Original Research Article

A study of methylprednisolone in cardiac surgery

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Abstract

Background: Cardiac surgery is associated with Post systematic inflammatory response. Use of steroids in cardiac surgery is controversial. **Aim and objective:** To study the effect of methylprednisolone in patients with cardiac surgery at a tertiary health care centre **Methodology:** Present study was a randomized control trial carried out on patients undergoing Coronary Artery Bypass Graft surgery. Total 60 patients were studied. Group 1 received intravenous methylprednisolone sodium succinate and Group 2 received intravenous isotonic sodium chloride solution. Study outcome was measured as major adverse event like death, myocardial infarction (MI), stroke, renal failure, or respiratory failure, occurring within 30 days, postoperative infections; postoperative atrial fibrillation; highest serum glucose concentration in the ICU and time to discharge from the ICU and from the hospital. **Results:** Extubation time in methyl prednisolone group (12.2± 1.3 hours) significantly hogher than normal saline group (10.1± 1.5 hours). Highest serum glucose concentration was significantly higher in MP group than NS group ($p<0.05$). Post operative infection was significantly higher in normal saline group (26.67%) than methyl prednisolone group (13.33%) ($p<0.05$).
Key Word: methylprednisolone, cardiac surgery.

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INTRODUCTION

Coronary artery bypass is most commonly performed cardiac surgery. Cardiac surgery improves cardiac symptoms and quality of life of patient. Though there are improvements in surgical techniques, anaesthesia techniques and post operative care cardiac surgery is associated with stroke, myocardial infarction, renal failure, respiratory failure and death. [1-4] Perioperative inflammatory response is also an important adverse effect associated with cardiac surgery. Inflammatory response is characterised by both cell and protein activation. It is intensified by surgical trauma, endotoxaemia and ischaemia reperfusion injury. [5,6] During cardiopulmonary bypass blood is exposed to inflammatory markers like tumour necrosis fator, interlukin 6 etc. These markers are cardio depressants. [7] Post operative systemic inflammatory response system (SIRS) is observed in cardiac surgery patients. Severity of SIRS varies between all patients. [8] SIRS is characterised by fever, leucocytosis, hypotension, respiratory failure, hemodynamic distrbances and organ failure. It increases risk of adverse effects like organ failure and death. [9] Previous studies evaluated the effects of corticosteroids on inflammatory mediators in cardiac surgery patients and found that corticosteroids attenuate the complement pathways associated with CPB. [10,11] some of the studies observed no effect of steroids in cardiac surgery. Various cortiocosteroids like dexamethasone and methyl prednisolone are used in cardiac surgery. Methyl prednisolone emerged as drug of choice in cardiac surgery. Methylprednisolone has better clinical efficacy in shock and sepsis. It has lesser side effects than other corticosteroids.

Present study was conducted to study the effect of methylprednisolone in patients of cardiac surgery.

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Aim and objective: To study the effect of methylprednisolone in patients with cardiac surgery at a tertiary health care centre

MATERIAL AND METHODS

Present study was a randomized control trial carried out at department of cardiac surgery at a tertiary health care centre. Study population was patients undergoing Coronary Artery Bypass Graft surgery.

Inclusion criteria:

1. Patients undergoing elective coronary artery bypass graft surgery
2. Patients in age group of 30-70 years
3. Patients with redo surgery

Exclusion criteria:

1. Patients receiving preoperative steroids
2. Patients requiring preoperative intravenous inotropic or vasoactive drugs
3. Patients requiring supplemental oxygen, or mechanical ventilation
4. Patients who undergone previous lung surgery

Study was approved by ethical committee of the institute. A valid written consent was taken from the patients after explaining study to them.

Data was collected with pre tested questionnaire. Data included demographic data. Detailed history was taken from the patients. Through clinical examination was done. Pre operative investigations were done in all patients for anaesthetic assessment. Total 60 patients were studied. Patients were randomized into two groups (30 each). Randomization was done by a statistician using computer generated random numbers. Group 1 received intravenous methylprednisolone sodium succinate and Group 2 received intravenous isotonic sodium chloride solution. After arrival to the operation room, standard anesthesia technique was used for all patients it included intravenous fentanyl (20 mg/kg), midazolam (150 mg/kg), and vecuronium bromide. All of the fentanyl was administered before sternotomy. 70% of calculated dose of midazolam was given before sternotomy remaining dose was used during rewarming. Group 1 patients received 30 mg/kg intravenous methylprednisolone during sternotomy and 30mg/kg methylprednisolone was given at the beginning of sternotomy. Group 2 patients received similar volumes of intravenous isotonic sodium chloride solution at the same time. Both the drugs were prepared by OT staff who was not the part of study. For controlling blood pressure, inhaled isoflurane, intravenous nitroglycerin was used before CPB. Hypothermic CPB (to a lowest temperature of 26°C) with a membrane oxygenator and crystalloid prime (2.0 L of lactated Ringer's solution and 50 mEq sodium bicarbonate) was used in all patients. Isoflurane was used by the perfusionist to maintain perfusion pressure in the range of 50 to 70 mm Hg. Intermittent antegrade hypothermic crystalloid cardioplegia was used in all patients. Separation from CPB was facilitated with intravenous dobutamine, norepinephrine, nitroglycerin. Hemodynamic measurements included heart rate, mean arterial pressure, central venous pressure, mean pulmonary artery pressure, and pulmonary artery occlusive pressure. After surgery, patients were transferred to the intensive care unit (ICU) and weaned from mechanical ventilation when there was no excessive ongoing blood loss and patients were cooperative and hemodynamically stable. Study outcome was measured as major adverse event like death, myocardial infarction (MI), stroke, renal failure, or respiratory failure, occurring within 30 days, postoperative infections; postoperative atrial fibrillation; highest serum glucose concentration in the ICU and time to discharge from the ICU and from the hospital. Data was analysed with SPSS version 22.

RESULTS

Table 1 shows Comparison between two groups. Mean age in group 1 was59.8± 4.2 years and group 2 was 58.4± 3.3 years. Male to female ratio in group 1 was 21:9 and group 2 was 20:10. Mean height in group 1 was 168.3± 14.7 cm and group 2 was 167.6± 15.3 cm. Mean weight in group 1 and group 2 was 68.1± 4.1 and 67.9± 3.1 kg respectively. Both the groups were comparable with respect to age, sex ratio, height and weight ($p>0.05$). Pre operative medication received by the patients were Beta blockers, Calcium channel blockers, ACE inhibitors, nitrates, digitalis, diuretics, insulin or oral antidiabetic and inhaled bronchodilators. Both the groups were comparable with respect to pre operative medication ($p> 0.05$). Isolated CABG was most commonly performed surgery in both the groups (60% and 56.67%) followed by CABG and valve surgery (26.67% and 23.33%). Single valve surgery was done in 13.33% and 16.67% patients in grou 1 and group 2 respectively. Repeat surgery was done in one patient in each group. Table 2 shows comparison of both the groups according to intraoperative variables. Anaesthetic drugs used in both the group was almost similar ($p>0.05$). Before CPB isoflurane was used in all patients. Nitroglycerine was used in 23.33% patients in methylprednisolone group and 16.67% in normal saline group. During CPB mean total heparin required was 305±89 mg and 285±64 mg in group 1 and group 2 respectively. Mean total cardioplegia required was 3102±994 ml in group 1 and 2967±982 ml in group 2. After CPB isoflurane was used in 5 patients in each group. Nitroglycerine was used in 6.67% patients in group 1 and 3.33% in group 2 patients. Dopamine was used in 19 (63.33%) and 18 (60%) in group 1 and group 2 respectively. Nor epinephrine was used in 16.67% patients in group 1 and 6.67% patients in group 2. Total protamine

used in group 1 and group 2 was 311± 81mg and 302± 78 mg respectively. Drugs required in both the groups before CPB, during CPB and after CPB was similar (p>0.05) (table 2) Intraoperative haemodynamic variables like mean heart rate, mean arterial pressure and oxygen saturation was similar in both the groups (p>0.05). Table 3 shows time required for procedures during operative procedure. Duration of procedure in methyl prednisolone was 244.6± 48.3 min. and in normal saline group was 243.5± 50.21 min. Duration of extracorporeal circulation in MP group and NS group was 123.4± 29.5 min and 125.6± 32.3 min respectively. Duration of aortic cross clamping was 86.3± 18.3 min and 85.5± 22.1 min in group 1 and group 2 respectively. In methyl prednisolone group 76.67% of patients required antifibrinolytic drugs and in normal saline group 80% of patients required antifibrinolytic drugs. Mean duration of procedure, mean duration of extracorporeal circulation and mean duration of aortic cross clamping were comparable in both the groups (p>0.05) Extubation time in methyl prednisolone group was 12.2± 1.3 hours and in extubation time in normal saline group was 10.1± 1.5 hours. This difference was statistically significant. (p<0.05) Post operative outcome in both the group was analysed in table 4. Duration of post mechanical ventilation was 8 hours in both the groups with interquartile range 0f 4-11 and 5-12 hours. Median of length of ICU stay in group 1 was 23 (18-25) hours and in group 2 it was 23 hours (18-26). Length of hospital stay was 8 days with interquartile range of 7-12 days in methyl prednisolone group. Length of hospital stay in group 2 was 10 days with interquartile range of 7-13 days. This difference was statistically significant.(p<0.05) Mean highest serum glucose concentration in ICU was 194± 42 mg/dl in methylprednisolone group and 176± 43 mg/dl in normal saline group. Highest serum glucose concentration was significantly higher in MP group than NS group (p<0.05). Atrial fibrillation was observed 30 % of patients in group 1 and 33.33% of patients in group 2. Delirium was seen in 6.67% and 10% patients in group 1 and group 2 respectively. Myocardial infarction was observed in one patient in each group post operatively. Stroke was observed among 2 patients in MP group and 1 patient in NS group. Renal failure was observed in 2 patients in MP group and 1 patient in NS group. 2 patients suffered from respiratory failure in each group. Post operative infection was significantly higher in normal saline group (26.67%) than methyl prednisolone group (13.33%) (p<0.05). Mortality was same in both the groups.

Table 1: Comparison of both the groups according to variables

Sr no	Variables	Group 1	Group 2	P value
1	Age (years)	59.8± 4.2	58.4± 3.3	<0.05
2	Male: female	21:9	20:10	<0.05
3	Height (cm)	168.3± 14.7	167.6± 15.3	<0.05
4	Weight (kg)	68.1± 4.1	67.9± 3.1	<0.05

Table 2: Comparison of both the groups according to intraoperative variables

Sr no	Intraoperative variables	Group 1	Group 2	P value
1	**Anaesthetic drug**			
2	Fentanyl (µg/kg)	20±0.4	20±0.3	p>0.05
3	Midazolam(µg/kg)	140±21	150± 31	p>0.05
4	Vecuronium (µg/kg)	20±0.3	20±0.3	p>0.05
5	**Before CPB (%)**			
6	Isoflurane use	30(100%)	30(100%)	p>0.05
7	Nitroglycerine use	7 (23.33%)	5 (16.67%)	p>0.05
8	**During CPB**			
9	Total heparin (mg)	305±89	285±64	p>0.05
10	Total cardioplegia (ml)	3102±994	2967±982	p>0.05
11	**After CPB (%)**			
12	Isoflurane use	5 (16.67%)	5(16.67%)	p>0.05
13	Nitroglycerin use	2 (6.67%)	1 (3.33%)	p>0.05
14	Dopamine use	19 (63.33%)	18 (60%)	p>0.05
15	Norepinephrine use	5 (16.67%)	2 (6.67%)	p>0.05
16	Total protamine used (mg)	311± 81	302± 78	p>0.05

Table 3: Comparison of both the groups according to intraoperative variables

Sr no	Operative variables	Group 1	Group 2	P value
1	Duration of procedure (min)	244.6± 48.3	243.5± 50.21	>0.05
2	Duration of extracorporeal circulation (min)	123.4± 29.5	125.6± 32.3	>0.05
3	Duration of aortic cross clamping (min)	86.3± 18.3	85.5± 22.1	>0.05
4	Use of antifibrinolytic drugs	23 (76.67%)	24 (80%)	>0.05

Table 4: Comparison of both the groups according to post operative outcome

Sr no	Post operative outcome	Group 1	Group 2	P Value
1	**Median (interquartile range)** Duration of post mechanical ventilation (hours)	8(4 -11)	8(5-12)	P> 0.05
2	Length of ICU stay (hours)	23 (18-25)	23 (18-26)	P> 0.05
3	Length of hospital stay (days)	8(7-12)	10(7-13)	**P><0.05**
4	**(Mean)** Highest serum glucose conc. In ICU	194± 42	176± 43	**P><0.05**
5	**(percentage)** Atrial fibrillation	9 (30%)	10(33.33%)	P> 0.05
6	Myocardial infarction	1(3.33%)	1(3.33%)	P> 0.05
7	Stroke	1(3.33%)	2 (6.67%)	P> 0.05
8	Renal failure	2 (6.67%)	1(3.33%)	P> 0.05
9	Respiratory failure	2 (6.67%)	2 (6.67%)	P> 0.05
10	Delirium	2(6.67%)	3(10%)	P> 0.05
11	Post operative infection	4 (13.33%)	8(26.67%)	**P<0.05**
12	Death	1 (3.33%)	1 (3.33%)	P> 0.05

DISCUSSION

In our study, Both the groups were comparable with respect to age, sex ratio, height and weight (p>0.05). Both the groups were comparable with respect to pre operative medication (p> 0.05). Isolated CABG was most commonly performed surgery in both the groups (60% and 56.67%) followed by CABG and valve surgery (26.67% and 23.33%). Drugs required in both the groups before CPB, during CPB and after CPB was similar (p>0.05) (table 2) In methyl prednisolone group 76.67% of patients required antifibrinolytic drugs and in normal saline group 80% of patients required antifibrinolytic drugs. Mean duration of procedure, mean duration of extracorporeal circulation and mean duration of aortic cross clamping were comparable in both the groups (p>0.05) Extubation time in methyl prednisolone group was 12.2± 1.3 hours and in extubation time in normal saline group was 10.1± 1.5 hours. This difference was statistically significant. (p<0.05) Similar finding were observed in Engelman RM *et al.*. [12] They found that methylprednisolone group (13.1 ± 2.3 hours) has prolonged extubation period than control group (10.5 ± 1.0.). Similarily Coffin LH *et al.* found prolonged respiratory support than control group. [12] Methyl prednisolone causes sodium and water retention leading to initiation of pulmonary edema in susceptible patients. [14] Median of length of ICU stay in group 1 was 23 (18-25) hours and in group 2 it was 23 hours (18-26). Length of hospital stay was 8 days with interquartile range of 7-12 days in methyl prednisolone group. Length of hospital stay in group 2 was 10 days with interquartile range of 7-13 days. This difference was statistically significant.(p<0.05) Prolonged intubation following cardiac surgery is associated with an increased risk of infection and a prolonged ICU length of stay. The Cochrane meta-analysis found a significant reduction in ICU stay by about 2 hours (95% CI, -2.8 to -1.8 hours) and hospital stay by about half a day (95% CI, -0.65 to -0.15). [15] similar findings were observed in previous studies. [16,17] In our study, Mean highest serum glucose concentration in ICU was 194± 42 mg/dl in methylprednisolone group and 176± 43 mg/dl in normal saline group. Highest serum glucose concentration was significantly higher in MP group than NS group (p<0.05). Similar to our study previous studies found increased hyperglycemia and increased insulin requirement in cardiac surgery patients in corticosteroids groups than control group. [18-21] Post operative infection was significantly higher in normal saline group (26.67%) than methyl prednisolone group (13.33%) (p<0.05). Mortality was same in both the groups. Hyperglycemia impairs T cell function increasing morbidity and mortality. [22] Similarily Dieleman JM *et al.* found significant increase in post operative infections in control group than methylprednisolone group. [15]

CONCLUSION

Methylprednisolone in cardiac surgery is not having additional beneficial effect in cardiac surgery patients.

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