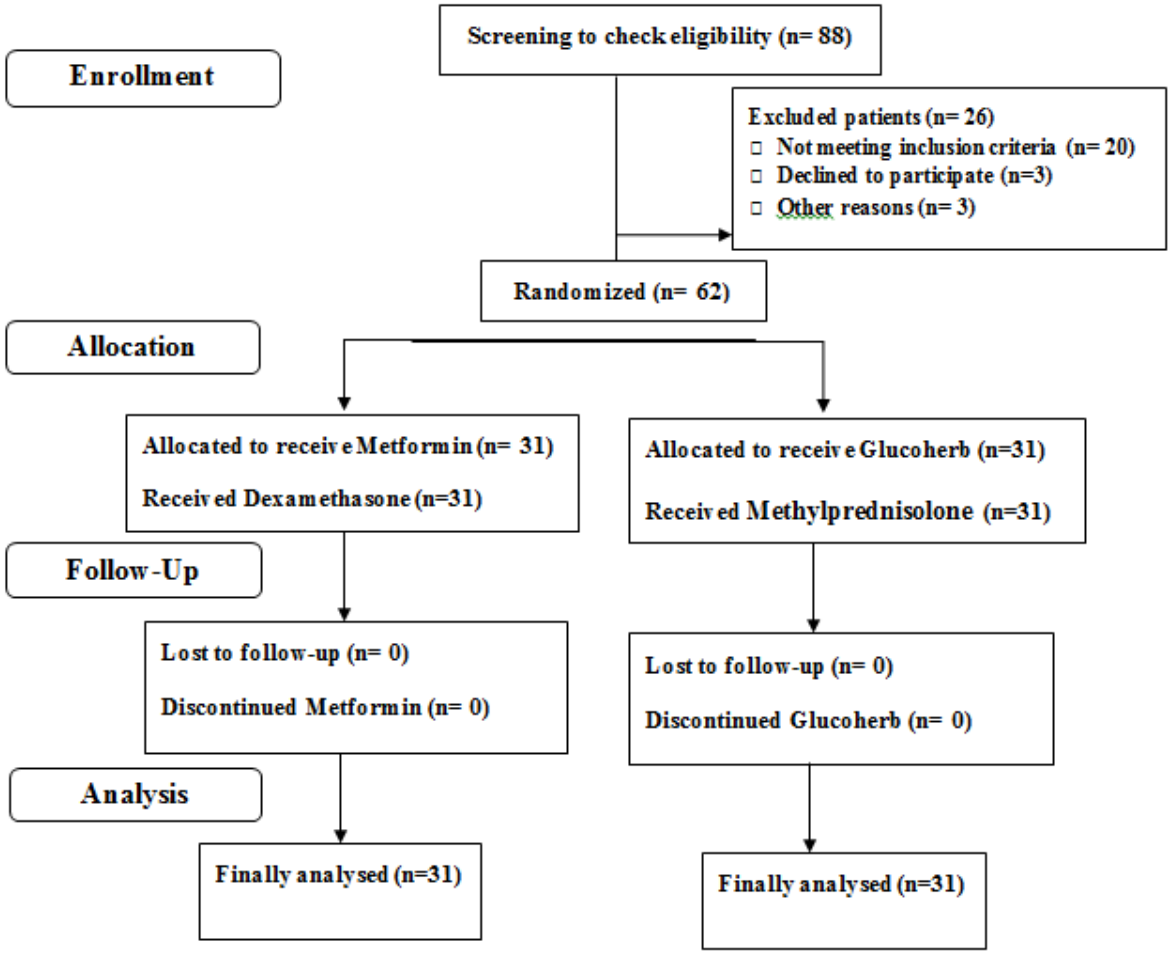

Figure 1. CONSORT flow chart showing the flow of patients through the trial.

presented as mean and standard deviation and qualitative data were reported as frequency and percentage. If the data had a normal distribution, Student's T-Test was used. If the data did not have a normal distribution, the Mann-Whitney U test and the Friedman nonparametric hypothesis test were used, and the Chi-test method was used when the data were categorical. A P-value less than 0.05 was considered significant. Data entry and analysis were performed using IBM SPSS Version 14.

The research followed the tenets of the Declaration of Helsinki. This research was approved by the ethics committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1398.225). It was also registered in the Iranian registry of clinical trials data registry (IRCT20170620034666N2).

Results

Patients were aged were 55.7±13.4 years (ranging from 46 to 60 years) in the dexamethasone group and 53.09±6.78 years (ranging from 40 to 60 years) in the methylprednisolone group with no statistically significant difference between the two groups (p=0.078; independent t-test). Besides, patient's gender did not differ significantly between the two groups (p=0.054) and none of the patients in the two groups needed inotropes. The mean duration of mechanical ventilation and ICU stay was significantly higher in the dexamethasone group than the methylprednisolone group; also, the mean bleeding volume in the dexamethasone group was significantly lower than in the methylprednisolone group (Table 1).

Table 1: Comparison of the mean duration of mechanical ventilation in the two groups.

Group	Mean	SD	P value
Dexamethasone	10.6	3.5	0.03
Methylprednisolone	8.8	2.8	

Table 2: Comparison of the mean stay at ICU in the two groups.

Group	Mean	SD	P value
Dexamethasone	63.9	17.1	0.001
Methylprednisolone	51.1	10.3	

Table 3: Comparison of the mean bleeding volume in the two groups.

Group	Mean	SD	P value
Dexamethasone	637.1	164.3	0.04
Methylprednisolone	716.9	192.3	

Discussion

This study was performed to compare the clinical results of the use of methylprednisolone and dexamethasone in the prime solution during cardiopulmonary bypass following CABG. The mean age of patients in the dexamethasone group was 55 years and in the methylprednisolone group was 53 years. The two groups are not significantly different regarding age and gender. Arrhythmia was not seen in the groups. In addition, none of the patients in the two groups needed inotropes. The mean duration of mechanical ventilation and stay at the ICU in the dexamethasone group was significantly higher than the methylprednisolone group, but the mean bleeding volume in the dexamethasone group was significantly lower than the methylprednisolone group.

Methylprednisolone reduces complement activation and IL-6 and IL-8 release and TNF, increase IL-10. Methylprednisolone leads to decrease neutrophil activation and migration into the lungs, decrease pulmonary lysosomal enzyme release, decrease post-operative radiographic abnormalities, and preservation of pulmonary vascular and alveolar architecture (4, 9, 12). Dexamethasone modulated the Systemic inflammatory response syndrome (SIRS) with lower pro-inflammatory (IL-6, IL-8) and higher anti-inflammatory (IL-10) IL levels and reduces the duration of mechanical ventilation and Patients were discharged from the intensive care unit earlier (13, 18, 24, 25). Therefore the use of corticosteroids is associated with a reduction in atrial fibrillation, stay in ICU and hospital, and mortality (26).

Interleukin-10 (IL-10) is described as a major immunoregulatory cytokine. It is originally called the "cytokine synthesis inhibitory factor" (CSIF) because of its inhibitory effects on the release of cytokines such as interferon-α (IFN-α), Tumor Necrosis Factor-alpha (TNF-α), interleukin-1 (IL-1), and Interleukin-6 (IL-6) (15-17). However, IL-1 and IL-6 contribute to hemodynamic instability after cardiopulmonary bypass; while, TNF-α is released by activated monocyte and macrophages and induces tachycardia and microvascular permeability and multiple organ failure; thus CPB-induced inflammation could lead to worse outcomes including myocardial ischemia, cardiac arrhythmias, and prolonged respiratory failure (2, 3, 5, 10, 12, 14, 17-21).

In one study it was demonstrated that patients who received glucocorticoids in cardiac surgery had a shorter hospital stay than those who did not receive glucocorticoids and had a better quality of life (27). In our study, this comparison was not possible because both study groups used corticosteroids, but the

methylprednisolone group had a shorter hospital stay time than the dexamethasone group, and this difference was statistically significant.

In a study by Whitlock et al. (26), out of 44 articles conducted on 3205 patients, the effect of corticosteroids on clinical results after CABG was evaluated and the patients received corticosteroids as prophylactic. In this study, the use of corticosteroids made low incidence of atrial fibrillation, postoperative bleeding, stay at the ICU, hospital stay, and mortality. In our study, the incidence of arrhythmias was zero i.e. corticosteroids showed a decreasing effect on the incidence of arrhythmias, which did not require inotropic drugs.

In the study by Ando et al. (28), the effect of hydrocortisone on infant mortality, length of stay at ICU, duration of ventilation, and the need for inotropes were investigated. Postoperative disability was not observed when the patients were hospitalized. The length of stay at the ICU did not differ between the two groups. However, in the test group, blood oxygen saturation was continuously improved and the duration of mechanical ventilation was shortened. This study was consistent with the results of our study because it favors the use of corticosteroids in reducing the length of hospital stay and bleeding after CABG. Other studies which have used corticosteroids support our findings in reduction of atrial fibrillation, stay at ICU and hospital, and mortality (26).

The use of pre-operative extra doses improves further, which is especially associated with reduced mechanical ventilation time (10, 16, 17, 22, 29). In another study, the effect of combination steroids (prescribing steroids during and before surgery) was compared with steroid therapy alone (during surgery); so, 29 patients who underwent CABG randomly received methylprednisolone before and during surgery and the length of stay at the ICU was shorter in the combined group, while more improvement was observed in other clinical outcomes (22). However, another study showed that administration of dexamethasone reduces interleukin-6 and interleukin-8 and increases interleukin-10 which could be correlated to the lower incidence of early postoperative fever and new-onset atrial fibrillation (20).

It was stated in another study dexamethasone caused an eightfold decrease in interleukin-6 levels and a greater than the threefold decrease in tumor necrosis factor-α level after CPB (30). Another study found that prescribing steroids reduced complement activation and prevent cytokine release (19). However, the use of methylprednisolone decreased interleukin-6 levels and tumor necrosis factor and increased interleukin-10 levels, which reduced lung protection and reduced the duration of mechanical ventilation (4, 10).

Corticosteroid downregulates TNF-α production by inhibiting TNF-α gene transcription (31). TNF-α causes multiple organ failure and cardiac arrhythmias and microvascular permeability (21). Dexamethasone inhibits the gene expression of the cyclooxygenase enzyme, which is one of the major enzymes in the conversion of arachidonic acid to prostaglandins. As a result, it reduces the amount of bleeding (13, 15, 24, 30). The current study demonstrated the effects of both dexamethasone and methylprednisolone.

This study had some limitations. First of all, we considered short-term outcome measures which should be completed with long-term outcome measures in future assessment. Second, we mainly focused on the cardiovascular system; however, other organ systems including the brain, viscera, and the coagulation system should be considered more extensively in future studies. Finally, failure to examine paraclinical variables such as International normalized ratio (INR) and other coagulation factors was one of the limitations of the study.

Conclusion

The results of the study showed that the mean duration of mechanical ventilation and ICU stay in the dexamethasone group was higher than the methylprednisolone group; however, the use of dexamethasone had the advantage of lower chance of bleeding.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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