Original Article

Effect of Low-dose Dexamethasone on Extra Vascular Lung Water in Patients Following On-pump Elective Primary Coronary Artery Bypass Graft Surgery

Madan Mohan Maddali, Niranjan Dilip Waje, Nishant Ram Arora, Sathiya Murthi Panchatcharam[1]

Department of Cardiac Anesthesia, National Heart Center, Royal Hospital, [1]Department of Studies and Research, Oman Medical Specialty Board, Muscat, Oman

Abstract

Background: The primary objective was to compare the effect of a low-dose dexamethasone as against a saline placebo on extravascular lung water index (EVLWI) in patients undergoing elective primary coronary artery bypass surgery. The secondary endpoints were to assess the effect of dexamethasone on other volumetric parameters (pulmonary vascular permeability index, global end diastolic volume index, and intrathoracic blood volume index), Vasoactive Inotrope Scores, hemodynamic parameters and serum osmolality in both groups. **Settings and Design:** Prospective observational study performed at a single tertiary cardiac care center. **Materials and Methods:** Twenty patients were randomized to receive either dexamethasone (steroid group, n = 10) or placebo (nonsteroid group, n = 10) twice before the institution of cardiopulmonary bypass (CPB). EVLWI and other volumetric parameters were obtained with the help of VolumeView™ Combo Kit connected to EV 1000 clinical platform at predetermined intervals. Hemodynamic parameters, vasoactive-inotropic Scores, hematocrit values were recorded at the predetermined time intervals. Baseline and 1st postoperative day serum osmolality values were also obtained. **Results:** The two groups were evenly matched in terms of demographic and CPB data. Intra- and inter-group comparison of the baseline EVLWI including other volumetric and hemodynamic parameters with those recorded at subsequent intervals revealed no statistical difference and was similar. Generalized estimating equation model was obtained to compare the changes between the groups over the entire study period which showed that on an average the changes between the steroid and nonsteroid group in terms of all volumetric parameters were not statistically significant. **Conclusions:** There were no beneficial effects of low-dose dexamethasone on EVLWI or other volumetric parameters in patients subjected to on-pump primary coronary bypass surgery. Hemodynamic parameters were also not affected. Probably, the advanced hemodynamic monitoring aided in optimal fluid management in the nonsteroidal group impacting EVLW accumulation.

Keywords: *Anti-inflammatory agents/pharmacology, dexamethasone/administration and dosage, extravascular lung water, heart diseases/surgery, inflammation/prevention and control*

Introduction

Cardiac surgery performed on cardiopulmonary bypass (CPB) is associated with a systemic inflammatory response resulting in organ dysfunction, and even multisystem organ failure.[1-3] Glucocorticoids have anti-inflammatory activity.[4] These drugs are low-cost, potent anti-inflammatory agents and therefore represent an appealing treatment option in this scenario.[4,5] It, therefore, seems reasonable to try to attenuate the inflammatory response with long-acting corticosteroids such as intravenous methylprednisolone or dexamethasone during cardiac surgery for a better outcome.[6] Studies have shown that corticosteroids may improve pulmonary gas exchange and reduce the need for postoperative inotropic support by attenuating increases in serum inflammatory markers.[4] Corticosteroids administration has also been shown to improve myocardial or pulmonary cell integrity with a reduction in the expression of endothelial adhesion molecules, complement activation, and cytokine release.[7] Despite the uncertainty about the effectiveness of corticosteroids in the reduction of major adverse events,[8,9] corticosteroid administration during cardiac surgery is part of routine care in many European hospitals.[10] High-dose (1 mg/kg) dexamethasone could result in inadequate

How to cite this article: Maddali MM, Waje ND, Arora NR, Panchatcharam SM. Effect of low-dose dexamethasone on extra vascular lung water in patients following on-pump elective primary coronary artery bypass graft surgery. Ann Card Anaesth 2019;22:372-8.

Address for correspondence:
Dr. Madan Mohan Maddali, Department of Cardiac Anesthesia, National Heart Center, Royal Hospital, P. B.No: 1331, P.C: 111, Seeb, Muscat, Oman. E-mail: madanmaddali@hotmail.com

Access this article online

Website: www.annals.in

DOI: 10.4103/aca.ACA_122_18

Quick Response Code:

serum glucose control and an increased re-thoracotomy to name a few adverse effects.[11-13] Low-dose corticosteroids were found to attenuate the systemic inflammation associated with CPB.[14] Small-dose dexamethasone therapy (8 mg at the start of anesthesia and CPB) enhanced patient-perceived quality of recovery scores in elective cardiac surgical patients.[15] The authors assumed that tissue edema is an indicator for inflammatory mediator activation and extravascular lung water index (EVLWI) could be considered as a surrogate marker of tissue edema following CPB. EVLWI can be measured perioperatively by transpulmonary thermodilution technique with the help of VolumeView/EV1000™ system (Edwards Lifesciences, Irvine CA, USA). It was hypothesized that a small dose of dexamethasone would attenuate inflammatory response as reflected by a reduction in EVLWI during open heart surgery.

The primary objective was to compare the effect on EVLWI measured at predetermined intervals of a low-dose intravenous dexamethasone (0.1 mg/kg) administered twice before the commencement of CPB as against a saline placebo in patients undergoing elective primary coronary artery bypass surgery. The secondary endpoints were to assess the effect of dexamethasone on other volumetric parameters pulmonary vascular permeability index (PVPI), global end-diastolic volume index (GEDVI), intrathoracic blood volume index (ITBVI), vasoactive inotrope score (VIS), hemodynamic parameters, and serum osmolality.

Materials and Methods

After obtaining the Institutional Medical Ethics and Scientific Research Committee approval (MESRC#4/2016) and an informed consent, 20 adult patients undergoing elective on-pump primary coronary artery bypass surgery were prospectively included in the study. Patients weighing <40 kgs and those with valvular abnormalities and/or arrhythmias were excluded from the study. Patients who were to undergo emergency coronary bypass surgery, combined bypass surgery and valve procedures, those patients on preoperative inotropic agents or needing intra-aortic balloon counter pulsations perioperatively, patients on steroid therapy, poorly controlled diabetes patients, patients with pulmonary disease or renal impairment and those with ejection fraction (EF) <30% were also excluded from the study. The 20 patients were allocated by computer-generated block randomization numbers using the block sizes of 2, 4, 6 to either the steroid group (n = 10) or the nonsteroid group (n = 10). Two qualified anesthesiologists were allotted for each case. A nurse anesthetist who is aware of the randomization code prepared either the intervention drug or normal saline in a 5 ml syringe labeled with the patient's hospital identity number. One anesthesiologist who was blinded to the randomization conducted the anesthesia for the patient and a second anesthesiologist also blinded to the drug administered collected all the data. Based on the randomization code, two syringes each containing either the intervention drug (dexamethasone [0.1 mg/kg drawn up to 5 ml total volume]) or saline (drawn up to 5 ml total volume) were kept ready by the nurse anesthesiologist to be administered at the appropriate time.

All patients were premedicated as per the institutional protocol. Under standard American Society of Anesthesiologists recommended monitoring modalities, general anesthesia was administered after adequate pre-oxygenation and following right radial artery cannulation under topical anesthesia. Anesthesia was induced with thiopental (2 mg/kg), midazolam (1–5 mg), and fentanyl (1–2 mcg/kg). Neuromuscular blockade was achieved with rocuronium (1–1.5 mg/kg). Pressure controlled mechanical ventilation was used in all patients. The respiratory rate, pressure control limits, inspired oxygen concentration, and positive end-expiratory pressure were adjusted to ensure a minimum tidal volume of 6–8 ml/kg, oxygen saturation of >95%, and end-tidal carbon dioxide levels of 36–38 mm Hg. Anesthesia was maintained with isoflurane in oxygen-enriched air, propofol infusion (2–5 mg/kg/hr), and intermittent fentanyl boluses.

Intraoperative transesophageal echocardiography was used routinely. In all patients, the right internal jugular vein was accessed with a quadruple lumen central venous catheter (8.5 Fr, ARROWg + ard Blue PLUS® Catheter, Arrow International, Inc., Reading, PA 19605 USA) and left femoral artery was cannulated with a VolumeView femoral artery catheter, from the femoral catheter kit (5Fr, VLVFC520, Edwards Lifesciences LLC, Irvine, CA, USA) provided in the VolumeView™ Combo Kit (VLV8R520, Edwards Lifesciences LLC, Irvine, CA, USA). All cannulations were performed aseptically under ultrasound guidance. The femoral arterial line was connected to a VolumeView sensor. The central venous line was connected to VolumeView thermistor manifold and the TruWave pressure transducer that was provided in the venous injectate kit by the manufacturer (VLVVKDT, Edwards Lifesciences LLC, Irvine, CA, USA). The femoral arterial line and the central venous line were in turn connected to EV1000 clinical platform. Bolus injections of 20 ml of cold saline (<8°C) through the thermistor manifold attached to the central venous line were used to obtain cardiac output values. The arterial pressure waveform derived continuous cardiac output monitoring system was then calibrated by accepting the mean of the three cardiac output readings that were obtained by transpulmonary thermodilution technique. Subsequent to calibration, the EV1000 clinical platform continuously displayed the patient's hemodynamic and volumetric data. Once the baseline data were collected the first bolus of dexamethasone or saline placebo was administered to the patient by the second anesthesiologist which was

about 30 min from the skin incision. The second bolus of dexamethasone was administered before the institution of CPB.

The volumetric parameters (EVLW, PVPI, GEDVI, and ITBV) and hemodynamic parameters (heart rate, mean arterial pressure, central venous pressure, stroke volume variation, calibrated cardiac output, calibrated stroke volume, and systemic vascular resistance) were recorded at predefined time intervals: T1: Baseline once the system was in place and before bolus of the drug or placebo administration, T2: Before institution of CPB and after the second bolus of drug or placebo administration, T3: After separation from CPB and protamine administration, T4: before shifting from operating room, T5:6 h. after aortic cross-clamp release and T6: 24 h after aortic cross-clamp release.

Demographic data such as age, BSA, BMI, EuroSCORE II, EF, and CPB data (total CPB time and aortic cross-clamp time) were recorded for each patient. For all patients, VIS, hematocrit at the predetermined time intervals was obtained along with the baseline and 1st postoperative day serum osmolality values. The VIS was calculated as described in the literature.[16] The formula used was as follows:

Inotrope Score (IS) = Dopamine dose (mcg/kg/min) + Dobutamine dose (mcg/kg/min) + 100 × Epinephrine dose (mcg/kg/min).

Vasoactive-Inotropic Score (VIS) = IS + 10 × Milrinone dose (mcg/kg/min) +10,000 × Vasopressin dose (units/kg/min) +100 × Norepinephrine dose (mcg/kg/min).

Baseline arterial blood gas values and blood sugar levels were obtained following radial arterial cannulation with patients receiving supplemental oxygen through a face mask. These were compared with those obtained following separation from CPB between both groups. Mean arterial pressure was maintained within 20% of the baseline values. Hypertension was treated with attempts at deepening the planes of anesthesia or by vasodilation. Fluid management in both the groups was based on the dynamic variables that were displayed on the EV1000 monitor. The objective of fluid administration in this study was to maintain the stroke volume variation <10%–13% to achieve a stroke volume index ≥35 ml/m^2 and a cardiac index >3l ts/m^2. Lactated Ringer's was often the crystalloid of choice and the volume of fluid administered was recorded for each patient. Vasopressors were administered only if patients were hypotensive with low cardiac output variables despite adequate volume optimization. The total intraoperative urine output was recorded and compared between both groups.

Statistical analysis

Data were analyzed using Statistical Package for Social Sciences version 22 (IBM Corp. Chicago, Illinois, USA). For descriptive purposes, continuous variables are presented as Mean and Standard Deviation. The outcome variables at the predetermined time intervals were compared using nonparametric approach using Mann–Whitney "U" test. Generalized estimating equation model was obtained to compare the average of changes between the groups over the time period. $P < 0.05$ was considered statistically significant.

The values of serum osmolality, blood sugar, and arterial blood gas parameters were analyzed using Mann–Whitney test. The differences in the pre- and post-CPB values were compared and a $P < 0.05$ was considered as statistically significant.

Results

Twenty patients completed the study. In view of the small sample size and to compare the variables between the two groups, the sum of ranks and the mean ranks were obtained using Mann–Whitney Test. The idea of applying the Mann–Whitney test was to rank the data for each condition, and then appreciate how different the two rank totals are. If there was a systematic difference between the two groups, then most of the high ranks would belong to one group, and most of the low ranks would belong to the other one. As a result, the rank totals would be quite different. On the other hand, if the two groups are similar, then high and low ranks would be distributed fairly evenly between the two groups and the rank totals would be quite similar.

There was no difference in demographic and CPB data between the groups [Table 1]. Between the two groups, there was no difference in the baseline arterial blood gas values and blood sugar levels as compared to those obtained following separation from CPB [Table 2]. The volume of fluid administered before CPB institution was comparable between the two groups [Table 1]. The urine output was also comparable [Table 2]. The hemodynamic parameters obtained following calibration by transpulmonary thermodilution of the arterial pressure waveform derived continuous cardiac output monitoring system were considered as baseline values. These values were compared with values obtained at the subsequent predetermined time intervals both within the groups as well as between the two groups [Table 3]. The results indicated that the mean ranks of each hemodynamic variable at the baseline as compared with subsequent readings within the group as well as between the two groups were comparable. The baseline VIS values were comparable at all subsequent time points between the groups. The mean ranks hematocrit values were also comparable throughout the study. Serum osmolality values were not normally distributed. Hence, a nonparametric approach using Mann–Whitney test for obtaining statistical significance was adopted. The baseline mean rank values of serum osmolality were comparable to those obtained on the 1st postoperative day in both groups ($P = 0.796$) [Table 3].

Table 1: Demographic and cardiopulmonary bypass data

Data	Steroid group (*n*=10)	Nonsteroid group (*n*=10)	Mean ranks*		*U*	*P**
			Steroid group (*n*=10)	Nonsteroid group (*n*=10)		
Age (years)	60.8±11	61.6±11	10.68	11.35	51.50	0.809
BSA	1.8±0.12	1.8±0.17	11.23	9.61	41.50	0.552
BMI	25.6±2.7	26.43±4.7	10.86	11.15	53.50	0.918
Euroscore II	1.3±0.8	1.3±0.41	9.14	11.19	34.50	0.442
EF %	52.7±6.47	48.5±4.7	12.86	8.95	34.50	0.152
CPB time (min)	108.7±18.02	106.80±20.92	11.14	10.85	53.50	0.918
ACC time (min)	65.5±16.12	71.3±25.44	10.68	11.35	51.50	0.809
Pre CPB fluid (ml/kg)	8.2±2.14	7.2±1.8	12.59	9.25	37.50	0.223

*Mann–Whitney test. BSA: Body surface area, BMI: Body mass index, CPB: Cardiopulmonary bypass, EF: Ejection fraction, ACC: Aortic cross clamp

Table 2: Comparison of the arterial blood gas parameters, blood sugar levels and urine output between steroid group and nonsteroid group

Variables	Mean ranks		*U*	*P**
	Steroid group (*n*=10)	Nonsteroid group (*n*=10)		
Arterial blood gas values				
pH				
Pre. CPB**-Post. CPB***	11.9	9.1	36	0.315
pO_2				
Pre. CPB**-Post. CPB***	12.3	8.7	32	0.190
pCO_2				
Pre. CPB**-Post. CPB***	12.9	8.1	26	0.075
Lactate				
Pre. CPB**-Post. CPB***	7.3	13.7	18	0.015
Blood sugar levels				
Pre. CPB**-Post. CPB****	11.9	9.1	36	0.315
Urine output	11.50	9.50	40	0.481

*Mann–Whitney test, **Pre. CPB: Baseline values following arterial line insertion with the patients on oxygen supplementation thorough a face mask prior to CPB institution, ***Post. CPB: Values at 30 min following separation from CPB, ****Post. CPB: Highest blood sugar values recorded following separation from CPB and prior to shifting to the ICU. ICU: Intensive care unit, CPB: Cardiopulmonary bypass

The baseline mean rank values of volumetric variables were compared with subsequent values obtained at the predetermined time points [Table 4]. The baseline EVLWI values were comparable between the steroid and nonsteroid groups [P = 1.0]. The subsequent mean rank values of EVLWI that were recorded at various time points were comparable in each group. Following separation from CPB, neither intra- nor inter-group differences in mean rank values of EVLWI were found as compared to their baseline values. There were no intra- or inter-group differences in PVPI, GEDVI, ITBVI values during the study.

Generalized estimating equation model was obtained to compare the changes between the groups over the entire study period [Figure 1]. Generalized estimating equation is a general statistical approach to fit a marginal model for longitudinal/clustered data analysis in biomedical studies.[17] Generalized estimating equation is used to estimate the parameters of a generalized linear model with a possible unknown correlation between outcomes. Under mild regularity conditions, parameter estimates from the generalized estimating equation are consistent even when the covariance structure is misspecified. Generalized estimating equation model was obtained to compare the changes between the groups over the time period for EVLWI, PVPI, GEDVI, and ITBVI [Figure 1]. On an average, the changes between the steroid and non-steroid group in terms of EVLWI, PVPI, GEDVI, and ITBVI were not statistically significant.

Discussion

Low-dose dexamethasone did not have any effect on EVLWI in patients who had coronary bypass surgery on CPB. The hypothesis that low-dose dexamethasone would reduce inflammatory response as reflected by a reduction in a surrogate marker, i.e., EVLWI was rejected.

Cardiac surgery and CPB induce an acute inflammatory response contributing to postoperative morbidity.[15] This inflammatory response often leads to tissue edema and organ failure. Corticosteroids are anti-inflammatory drugs that can reduce the inflammatory response and suppress the immune response. It has been suggested that steroids exhibit a cytoprotective effect in patients undergoing CPB.[18] Steroids inhibit increases in interleukin 6 and 8 levels during open heart surgery.[19] Corticosteroid treatment before CPB was shown to have cardioprotective effects due to the reduction of perioperative release of systemic and myocardial inflammatory mediators.[20] Corticosteroid prophylaxis during cardiac surgery was associated with a salutary effect on pulmonary function.[6,21] These beneficial effects of steroid therapy may be attributed to the attenuation of the perioperative systemic inflammatory response syndrome

Table 3: Comparison of hemodynamic parameters at each time point between steroid group and nonsteroid group using Mann-Whitney test

Variables*	Mean ranks		*U*	*P*
	Steroid group (*n*=10)	Nonsteroid group (*n*=10)		
HR				
HR1-HR2	11.64	10.30	48.0	0.65
HR1-HR3	11.91	10.00	45.0	0.51
HR1-HR4	13.09	8.70	32.0	0.11
HR1-HR5	12.36	9.50	40.0	0.31
HR1-HR6	9.86	12.30	42.0	0.39
MAP				
MAP1-MAP2	10.95	11.05	54.5	0.97
MAP1-MAP3	9.86	12.25	42.5	0.39
MAP1-MAP4	11.68	10.25	47.5	0.61
MAP1-MAP5	10.64	11.40	51.0	0.51
MAP1-MAP6	10.55	11.50	50.0	0.76
CVP				
CVP1-CVP2	9.14	13.05	34.5	0.15
CVP1-CVP3	9.41	12.75	37.5	0.22
CVP1-CVP4	11.55	10.40	49.0	0.71
CVP1-CVP5	11.05	10.95	54.5	0.97
CVP1-CVP6	10.86	11.15	53.5	0.92
SVV				
SVV1-SVV2	12.00	9.90	44.0	0.47
SVV1-SVV3	12.73	9.10	36.0	0.20
SVV1-SVV4	12.45	9.40	39.0	0.28
SVV1-SVV5	12.45	9.40	39.0	0.28
SVV1-SVV6	12.73	9.10	36.0	0.20
CI				
CI1-CI2	11.64	10.30	48.0	0.65
CI1-CI3	9.00	13.20	33.0	0.13
CI1-CI4	11.09	10.90	54.0	0.97
CI1-CI5	10.55	11.50	50.0	0.76
CI1-CI6	9.41	12.75	37.5	0.22
SVI				
SVI1-SVI2	11.00	11.00	55.0	1.00
SVI1-SVI3	9.18	13.00	35.0	0.17
SVI1-SVI4	10.32	11.75	47.5	0.61
SVI1-SVI5	10.14	11.95	45.5	0.51
SVI1-SVI6	10.23	11.85	46.5	0.56
SVRI				
SVRI1-SVRI2	12.09	9.80	43.0	0.43
SVRI1-SVRI3	10.82	11.20	53.0	0.92
SVRI1-SVRI4	10.82	11.20	53.0	0.92
SVRI1-SVRI5	11.18	10.80	53.0	0.92
SVRI1-SVRI6	12.18	9.70	42.0	0.39
VIS				
VIS1-VIS2	10.45	10.55	49.5	0.97
VIS1-VIS3	10.40	10.60	49.0	0.97
VIS1-VIS4	8.80	12.20	33.0	0.22
VIS1-VIS5	8.5	12.25	32.5	0.19
VIS1-VIS6	10.0	11.0	45.0	0.74
HCT				
HCT1-HCT2	10.05	12.05	44.5	0.47
HCT1-HCT3	12.82	9.00	35.0	0.17
HCT1-HCT4	13.36	8.40	29.0	0.07
HCT1-HCT5	12.95	8.85	33.5	0.13
HCT1-HCT6	12.45	9.40	39.0	0.28
Serum osmolality	10.85 (base line)	10.15 (1st postoperative day)	46.5	0.8

*: $P < 0.05$ statistically significant, HR: Heart rate, HCT: Hematocrit, VIS: Vasoactive index score, SVRI: Systemic vascular resistance index, SVI: Stroke volume index, CI: Cardiac index, SVV: Stroke volume variation, CVP: Central venous pressure, MAP: Mean arterial pressure

and were pathophysiologic goal of the single high-dose corticosteroid treatment.[8-10,14]

While on the subject of the beneficial effects of high-dose steroid therapy during cardiac surgery, there are simultaneous reports supporting the efficacy of a low-dose corticosteroid protocol in terms of inflammatory mediator suppression.[22,23] It has been suggested that a low dose corticosteroid therapy might beneficially influence outcomes without producing adverse events in cardiac surgical patients.[8,14] High doses of steroids during cardiac surgery were shown to have detrimental effects on pulmonary function, glycemic control, and postoperative tracheal extubation times.[24,25] Therefore, if steroid benefit could be derived through the suppression of the inflammatory cascade using a low dose, high doses of steroid administration over a prolonged duration might not be necessary.

A small dose of dexamethasone (8 mg) administered twice to cardiac surgical patients improved the quality of recovery scores after elective cardiac surgery.[15] The authors of the present study assumed that since a small dose of a corticosteroid appears to be efficacious in suppression of inflammatory cascade and also shown to improve the recovery scores, probably a patient weight adjusted low-dose dexamethasone could be investigated. Hence, dexamethasone at a dosage of 0.1 mg/kg was investigated in this current study. A rapid fall in plasma levels of corticosteroids on the initiation of CPB because of hemodilution was described earlier.[15] Based on this observation, weight-adjusted dexamethasone or bolus was administered twice before institution of CPB in this study.

Dexamethasone was found to enhance patient comfort through several direct mechanisms such as reducing nausea/vomiting, shivering, and fatigue.[15] The indirect mechanisms might be due to its beneficial action of attenuation of inflammation.[15] This specific action of dexamethasone on inflammatory cascade was what was investigated in this study.

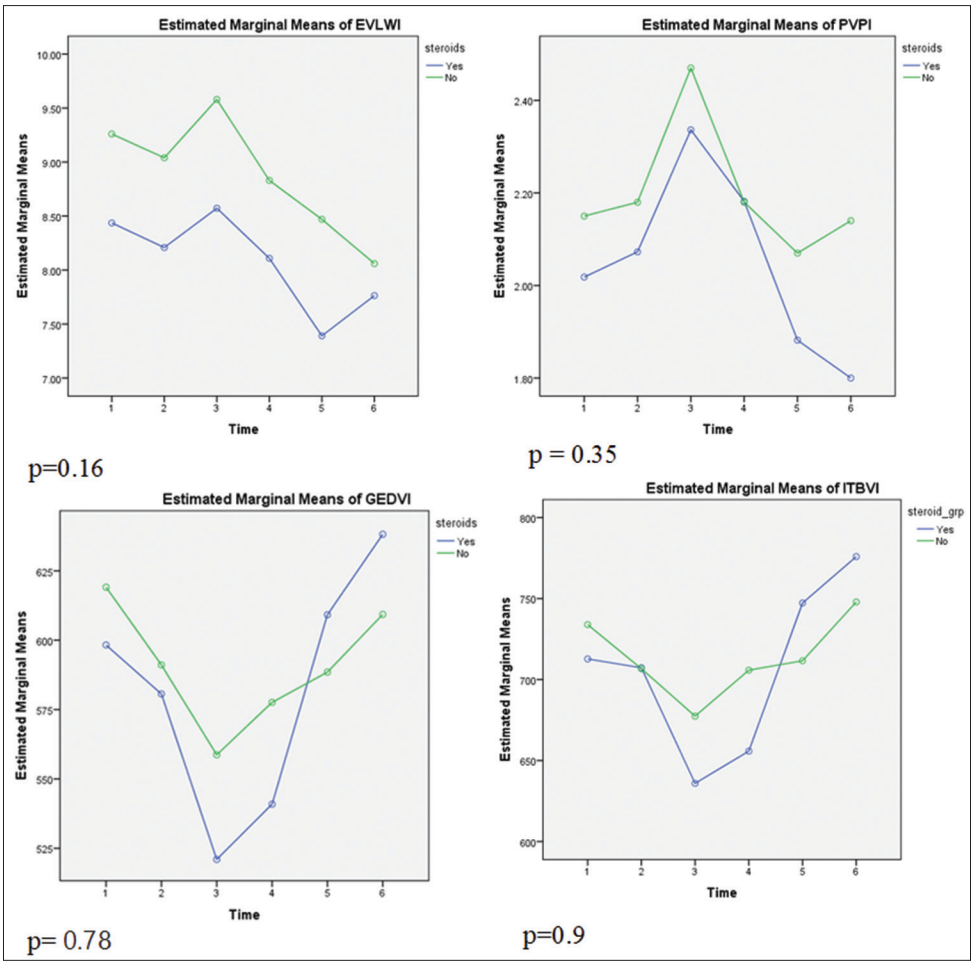

Figure 1: Comparison of estimated marginal means of extravascular lung water index, pulmonary vascular permeability index, Global End Diastolic Volume Index Intrathoracic Blood Volume Index [ITBVI] measurements

EVLWI was deemed to be a surrogate marker for tissue edema that could occur as a result of inflammatory mediator release during cardiac surgery on CPB. The beneficial effect of a low-dose dexamethasone on reducing EVLWI was explored in this study. Vascular permeability can be increased by an inflammatory reaction during CPB and result in increased EVLWI despite normal to low intravascular fluid status and hydrostatic pressure. Hence, PVPI was also studied. Factors such as fluid overload, decreased myocardial contractility could contribute to increase in EVLWI. While assessing preload, it is known that higher central venous pressure and/or a higher pulmonary capillary wedge pressure are not reliable indicators for this purpose. Therefore, a volumetric parameter like GEDVI was also measured in the current study. Global EF offers a complete picture of the overall cardiac contractility which was also obtained for all patients. Hematocrit and serum osmolality were measured in both groups to identify if they could be contributing to EVLWI values. However, these parameters were comparable in both groups.

Previous studies have shown that corticosteroids can reduce the need for postoperative inotropic support.[4] Murphy *et al.* could not demonstrate any beneficial effects of low dose dexamethasone on cardiac function.[15] In the current study, the VIS was similar between the steroid and nonsteroid groups exhibiting no beneficial effect of low-dose steroid on hemodynamic parameters.

There are several limitations to this study. First, the sample size comprises only 20 patients. Second, only low-risk patients were investigated. Third, as the sample size was small, no increased risk of steroid-related infection was observed.

Conclusions

Low-dose dexamethasone did not have any effect on EVLWI or other volumetric parameters in patients subjected to on-pump primary coronary bypass surgery. There were no beneficial effects of dexamethasone on hemodynamic parameters as well. Probably, the advanced hemodynamic monitoring aided in optimal fluid management in the nonsteroidal group impacting EVLW accumulation thereby nullifying the beneficial effects of a low-dose dexamethasone.

Financial support and sponsorship

Nil.

Table 4: Comparison of difference in volumetric parameters at each time point between steroid group and nonsteroid group using Mann-Whitney test

Variables	Mean ranks		*U*	*P*
	Steroid group (*n*=10)	Nonsteroid group (*n*=10)		
EVLWI				
EVLWI1-EVLWI2	11.00	11.00	55.0	1.00
EVLWI1-EVLWI3	10.91	11.10	54.0	0.97
EVLWI1-EVLWI4	10.50	11.55	49.5	0.71
EVLWI1-EVLWI5	11.27	10.70	52.0	0.86
EVLWI1-EVLWI6	10.68	11.35	51.5	0.81
PVPI				
PVPI1-PVPI2	10.41	11.65	48.5	0.65
PVPI1-PVPI3	10.45	11.60	49.0	0.71
PVPI1-PVPI4	9.36	12.8	37.0	0.22
PVPI1-PVPI5	10.27	11.80	47.0	0.61
PVPI1-PVPI6	11.68	10.25	47.5	0.61
GEDVI				
GEDVI1-GEDVI2	10.95	11.05	54.5	0.97
GEDVI1-GEDVI3	11.55	10.40	49.0	0.71
GEDVI1-GEDVI4	11.41	10.55	50.5	0.76
GEDVI1-GEDVI5	10.09	12.00	45.0	0.51
GEDVI1-GEDVI6	10.55	11.50	50.0	0.76
ITBVI				
ITBVI1-ITBVI2	10.73	11.30	52.0	0.86
ITBVI1-ITBVI3	10.91	11.10	54.0	0.97
ITBVI1-ITBVI4	11.73	10.20	47.0	0.61
ITBVI1-ITBVI5	10.36	11.70	48.0	0.65
ITBVI1-ITBVI6	10.73	11.30	52.0	0.86

EWLWI: Extravascular lung water index, PVPI: Pulmonary vascular permeability index, GEDVI: Global end diastolic volume index, ITBVI: Intrathoracic blood volume index

Conflicts of interest

There are no conflicts of interest.

References

1. Asimakopoulos G. Systemic inflammation and cardiac surgery: An update. Perfusion 2001;16:353-60.
2. Holmes JH 4th, Connolly NC, Paull DL, Hill ME, Guyton SW, Ziegler SF, *et al.* Magnitude of the inflammatory response to cardiopulmonary bypass and its relation to adverse clinical outcomes. Inflamm Res 2002;51:579-86.
3. Paparella D, Yau TM, Young E. Cardiopulmonary bypass induced inflammation: Pathophysiology and treatment. An update. Eur J Cardiothorac Surg 2002;21:232-44.
4. Chaney MA. Corticosteroids and cardiopulmonary bypass: A review of clinical investigations. Chest 2002;121:921-31.
5. Wan S, LeClerc JL, Vincent JL. Inflammatory response to cardiopulmonary bypass: Mechanisms involved and possible therapeutic strategies. Chest 1997;112:676-92.
6. Dieleman JM, Nierich AP, Rosseel PM, van der Maaten JM, Hofland J, Diephuis JC, *et al.* Intraoperative high-dose dexamethasone for cardiac surgery: A randomized controlled trial. JAMA 2012;308:1761-7.
7. Warren OJ, Watret AL, de Wit KL, Alexiou C, Vincent C, Darzi AW, *et al.* The inflammatory response to cardiopulmonary bypass: Part 2 – Anti-inflammatory therapeutic strategies. J Cardiothorac Vasc Anesth 2009;23:384-93.
8. Whitlock RP, Chan S, Devereaux PJ, Sun J, Rubens FD, Thorlund K, *et al.* Clinical benefit of steroid use in patients undergoing cardiopulmonary bypass: A meta-analysis of randomized trials. Eur Heart J 2008;29:2592-600.
9. Dieleman JM, van Paassen J, van Dijk D, Arbous MS, Kalkman CJ, Vandenbroucke JP, *et al.* Prophylactic corticosteroids for cardiopulmonary bypass in adults. Cochrane Database Syst Rev 2011;5:CD005566. doi: 10.1002/14651858.CD005566.pub3.
10. Whitlock RP, Rubens FD, Young E, Teoh KH. Pro: Steroids should be used for cardiopulmonary bypass. J Cardiothorac Vasc Anesth 2005;19:250-4.
11. Vogelzang M, Hoekstra M, Drost JT, Janse M, van der Horst IC, Boonstra PW, *et al.* The impact of a reduced dose of dexamethasone on glucose control after coronary artery bypass surgery. Cardiovasc Diabetol 2007;6:39.
12. Duncan AE, Abd-Elsayed A, Maheshwari A, Xu M, Soltesz E, Koch CG, *et al.* Role of intraoperative and postoperative blood glucose concentrations in predicting outcomes after cardiac surgery. Anesthesiology 2010;112:860-71.
13. van Osch D, Dieleman JM, Nathoe HM, Boasson MP, Kluin J, Bunge JJ, *et al.* Intraoperative high-dose dexamethasone in cardiac surgery and the risk of rethoracotomy. Ann Thorac Surg 2015;100:2237-42.
14. Ho KM, Tan JA. Benefits and risks of corticosteroid prophylaxis in adult cardiac surgery: A dose-response meta-analysis. Circulation 2009;119:1853-66.
15. Murphy GS, Sherwani SS, Szokol JW, Avram MJ, Greenberg SB, Patel KM, *et al.* Small-dose dexamethasone improves quality of recovery scores after elective cardiac surgery: A randomized, double-blind, placebo-controlled study. J Cardiothorac Vasc Anesth 2011;25:950-60.
16. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, *et al.* Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. Pediatr Crit Care Med 2010;11:234-8.
17. Wang M, Kong L, Li Z, Zhang L. Covariance estimators for generalized estimating equations (GEE) in longitudinal analysis with small samples. Stat Med 2016;35:1706-21.
18. Kawamura T, Inada K, Nara N, Wakusawa R, Endo S. Influence of methylprednisolone on cytokine balance during cardiac surgery. Crit Care Med 1999;27:545-8.
19. Kawamura T, Inada K, Okada H, Okada K, Wakusawa R. Methylprednisolone inhibits increase of interleukin 8 and 6 during open heart surgery. Can J Anaesth 1995;42:399-403.
20. Liakopoulos OJ, Schmitto JD, Kazmaier S, Bräuer A, Quintel M, Schoendube FA, *et al.* Cardiopulmonary and systemic effects of methylprednisolone in patients undergoing cardiac surgery. Ann Thorac Surg 2007;84:110-8.
21. Tassani P, Richter JA, Barankay A, Braun SL, Haehnel C, Spaeth P, *et al.* Does high-dose methylprednisolone in aprotinin-treated patients attenuate the systemic inflammatory response during coronary artery bypass grafting procedures? J Cardiothorac Vasc Anesth 1999;13:165-72.
22. Teoh KH, Bradley CA, Gauldie J, Burrows H. Steroid inhibition of cytokine-mediated vasodilation after warm heart surgery. Circulation 1995;92:II347-53.
23. Whitlock RP, Young E, Noora J, Farrokhyar F, Blackall M, Teoh KH, *et al.* Pulse low dose steroids attenuate post-cardiopulmonary bypass SIRS; SIRS I. J Surg Res 2006;132:188-94.
24. Chaney MA, Durazo-Arvizu RA, Nikolov MP, Blakeman BP, Bakhos M. Methylprednisolone does not benefit patients undergoing coronary artery bypass grafting and early tracheal extubation. J Thorac Cardiovasc Surg 2001;121:561-9.
25. Chaney MA, Nikolov MP, Blakeman B, Bakhos M, Slogoff S. Pulmonary effects of methylprednisolone in patients undergoing coronary artery bypass grafting and early tracheal extubation. Anesth Analg 1998;87:27-33.