Original article

The effect of dexamethasone prophylaxis on postoperative delirium after cardiac surgery: A randomized trial

Davoud Mardani[1], Hamid Bigdelian[2]

[1] Department of Nursing, School of Medicine Isfahan University of Medical Sciences, Isfahan, Iran. [2] Department of Cardiac Surgery, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

BACKGROUND: Coronary artery bypass graft is commonly associated with post cardiac surgery delirium. Proinflammatory processes play an important role in the pathogenesis of postoperative delirium. Therefore, dexamethasone might have a beneficial effect on the reduction of this complication. **METHODS:** This randomized clinical trial was conducted with the objective of the evaluation of dexamethasone effects on postoperative delirium and complications after cardiac surgery. The eligible patients were divided into 2 groups of dexamethasone with 43 patients and placebo with 50 patients. The dexamethasone group took 8mg dexamethasone before induction of anesthesia followed by 8mg every 8 hour for 3 days and the other group received placebo in the same way. **RESULTS:** all patients were assessed by a mini mental status questionnaire and psychiatric interviewing with the aim of diagnosing delirium. Extubation time of the dexamethasone group was significantly reduced. Our results showed that in the first postoperative day delirium, extubation time, and intensive care unit length of stay significantly decreased in the dexamethasone group without increasing serious complications such as infectious diseases. After administration of dexamethasone only hyperglycemia as an adverse event was increased in the dexamethasone group. Other complications of renal, cardiac, cerebrovascular and respiratory system did not show any significant differences between the two groups. **CONCLUSIONS:** postoperative delirium is in correlation with costly adverse events after cardiac surgery. Our data suggested that preoperative administration of dexamethasone might safely protect the brain of patients who undergone cardiac surgery against postoperative delirium.

KEYWORDS: Cardiopulmonary Bypass, Delirium, Coronary Artery Bypasses Grafting, Dexamethasone

BACKGROUND

Complications of CABG vary from minor symptoms to fatal brain injuries. Impairment of memory, concentration, and language comprehension are related to postoperative cognitive disorders.[1-3] Cognitive impairment occurs in about 15-80% of patients who have undergone CABG, and is associated with increased mortality, hospital lengths of stay and long-term effects on the individuals life.[4,5]

The main cause of these neuropsychological impairments is still unknown; nevertheless evidences suggest that cardiopulmonary bypass (CPB) is an important trigger for neuropsychological disorders after cardiac surgery.[6] Cardiopulmonary bypass causes systemic inflammatory response syndrome (SIRS) which is understood to be associated with cognitive decline.[7,8] Enzymes and proinflammatory cytokines, which are released by monocytes and neutrophils in collaboration with reactive oxygen species, may result in cerebral damage and brain edema secondary to vasodilatation and fluid leak into brain tissue.[9-11]

Corticosteroid therapy as an anti-inflammatory strategy can interrupt the inflammatory events after CPB.[12,13] Potential Inhibition of proinflammatory response by corticosteroids might have outcomes such as improvement of myocardial function, reduction of extubation time, shortening of intensive care unit and hospital length of stay.[13,14] The beneficial effect of dexamethasone on neurological sequelae has been showed previously, but its value in the context of cardiac surgery still remains controversial.[12,15] Despite the high incidence of neurologic deficits and importance of the immediate postoperative period, few literature have been found which evaluate this period.[16] According to our searches, there is little knowledge about the effects of dexamethasone on post cardiac surgery cognitive disorders. Therefore, this study was conducted with the aim of evaluating dexamethasone effects on postoperative delirium and complications after cardiac surgery.

METHODS

Study design

After receiving institutional committee approval,

Address for correspondence: Hamid Bigdelian, Department of Cardiac surgery, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: Bigdelian@med.mui.ac.ir
Received: 17-12-2011; **Revised:** 24-01-2012; **Accepted:** 21-02-2012

this randomized clinical trial was performed from January of 2009 to February 2011 in Chamran Heart Center, which is one of the teaching hospitals of Isfahan University of Medical Sciences. The exclusion criteria were; inability to read and write, prolonged intubation, longer duration of CPB (more than 3 hours), older than 80 years of age, EF lower than 20%, hemodynamic instability, history of delirium, and emergency operation. Totally, 110 patients who had undergone CABG were eligible for this study. Informed consents were obtained from patients before their participation and they were randomly divided into two groups of the same size (n = 55). During the study 17 patients were excluded because of death (n = 9), intubation of more than 24 hours (n = 5), and refusal to complete the survey (n = 3). Hence, in total 93 patients remained in the groups of dexamethasone (DEX (n) = 43), and placebo (PCB (n) = 50). Patients received dexamethasone or placebo as follows: 8mg of intravenous dexamethasone was administrated to the dexamethasone group immediately before surgery and was followed by 8mg (2ml) every 8 hours for the first 3 postoperative days. This method was repeated for the placebo group using an equal volume of normal saline 0.9% (as placebo) instead of dexamethasone.

Anesthesia and surgical methods

After performing routine care and cardio-respiratory monitoring for all subjects, they received a constant anesthesia. Surgery was performed under moderate hypothermia (28-30◦/c) approach. After institution of CPB at flow rate of 2.4 $L.min^{-1}.M^{-2}$, the aorta was cross-clamped and potassium cardioplegia was administrated. During surgery, radial arterial pressure was preserved in the range of 60-80 mmHg with low dose norepinephrine. After anastomosing grafts and repairing valves (if it was indicated), the cross-clamp was removed and patients were rewarmed. Moreover, after transferring patients to intensive care unit (ICU), all of them profited from protocolled managements including sitting of mechanical ventilation, fast-tracking, administrating of low dose nitrates and dobutamine, and antibiotic therapy. Blood glucose was routinely monitored in ICU at 6-hour intervals and hyperglycemia was managed according to ICU protocol by continuous infusion of insulin. The target goal of blood glucose was 80-180 mg/dl in this protocol.

Psychological methods

The participants' cognitive status was assessed by using mini-mental status examination (MMSE) as a screening method for diagnosing probable cognitive impairment. The MMSE questionnaire was completed on the preoperation day (PROD)and first, second, and third postoperation days (POD1, 2, 3) for each participant. Patients were not examined on the operation day because of surgery, anesthesia, intubation, and psychological stresses. The MMSE screening questionnaire, which evaluates general mental status, includes 11 items with the maximum score of 30 points.[17] A total score of less than 23 was considered as a possible indicator for cognitive impairment. Hence, the diagnostic criteria for the confirmation of diagnosis in patients, who had obtained a score of 23 or less were based on the DSM-IV criteria. In other words, delirium was diagnosed if the DSM-IV criteria were met in a patient.

Data analysis

All analysis was performed by the SPSS software (version 16, SPSS Inc. , Chicago, IL, USA). Continuous variables of study described by mean and standard deviation values are shown by mean ± standard deviation (SD) in this study. Additionally, Frequency and percentage of categorical variables are represented as frequency (percent) and determined by means of descriptive statistic. Continuous variables analysis was performed by independent-sample t-test. In order to find any noticeable difference between and within groups, categorical statistics was analyzed by $\chi 2$ or Fisher's exact test (as appropriate). In all of the tests, P-value < 0.05 was considered as significant level.

RESULTS

A total of 93 patients participated in the study groups (DEX and PCB). Table 1 consists of the summarization of comparisons of pre-, intra-, and postoperative characteristics for the two groups. As shown in table 1, there is no significant difference in the preoperative baseline characteristics of the groups.. Analysis of postoperative data revealed that the patients of DEX group were intubated for a significantly shorter time (p = 0.04). The mean extubation time of DEX group was 9.18 ± 2.40 hours, but for PCB group it was 10.56 ± 3.86 hours. One other significant difference was seen in mean of postoperative blood sugar between groups (p = 0.007); the DEX group had mean blood glucose of 245 ± 68 mg/dl versus 212 ± 45 mg/dl in PCB group.

The psychometric results of the MMSE questionnaire on pre and postoperative days are presented in table 2. According to these results, there is no significant difference between the scores of DEX and PCB groups in PROD (28.63 ± 3.06 vs. 27.84 ± 3.15, respectively, p = 0.1). Although, the DEX group compared to the PCB group obtained higher scores in POD1 (27.53 ± 3.44 vs. 25.78 ± 4.70, respectively,

p = 0.04). DEX group had significantly higher scores than PCB group in POD2 (28.12 ± 2.66 vs. 26.26 ± 4.20, respectively, p = 0.04). The Scores of POD3 did not show any meaningful difference between the DEX and PCB groups (28.00 ± 3.08 vs. 27.40 ± 3.20, respectively, P=0.36).

Table 3 demonstrates statistics of delirium incidences and shows that in this study none of the subjects was diagnosed as delirious in PROD. The results of POD1 exhibited a significant reduction of delirium incidence in DEX in contrasted with PCB group (4(9.3%) vs. 13 (26%), respectively, p = 0.03). The results of POD2 did not show any significant differences between DEX and PCB groups (2(4.7%) vs. 5(10%), respectively, p = 0.40). In the same way, there is no statistical difference in the number of patients who suffered from delirium between DEX and PCB groups in POD3 (1(2.3%) vs. 1(2%), respectively, p = 1).

As displayed in table 4, the results showed that the patients of DEX group with 2.86 ± 1.3 days had a shorter intensive care unit (ICU) length of stay (LOS) than the patients of PCB group with 3.68 ± 1.33 days. In addition, the hospital LOS for DEX group was 12.93 ± 1.03 days versus 13.64 ± 1.75 days for the PCB group. Therefore, both parameters of ICU and hospital LOS were significantly shorter in the DEX group (p = 0.004, p = 0.02, respectively).

Table 5 depicts a comparison of postoperative complications between the two groups. Analysis of these variables shows that there is no significant difference in postoperative complication rates. The results show that occurrences of deep sternal wound infection (DSWI), leg infection, sepsis, and pneumonia did not statistically differ between the groups. In addition, occurrence of cardiac complications including acute myocardial infarction (AMI), cardiac arrest, atrioventricular block (AVB), atrial fibrillation (AF), and low cardiac output state were not statistically different between the two groups. There was no significant difference in cerebrovascular (transient ischemic attack (TIA), stroke), respiratory (acute respiratory failure (ARF)), and renal (acute tubular necrosis (ATN), renal failure) systems between the two groups.

Table 1. Comparison of medical Characteristics between the groups

	Total patients (N = 93)		
Characteristics	**Dexamethasone group (N = 43)**	**Placebo group (N = 50)**	
	N (%) or Mean ± SD	**N (%) or Mean ± SD**	**P-value**
Preoperative			
Age (year)	64.55 ± 11.10	60.04 ± 12.77	0.07
LVEF (%)	51.04 ± 5.40	51.90 ± 4.39	0.41
male gender	36(83.7)	44(88)	0.55
CVA	3(7)	4(8)	1
CRF	2(4.7)	1(2)	0.59
DM	3(7)	5(10)	0.72
Hypertension	11(25.6)	9(18)	0.37
COPD	2(4.7)	1(2)	0.59
Smoking	19(44.2)	23(40)	0.86
Carotid Bruit	3(7)	3(6)	1
Alcohol	3(7)	5(10)	0.72
Recent MI	4(9.3)	5(10)	1
Intraoperative			
IABP	3(7)	4(8)	1
CABG	41(95)	42(84)	0.1
CABG + Valve surgery	2(4.7)	8(16.8)	0.1
Grafts	3.07 ± 0.55	3.20 ± 0.72	0.39
Cross-clamp time	81 ± 11	86 ± 11	0.06
Pump time	108 ± 19	109 ± 18	0.92
Hemoglobin(mg/dl)	8.58 ± 1.05	8.28 ± 1.19	0.19
Temperature(◦/c)	28.51 ± 0.55	28.68 ± 0.62	0.15
Postoperative			
Drainage(ml)	807 ± 506	748 ± 496	0.58
P.C > 2unit	12(27.9)	8(16)	0.16
FFP > 2 unit	15(34.9)	13(26)	0.35
Blood sugar (mg/dl)	245 ± 68	212 ± 45	0.007
Extubation time(hr)	9.18 ± 2.40	10.56 ± 3.86	0.04

LVEF: left ventricular rejection fraction, CVA: cerebrovascular accidents, CRF: chronic renal failure, DM: Debates Mellitus, COPD: chronic obstructive pulmonary disease, MI: myocardial infarction, IABP: intra-aortic balloon pump, CABG: coronary arteries bypass graft, P.C: Packed cell, FFP: fresh frozen plasma.

Table 2. Comparison of MMSE scores between the groups

	Total Patients (N = 93)		
MMSE Scores	Dexamethasone group (N = 43)	Placebo group (N = 50)	
	Mean ± SD	Mean ± SD	P-value
PROD	28.63 ± 3.06	27.84 ± 3.15	0.10
POD1	27.53 ± 3.44	25.78 ± 4.70	0.04
POD2	28.12 ± 2.66	26.26 ± 4.20	0.04
POD3	28.00 ± 3.08	27.40 ± 3.20	0.36

MMSE: mini mental status examination, PROD: preoperative day, POD1: first operative day, POD2: second operative day, POD3: third operative day.

Table 3. Comparison of Delirium incidences between the groups

	Total patients (N = 93)		
Delirium	Dexamethasone group (N = 43)	Placebo group (N = 50)	
	N (%)	N (%)	P-value
PROD	0	0	-
POD1	4(9.3)	13(26)	0.03
POD2	2(4.7)	5(10)	0.40
POD3	1(2.3)	1(2)	1

PROD: preoperative day, POD1: first operative day, POD2: second operative day, POD3: third operative day.

Table 4. Comparison of Hospital outcomes between the groups

	Total Patients (N = 93)		
outcome	Dexamethasone group (N = 43)	Placebo group (N = 50)	
	Mean ± SD	Mean ± SD	P-value
ICU LOS(day)	2.86 ± 1.3	3.68 ± 1.33	0.004
Hospital LOS(day)	12.93 ± 1.03	13.64 ± 1.75	0.02

ICU: intensive care unit length of stay, LOS: Length of stay

Table 5. Comparison of post-operative complications between the groups

	Total Patients (N = 93)		
Complications	Dexamethasone group (N = 43)	Placebo group (N = 50)	
	N (%)	N (%)	P-value
Infections			
DSWI	1(2.3)	0(0)	0.46
Sepsis	0(0)	1(2)	1
Leg Infection	0(0)	1(2)	1
Pneumonia	2(4.7)	0(0)	0.21
Cardiac			
Arrest	1(2.3)	0(0)	0.46
AVB	2(4.7)	3(6)	1
AF	5(11.6)	11(22)	0.18
AMI	1(2.3)	0(0)	0.46
LCOS	2(4.7)	3(6)	1
Cerebrovascular			
TIA	3(7)	5(10)	0.72
Stroke	1(2.3)	3(6)	0.62
Respiratory			
ARF	2(4.7)	2(4)	1
Renal			
ATN	2(4.7)	3(6)	1
Renal Failure	0(0)	0(0)	-
Other			
Fever	4(9.3)	8(16)	0.33
Reoperation	2(4.7)	1(2)	0.59

DWSI: deep sternal wound infection, AVB: atrioventricular block, AF: atrial fibrillation, AMI: acute myocardial infarction, LCOS: low cardiac output state, TIA: transient ischemic attack, ARF: acute respiratory failure, ATN: acute tubular necrosis.

DISCUSSION

Generally, post cardiac surgery delirium may be due to complicated neurobiological factors, such as inflammatory responses, cytokines, and hypoxemia.[5] These factors predispose patients for delirium after establishment of CPB. Ischemia-reperfusion damage during cardiopulmonary bypass leads to activation of inflammatory cytokines, oxidative stress, and production of reactive oxygen species, which increase blood brain barrier (BBB) permeability.[18,19] Breakdown of BBB integrity precipitate destruction of brain parenchyma.[20] Finally, infiltration of Inflammatory cells into the damaged cerebral tissue causes extension of water inflow into the brain which leads to brain edema and cell dysfunction.[9,20,21] In summary, an overload of proinflammatory cytokines inflowing into the brain can cause dysfunction of the autonomic nervous and neuroendocrine systems that may result in delirium.[22] Consequently, dexamethasone with its modulatory effect on inflammatory mediators (tissue plasminogen activator, IL-6, IL8, and TNF-α) and disruption of above processes might have positive effects on reduction of delirium after utilization of CPB.[23] We believed that dexamethasone protected the brain by the interruption of this consequence.

According to our knowledge, there is no study that has evaluated dexamethasone effect on delirium incidence after cardiac surgery. In the present study we focused on the effect of administration of dexamethasone on postoperative incidence of delirium. Furthermore, this study compares the rates of complications and secondary outcomes between groups during hospitalization.

In our study we used MMSE questionnaire as a primary screening tool. The results did not show any significant difference in PROD, which means that the global mental status of both of DEX and PCB groups, were the same. Unsurprisingly, the MMSE scores decreased after cardiac surgery. Although, according to the results of POD1 this significant decrease was more obvious in the PCB group rather than DEX group. In the same way, MMSE scores of POD2 shows that the patients of DEX group had a better cognitive status in comparison to PCB group. Although, It is shown that delirium is associated with lower MMSE scores in several studies, there are some other studies which do not prove the correlation of MMSE scores and delirium.[5,24,25] This discrepancy may be related to some issues of sensitivity/specificity of the MMSE test and its limitations. In addition, it was previously shown that the highest sensitivity to cognitive impairments is in cutoff point 23/24 that can indicate possible cognitive impairment.[25,26] Therefore, it is recommended that diagnosis with MMSE be based on the clinical features of patients.[26]

As mentioned above, unfortunately MMSE is not a very reliable diagnostic test. Thus, psychiatric interviewing is the choice approach for validation of diagnosis of delirium. Similar to MMSE scores, the incidence of delirium was lower in DEX group in POD1, and 2, though only the result of POD1 was significant. The incidence of delirium in POD3 was very similar in both groups. We believe that these results are not statistical errors and dexamethasone really protects the brain against damages. We hypothesize that the maximum effect of dexamethasone is on first postoperative days because maximum inflammatory responses occur during this period. As mentioned above, establishment of CPB by activation of proinflammatory cytokines is expressed as SIRS, which can effect cerebrum by several mechanisms including of hypoxia and increasing vascular permeability, and secondary brain tissue damage and edema. Previously, the studies found that dexamethasone protect the brain and its global function (e.g., learning, memory) by reduction of cerebral tissue death that is due to cytokines and ischemia.[27] The result of our study is a new evidence for the cerebral protective effect of dexamethasone. On the other hand, there is a strong relationship between cortisol and cognitive impairment disorders. Dexamethasone with its negative feedback on HPA axis initiates decreasing of cortisol and theoretically may be a useful strategy for decreasing post cardiac surgery deliriums.[28] Researchers, who studied this mechanism of dexamethasone, however not after CPB, discovered a wide range of contradictory results.[28] With regard to these controversies it should be mentioned that the effect of dexamethasone on cognition is dose dependent. In detail, cortisol has an inverted U-shaped dose response effect on cognition, which means the presence of an extreme low/high level of serum cortisol (which is regulated by dexamethasone level) can cause the brain to show cognitive symptoms. IT seems that dexamethasone might worsen the mental condition of people with some pathological disturbances (e.g. Cushing syndrome, and Alzheimer's disease), which suffer from HPA axis dysregulation.[28,29] In comparison with other triggers, pathogenesis of post cardiac surgery delirium is linked with inflammatory phenomena.[30] The researcher believes dexamethasone reduced delirium incidence with its anti-inflammatory properties because the greatest difference was seen in

closest times to CPB. In other words, in comparison with the PCB group, the DEX group had a lower incidence in both POD1, and 2 but only in POD1 was significant which this day is nearer to CPB.

In one study, the advantageous effects of dexamethasone in reduction of inflammatory responses after CPB manifested as decreased adverse effects and consequently better outcomes after cardiac surgery.[31] This was also experienced by Prasongsukarn et al. who reported that consequential unfavorable events of cardiac surgery, which were assumed to be related to reduction of inflammatory cascade and cytokines, were significantly reduced.[23] Results of their study showed significant reduction of AF rhythm occurrence after steroid therapy followed by cardiac surgery. This report is in accordance with our results which showed AF occurred in DEX group with a lower incidence, however, this decline was not statistically significant. In contrast with our results, the study of Prasongsukarn et al. showed that corticosteroids were associated with longer hospital LOS. This could be due to more complications that were seen in their steroid group. The incidence of postoperative complications between our groups (DEX and PCB) did not show any significant difference. A recent meta-analysis, which evaluated effects of steroids on post cardiac surgery complications indicated that ICU and hospital LOS has been totally reduced after administration of steroids.[32]

One major concern related to prophylaxis of dexamethasone is the risk of increase in postoperative infections.[33] It is known that dexamethasone may have an association with higher incidences of infectious disease due to immunosuppression and hyperglycemia. Our results show that blood glucose of DEX group was significantly higher than PCB group nevertheless postoperative rate of infections was not significant different between DEX and PCB groups. We suppose that a low dose of dexamethasone cannot noticeably increase incidence of postoperative infections because dexamethasone effect is dose dependent. Other studies which support our results stated that dexamethasone was not absolutely associated with higher incidences of infections.[32,33]

In addition we found that DEX group had better outcomes than PCB group. The result of the current study indicated that the patients of DEX group had significantly shorter time of intubation. This finding is relatively important because longer intubation time is related with more complications (e.g. ventilator associated pneumonia, and so forth). This was also experienced in the study of Yared et al., who confirm the valuable effect of dexamethasone in early extubation of patients after cardiac surgery.[14] They stated that this effect might be due to reduction of shivering and fever. Furthermore, we believe that another reason of early extubation was lower incidence of delirium in DEX group. Administration hypnotic-sedative agents cause lower incidences of delirium, which can result in earlier awakening and extubation of patients. However, full consciousness of patients is necessary for extubation and administration of hypnotic-sedative medications may delay this awakening of patients. Therefore, dexamethasone could cause early extubation due to protection of brain against cognitive decline and delirium.

Literatures recommended that anti-inflammatory strategies such as administration of glucocorticoids, might improve cognitive dysfunction after cardiac surgery, despite the lack of information about effects of dexamethasone on delirium after CPB.[34] Our results might be a proof for such recommendations. These results showed that dexamethasone maintains a significantly higher brain function after establishment of CPB without any serious complications. In other words, prophylaxis of dexamethasone can place on perioperative management of patients who have undergone cardiac surgery.

Although, we take into account the probability of several known and unknown factors that may influence our results. In this regard, it is supposed that post cardiac surgery delirium is related to Intraoperative factors such as complexity of surgery, longer duration of cardiopulmonary bypass, cross-clamp time, and using of IABP. Therefore, we were concerned about the possibility of synergetic interference of these factors, which might contribute to higher incidence of delirium in PCB. By taking into consideration the limitations of our study; we are declaring that approval of prophylaxis of dexamethasone need to conduction of similar studies by same methodology but with larger subject population. According to our knowledge many factors influence the mental response to corticosteroids such as subjects' mood, medications, and even their hormonal level. Finally, our results strongly support that prophylaxis of dexamethasone can effectively reduce post cardiac surgery delirium.

ACKNOWLEDGMENTS

This trial has been registered in the Iranian Registry of Clinical Trials (ID: IRCT201202229108N1). The authors would like to thank all participating patients and all

who gave us the chance of accomplishing this study. We greatly appreciate the support and participation of our coworkers and nurses of the ICUs of the Chamran heart center.

REFERENCES

1. Fadaei S, Janighorban M, Mehrabi T, Ahmadi SA, Mokaryan F, Gukizade A. Effects of cognitive behavioral counseling on body Image following mastectomy. J Res Med Sci 2011; 16(8): 1047-54.
2. Oghabian MA, Batouli SA, Norouzian M, Ziaei M, Sikaroodi H. Using functional Magnetic Resonance Imaging to differentiate between healthy aging subjects, Mild Cognitive Impairment, and Alzheimer's patients. J Res Med Sci 2010; 15(2): 84-93.
3. Ramlawi B, Rudolph JL, Mieno S, Feng J, Boodhwani M, Khabbaz K, et al. C-Reactive protein and inflammatory response associated to neurocognitive decline following cardiac surgery. Surgery 2006; 140(2): 221-6.
4. Rosengart TK, Sweet JJ, Finnin E, Wolfe P, Cashy J, Hahn E, et al. Stable cognition after coronary artery bypass grafting: comparisons with percutaneous intervention and normal controls. Ann Thorac Surg 2006; 82(2): 597-607.
5. Hopkins RO, Jackson JC. Assessing neurocognitive outcomes after critical illness: are delirium and long-term cognitive impairments related? Curr Opin Crit Care 2006; 12(5): 388-94.
6. Stroobant N, Van NG, Belleghem Y, Vingerhoets G. Short-term and long-term neurocognitive outcome in on-pump versus off-pump CABG. Eur J Cardiothorac Surg 2002; 22(4): 559-64.
7. Kozora E, Kongs S, Collins JF, Hattler B, Baltz J, Hampton M, et al. Cognitive outcomes after on- versus off-pump coronary artery bypass surgery. Ann Thorac Surg 2010; 90(4): 1134-41.
8. Reis MD, Gommers D, Struijs A, Dekker R, Mekel J, Feelders R, et al. Ventilation according to the open lung concept attenuates pulmonary inflammatory response in cardiac surgery. Eur J Cardiothorac Surg 2005; 28(6): 889-95.
9. Gazit AZ, Huddleston CB, Checchia PA, Fehr J, Pezzella AT. Care of the pediatric cardiac surgery patient--part 1. Curr Probl Surg 2010; 47(3): 185-250.
10. Franke A, Lante W, Markewitz A, Weinhold C. In vitro restoration of post-operatively decreased IFN-gamma levels after cardiac surgery and its effect on pro- and anti-inflammatory mediators. J Surg Res 2006; 136(2): 266-72.
11. Parnell AD, Massey NJ. Postoperative care of the adult cardiac surgical patient. Anaesthesia & intensive care medicine 2009; 10(9): 430-6.
12. Larmann J, Theilmeier G. Inflammatory response to cardiac surgery: cardiopulmonary bypass versus non-cardiopulmonary bypass surgery. Best Pract Res Clin Anaesthesiol 2004; 18(3): 425-38.
13. Marik PE, Fromm R. The efficacy and dosage effect of corticosteroids for the prevention of atrial fibrillation after cardiac surgery: a systematic review. J Crit Care 2009; 24(3): 458-63.
14. Yared JP, Starr NJ, Torres FK, Bashour CA, Bourdakos G, Piedmonte M, et al. Effects of single dose, postinduction dexamethasone on recovery after cardiac surgery. Ann Thorac Surg 2000; 69(5): 1420-4.
15. Irazuzta J, Pretzlaff RK, DeCourten-Myers G, Zemlan F, Zingarelli B. Dexamethasone decreases neurological sequelae and caspase activity. Intensive Care Med 2005; 31(1): 146-50.
16. Bickert AT, Gallagher C, Reiner A, Hager WJ, Stecker MM. Nursing neurologic assessments after cardiac operations. Ann Thorac Surg 2008; 85(2): 554-60.
17. Nelson A, Fogel BS, Faust D. Bedside cognitive screening instruments. A critical assessment. J Nerv Ment Dis 1986; 174(2): 73-83.
18. Hoffman WH, Stamatovic SM, Andjelkovic AV. Inflammatory mediators and blood brain barrier disruption in fatal brain edema of diabetic ketoacidosis. Brain Res 2009; 1254: 138-48.
19. Joashi U, Tibby SM, Turner C, Mayer A, Austin C, Anderson D, et al. Soluble Fas may be a proinflammatory marker after cardiopulmonary bypass in children. J Thorac Cardiovasc Surg 2002; 123(1): 137-44.
20. Wasserman JK, Schlichter LC. Minocycline protects the blood-brain barrier and reduces edema following intracerebral hemorrhage in the rat. Exp Neurol 2007; 207(2): 227-37.
21. Nakamura K, Ueno T, Yamamoto H, Iguro Y, Yamada K, Sakata R. Relationship between cerebral injury and inflammatory responses in patients undergoing cardiac surgery with cardiopulmonary bypass. Cytokine 2005; 29(3): 95-104.
22. Ebersoldt M, Sharshar T, Annane D. Sepsis-associated delirium. Intensive Care Med 2007; 33(6): 941-50.
23. Prasongsukarn K, Abel JG, Jamieson WR, Cheung A, Russell JA, Walley KR, et al. The effects of steroids on the occurrence of postoperative atrial fibrillation after coronary artery bypass grafting surgery: a prospective randomized trial. J Thorac Cardiovasc Surg 2005; 130(1): 93-8.
24. van der Mast RC, van den Broek WW, Fekkes D, Pepplinkhuizen L, Habbema JD. Incidence of and preoperative predictors for delirium after cardiac surgery. J Psychosom Res 1999; 46(5): 479-83.
25. Jankowski CJ, Trenerry MR, Cook DJ, Buenvenida SL, Stevens SR, Schroeder DR, et al. Cognitive and functional predictors and sequelae of postoperative delirium in elderly patients undergoing elective joint arthroplasty. Anesth Analg 2011; 112(5): 1186-93.
26. Wind AW, Schellevis FG, Van SG, Scholten RP, Jonker C, Van Eijk JT. Limitations of the Mini-Mental State Examination in diagnosing dementia in general practice. Int J Geriatr Psychiatry 1997; 12(1): 101-8.
27. Feng Y, Rhodes PG, Liu H, Bhatt AJ. Dexamethasone induces neurodegeneration but also up-regulates vascular endothelial growth factor A in neonatal rat brains. Neuroscience 2009; 158(2): 823-32.
28. Belanoff JK, Gross K, Yager A, Schatzberg AF. Corticosteroids and cognition. J Psychiatr Res 2001; 35(3): 127-45.
29. Gurevich D, Siegel B, Dumlao M, Perl E, Chaitin P, Bagne C, et al. HPA axis responsivity to dexamethasone and cognitive impairment in dementia. Prog Neuropsychopharmacol Biol Psychiatry 1990; 14(3): 297-308.
30. Gao L, Taha R, Gauvin D, Othmen LB, Wang Y, Blaise G. Postoperative cognitive dysfunction after cardiac surgery. Chest 2005; 128(5): 3664-70.
31. El Azab SR, Rosseel PM, de Lange JJ, Groeneveld AB, van SR, van Wijk EM, et al. Dexamethasone decreases the pro- to anti-inflammatory cytokine ratio during cardiac surgery. Br J Anaesth 2002; 88(4): 496-501.
32. Cappabianca G, Rotunno C, de Luca Tupputi SL, Ranieri VM, Paparella D. Protective effects of steroids in cardiac surgery: a meta-analysis of randomized double-blind trials. J Cardiothorac Vasc Anesth 2011; 25(1): 156-65.
33. Price J, Tee R, Lam BK, Hendry P, Green MS, Rubens FD. Current use of prophylactic strategies for postoperative atrial fibrillation: a survey of Canadian cardiac surgeons. Ann Thorac Surg 2009; 88(1): 106-10.
34. Kadoi Y. Pharmacological neuroprotection during cardiac surgery. Asian Cardiovasc Thorac Ann 2007; 15(2): 167-77.

How to cite this article: Mardani D, Bigdelian H. The effect of dexamethasone prophylaxis on postoperative delirium after cardiac surgery: A randomized trial. J Res Med Sci 2012; 17(Spec 1): S113-S119.

Source of Support: Nill, **Conflict of Interest:** Finally, it must be mention that there is no financial or any other kind of conflict of interests for reporting in this manuscript.