The Changes in Cortisol Levels during Cardiac Surgery: A Randomized Double-Blinded Study between Two Induction Agents Etomidate and Thiopentone

Manee Raksakietisak MD*,
Chutimart Ngamlamiad MD*, Thitiganya Duangrat MD*,
Suvit Soontarinka MD*, Kasana Raksamani MD*

** Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Objective: *To study the changes in cortisol levels during and after cardiac surgery after an inductive dose of either etomidate or thiopentone and their consequences.*

Material and Method: *A prospective, randomized, double-blinded study was conducted in 26 patients undergoing elective cardiac surgery. They received either etomidate or thiopentone for induction. Serum cortisol levels were measured preoperatively, and then at 2-, 4-, 8-, and 24-hour. All of the patients received standard anesthesia and surgery. The data also included patients perioperative management and outcome.*

Results: *There is no difference in patients' characteristics. The baseline plasma morning cortisols in the two groups were comparable (11.7±7.5 mcg/dL in etomidate group vs. 12.0±8.2 mcg/dL in thiopentone group). In both groups, during surgery, the cortisol levels rose to higher levels and reached peak levels at four to eight hours and related to surgical stress. At all times, the etomidate group had lower cortisol levels but only at 8-hour, the etomidate group had significantly lower cortisol level (39.9±14.2 vs. 65.9±20.0 mcg/dL). At 24 hours, in both groups, cortisol levels were lower than at 8-hour but did not return to normal baseline levels. There were no differences in the dose of inotropic use and ICU stay. However, surprisingly the etomidate group had shorter hospital stay.*

Conclusion: *A single dose of etomidate used for induction in elective cardiac patients can partially and reversibly inhibit of the cortisol synthesis for, at least, 24 hours, but its association with any hemodynamic consequences cannot be concluded.*

Registration: *ClinicalTrials.gov as NCT01495949.*

Keywords: *Cortisol, Adrenal insufficiency, Cardiac surgery, Etomidate*

J Med Assoc Thai 2015; 98 (8): 775-81
Full text. e-Journal: *http://www.jmatonline.com*

The anesthetic inductive agents could cause unstable hemodynamic in patients with compromised left ventricular function[1]. Etomidate has been widely used in this group of patients because it results in stable hemodynamic. It has been known that even a single dose of etomidate can suppress adrenal function leading to adrenal insufficiency. This effect was temporary and its clinical significance is still unclear[2-5]. Etomidate causes inhibition of the enzyme 11β-hydroxylase, which converts 11-deoxycortisol to cortisol, thereby, decrease cortisol levels[6].

Meta-analysis showed that etomidate increased risk of adrenal insufficiency 1.64 times (95% CI 1.52-1.77), but the mortality rate was not clearly affected[3]. However, etomidate remains a popular drug widely used in emergency rooms and trauma, although adrenal suppression has been occasionally reported[4,7]. In cardiac surgery, with the use of cardiopulmonary bypass machine, which can stimulate stress hormones, the stress responses have resulted in increased cortisol secretion during and after the surgery[8-10].

The present study aimed to compare the changes in cortisol levels during and after cardiac surgery after a single dose of either etomidate or thiopentone, and their hemodynamic consequences.

Material and Method

This prospective, randomized, controlled, double-blinded study was performed between October 2011 and September 2012 in Siriraj Hospital, Mahidol University, Bangkok, Thailand. The study was approved by the Ethics Committee of Siriraj Hospital (507/2554 (EC1)), and registered with ClinicalTrials.gov

Correspondence to:
Raksakietisak M, Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand.
Phone: +66-2-4197989, +66-2-4113256
E-mail: manee.rak@mahidol.ac.th, manee95@hotmail.com

as NCT01495949. All patients had given informed consent. We included 26 patients who were 60 years old or older undergoing elective coronary artery bypass grafting (CABG), or valve replacement, or combined procedure, and other procedures using cardiopulmonary bypass (CPB). Exclusion criteria were age below 60 years, diagnosed or suspected adrenal insufficiency, history of steroid use within 1 year, redo-cardiac surgery, emergency procedure, preoperative use of inotrope or vasopressor, already intubated, and creatinine >2.0 mg/dL. Many cardiac anesthesiologists in our hospital routinely gave steroid as a part of anesthetic regimen and many never use etomidate in fear of adrenal suppression so only a few agreed with the study protocol.

To avoid the confounding effect of circadian rhythm of cortisol secretion, all selected operations were performed in the morning. Randomization was performed by using concealed envelopes. Patients were divided into two groups to receive either etomidate (Etomidate-®Lipuro, B. Braun, Germany) or thiopentone (Anesthal®, Jagsopal pharmaceutical, India) for induction. The induction drug was prepared in a 20 ml syringe containing either etomidate 2 mg/ml or thiopentone 25 mg/ml. This syringe and extension tube was wrapped by non-transparent material and contained in syringe pump before being handed to the in-charge anesthesiologist.

The premedication consisted of oral midazolam (5 mg or 1/3 tablet) given one hour before induction and oxygen cannula three liters/minute was given after premedication. The non-invasive monitoring consisted of electrocardiography with ST-segment analysis of leads II and V5, pulse oximetry, and non-invasive blood pressure. Before induction, the radial artery catheter was inserted for invasive arterial pressure monitoring and blood sample was drawn for baseline plasma cortisol level. Induction of anesthesia was performed with fentanyl 3 mcg per kg, midazolam 0.05 mg per kg and the study drug was given by titration 1-2 ml with syringe pump in order to achieve loss of consciousness. A single dose of rocuronium (0.6 mg per kg) was given to facilitate endotracheal intubation. After intubation, central venous or pulmonary artery catheter was inserted into the right internal jugular vein. The transesophageal echocardiography was also used in some cases. Anesthesia was maintained with sevoflurane, air, oxygen, additional doses of fentanyl, rocuronium, and midazolam. The blood cortisol levels were measured at 0 hour (before induction), 2- (during surgery), 4- (near the end of surgery), 8- hours (early period in ICU), and 24-hour (the next day morning) respectively. Apart from inductive agent, patients in the two groups were managed identically. The surgery was performed as the standard procedures. When weaning off cardiopulmonary bypass (CPB), the intravascular volume was optimized and dobutamine (first inotropic drug) was titrated to achieve good cardiac output and blood pressure. If it was not successful, the second inotrope or vasopressor would be used by anesthesiologist upon the patients' conditions. At the end of the operation, patients remained sedated, intubated, and transferred to the cardiac intensive care unit. The postoperative care included maintaining hemodynamic, ventilator support, fluid management, and standardized pain management. The ICU doctors and nurses were unaware of the patients' group and extubation was made when the patient met extubation criteria. The recorded data included cortisol levels, the amount of insulin used to achieve blood glucose levels of 140 to 180 mg/dL[11], the amount and duration of inotropic and vasopressor used, length of ICU stay, length of hospital stay. In normal situation, the serum cortisol <15 mcg/dL is diagnosed as adrenal insufficiency[12]. We did not use synthetic ACTH stimulation test because the surgical stress from cardiac surgery was more pronounced than ACTH stimulation test[13,14]. Primary outcome was the comparison between the changes in cortisol levels in two groups of the patients. Secondary outcome included the requirement of inotropes and/or vasopressor drugs (amounts and duration), the duration of ICU stay, and the length of the hospital stay.

Statistical analysis

The sample size calculated from the study of Hildreth et al[4] who found the increasing cortisol level in etomidate group = 4.2±4.9 mcg/dL and other group = 11.2±6.1 mcg/dL, type I error = 0.05, 2-sided and power of the test = 80%, 13 patients were needed for each group.

The data were collected and analyzed using Statistics SPSS, version 21. Quantitative variables were demonstrated as mean and standard deviation. Nominal variables were reported as frequencies and percentages. Comparisons between the two groups used Student's t-test for quantitative variables, the Chi-square test for qualitative variables, the Mann-Whitney U test for nonparametric continuous variables. Cortisol levels and dobutamine dosage were compared between the

groups using mean (SD) and t-test for comparison. The Levine's test was used for equality of variances. A *p*-value of less than 0.05 was considered statistically significant.

Results

Twenty-six patients were enrolled in the present study. Two patients in thiopentone group were excluded from study because of changing surgical plans to more complex surgery (Fig. 1). No protocol violation and all patients were analyzed per protocol. There were no differences in patients' characteristics. All of the patients had American Society of Anesthesiologists (ASA) physical status 3. The mean (SD) of left ventricular ejection fraction (LVEF) and the number of patients who had LVEF <40% were not different in both groups. Surgical procedures were coronary artery bypass graft (CABG), valvular repair or replacement, combined surgery (valve surgery + single vessel bypass graft), and myomectomy (Table 1).

No differences were seen in the duration of anesthetic time and CPB time between groups, although thiopentone group had longer aortic clamp time (91 minutes vs. 78 minutes) but did not reach statistically significant level. In the thiopentone group, the patients received more platelets transfusion (Table 2).

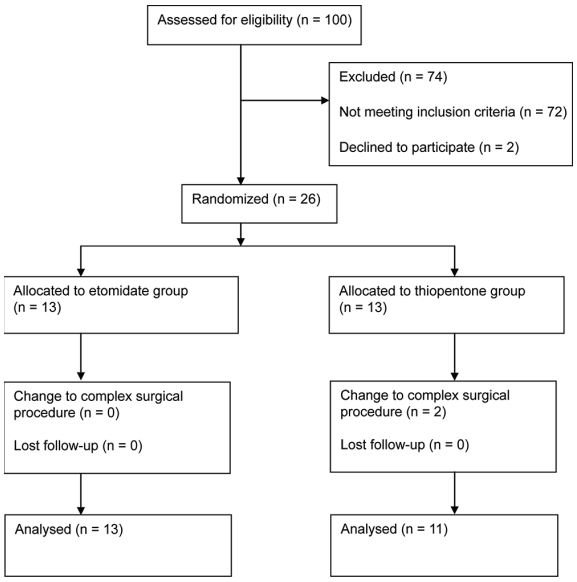

Fig. 1 Consort diagram of the study.

Plasma cortisol levels were measured at 0-(before induction), 2-, 4-, 8-, and 24-hour. The baseline plasma cortisol before anesthetic induction was 11.7±7.5 mcg/dL in etomidate group and in 12.0±8.2 mcg/dL thiopentone group ($p = 0.921$). The baselines of two groups were comparable. The cortisol

Table 1. Preoperative patient characteristics

	Etomidate (n = 13)	Thiopentone (n = 11)	*p*-value
Age (year)	67.5±6.7	70.7±6.7	0.561
Gender (female/male)	4/9	5/6	0.458
ASA class III	13 (100%)	11 (100%)	1.000
Diabetes mellitus	5 (38%)	5 (45%)	0.729
Hypertension	9 (69%)	9 (82%)	0.478
Cerebrovascular accident (CVA)	1 (7.6%)	1 (9.1%)	0.902
Diagnosis			N/A
Coronary artery disease (CAD)	9 (69%)	5 (45%)	
Valvular heart disease (VHD)	1 (7%)	4 (36%)	
CAD and VHD	3 (23%)	1 (9%)	
Others	0 (0%)	1 (9%)	
CAD degree			0.570
Tripple vessel	9 (69%)	3 (27%)	
Tripple vessel with left main	2 (15%)	2 (18%)	
Other	2 (15%)	6 (55%)	
Ejection fraction (%)	59±15	61±17	0.806
Euroscores	1.37±0.77	1.85±0.67	0.486

N/A = not available
Values are mean ± SD or number (%)

levels in both groups rose to higher levels and got their peak levels at 4-hour. Although the cortisol levels in thiopentone group were higher than etomidate at 2- and 4-hour, they did not reach statistically significant differences. However, at 8-hour, the etomidate group had plasma cortisol significantly lower than thiopentone group (39.9±14.2 mcg/dL vs. 65.9±20.0 mcg/dL). At 24 hours, cortisol levels were lower than at 8-hour but did not return to normal baseline levels (Fig. 2).

None had clinical signs of adrenal crisis (unexplained hypotension, hyponatremia, hyperkalemia, or hypoglycemia).

Dobutamine was first inotropic drug administered in both groups. The dobutamine requirements were similar between groups. One patient in thiopentone group, who had LVEF 27%, used second inotropic drug (epinephrine).

In ICU, no patients had serious complications or death. The thiopentone group had longer ventilator time and ICU length of stay, although it was not statistically significant. Most patients stayed in ICU for two days and could be discharged safely to cardiac ward. No differences in total insulin consumption in first 24 hours. The serious complications did not differ between groups. Three patients in each group had new onset of atrial fibrillation. In etomidate group, one patient had delirium. In thiopentone group, one patient had bradycardia requiring permanent pacemaker, and one patient had cardiogenic pulmonary edema. One patient in thiopentone group had a pre-surgical length of stay that was extremely long (40 days) due to preoperative pneumonia and stroke but postsurgical length of stay was only 10 days. Nevertheless, the length of hospital stay after surgery in etomidate group was significantly shorter than thiopentone group (p = 0.024) (Table 3).

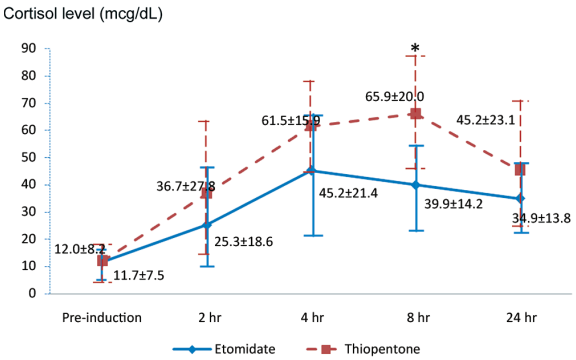

Fig. 2 Cortisol levels at different time points, * p<0.05.

Table 2. Intraoperative data

	Etomidate (n = 13)	Thiopentone (n = 11)	p-value
Anesthetic time (minute)	313±104	328±43	0.636
Surgical time (minute)	251±105	270±65	0.616
Aortic clamp time (minute)	78±33	91±36	0.358
CPB time (minute)	113±41	113±45	0.981
Fluid requirement			
Crystalloid (ml)	1,873±689	1,854±878	0.540
PRC (unit)	2 (0, 5)	2 (0, 6)	0.860
FFP (ml)	89±220	307±417	0.141
Platelets (unit)	0 (0, 4)	5 (0, 10)	0.008*
Cryoprecipitate (unit)	0 (0, 0)	0 (0, 10)	0.277

PRC = packed red-cell; FFP = fresh frozen plasma
Values are mean ± SD or median (P25, P75), * p<0.05 between groups

Table 3. Postoperative data

	Etomidate (n = 13)	Thiopentone (n = 11)	p-value
Ventilator time (hour)	14.5±8.0	27.6±40.8	0.229
ICU time (hour)	44.6±32.9	62.2±47.0	0.256
Length of stay after surgery (days)	6.5±1.6	11.2±6.6	0.024*
Length of total hospital stay (days)	8.8±2.7	18.5±12.4	0.012*

ICU = intensive care unit
Values are mean ± SD, * p<0.05

Discussion

Several studies have reported adrenal insufficiency in patients with the use of etomidate in several settings such as rapid sequence induction in emergency room, trauma, and ICU[3-5,7].

Cardiac surgery and the initiation of cardiopulmonary bypass produce a significant stimulus for the endogenous releases of catecholamines and stress hormones. The process could increase blood concentrations of cortisol, adrenaline, and others[8-10,13].

The present study found that the single use of etomidate at induction of anesthesia in patients undergoing elective cardiac surgery led to adrenal suppression at least 24 hours. The cortisol levels rose to higher levels and reached its peak four to eight hours after administration, which were related to the surgical stress. At all times, the etomidate group had lower cortisol levels (about 70% of the thiopentone group) but high enough to cover the surgical stress. The lower cortisol levels in etomidate group were not associated with clinical signs of adrenal crisis or increasing in requirement of inotrope (dobutamine) for weaning from CPB. The hemodynamic consequences in cardiac patient might be related with several factors such as preoperative LVEF, preoperative patient's status, comorbidity, aortic clamp time, and CPB duration.

Concordance with the present study, in the systemic review by Albert et al[3] concluded that etomidate inhibited adrenal hormone synthesis immediately and persisted for approximately 12 to 24 hours. Cortisol levels after etomidate were approximately 50% of levels observed without etomidate during comparable stress and associated with slightly increased mortality (RR 1.19, 95% CI 1.10-1.30), significance in subgroup with sepsis. In this review, they concluded that the critically ill or sepsis patients may prone to decrease cortisol synthesis, so even with single dose of etomidate may contribute to the morbidity in these patients. Another reviewed by Hohl et al[14] concluded that there was no available evidence to demonstrate that etomidate had a significant effect on mortality. From our study, the etomidate group surprisingly had shortened hospital stay. This reason may be explained by the different population, elective cardiac patients were neither shock nor sepsis[15].

Iribarren et al[2] mentioned that both relative adrenal insufficient (RAI) and lower cortisol levels were associated with increased need for vasoactive drugs for coming off CPB and in postoperative period. They concluded that the use of etomidate should be minimized in elective cardiac surgery. However, Iribarren's study[2] was prospective cohort study, and the etomidate was used according to anesthesiologist's decision. Etomidate might be chosen in sicker cardiac patient and led to the need for higher dose of inotropic drug for weaning from CPB. Morel et al[16] conducted a prospective randomized trial of 100 cardiac patients undergoing cardiac surgery and receiving etomidate or propofol and found relative adrenal insufficiency (RAI) was higher in etomidate group lasting more than 24 hours but no effect in norepinephrine requirement. Our results were comparable with the results from Morel et al[16] although we did not use ACTH stimulation test as a criteria for RAI. We also found no differences in inotropic use but our sample size was too small (calculated from expected differences in cortisol levels) to draw a conclusion about inotropic usage. Etomidate partially and reversibly inhibits adrenal cortisol synthesis, so the etomidate does not strongly suppress cortisol levels and it might not affect the use of inotropes when coming off CPB and in postoperative period. However, asymptomatic RAI was common and occasionally seen in cardiac patients[17].

In our hospital, the laboratory measures total plasma cortisol, not active free cortisol. In general, we assume that there is a good correlation between total cortisol and free cortisol. However, this might not be true, especially in patients with low albumin level. Some studies showed that free cortisol might fall greater when stress occurred[13,15].

One might suggest giving corticosteroid after etomidate induction for prevention of RAI. Payen et al[18] found that moderate dose of hydrocortizone (200 mg/day for 42 hours) had no benefit to overcome etomidate-related adrenal insufficiency.

Wagner et al[19] retrospectively reviewed the use of etomidate and outcomes in cardiac patients and concluded that there was no suggestive evidence that etomidate was associated with unfavorable outcomes such as severe hypotension, longer ventilator hours, longer length of hospital stay, or increasing in-hospital mortality.

As a whole, the authors believe that the etomidate could be used safely in elective uncomplicated cardiac patients without increasing in mortality and morbidity.

Limitations

The present study did not follow plasma cortisol levels after 24 hours. The influence of cortisol

inhibition might persist more than 24 hours. We did not know when the cortisol levels could have returned to their baselines. The cortisol synthesis inhibition by etomidate might last longer than we would have expected. The number of the participants was too small to draw a conclusion about the differences in inotropic uses.

Conclusion

A single dose of etomidate used for induction of anesthesia in elective cardiac patients can decrease cortisol synthesis at least 24 hours. Whether it is associated with increased consumption of inotropic agents. However, the cardiac anesthesiologist should be concerned about the inhibition of the cortisol synthesis, especially in patients who were suspected of adrenal insufficiency.

What is already known on this topic?

A single dose of etomidate during anesthetic induction can suppress cortisol synthesis.

What this study adds?

The etomidate partially (about 30%) and reversibly suppresses cortisol synthesis and has its peak effect four to eight hours after administration and still has some effect at 24 hours.

Acknowledgement

The present study was supported by the Siriraj Research Development Fund, Faculty of Medicine Siriraj Hospital, Mahidol University. The authors would like to thank Miss Nichapat Sookri, my research assistant for her great help with paper work, and Mr. Suthipol Udompunthurak for his statistical assistance.

Potential conflicts of interest

None.

References

1. Singh R, Choudhury M, Kapoor PM, Kiran U. A randomized trial of anesthetic induction agents in patients with coronary artery disease and left ventricular dysfunction. Ann Card Anaesth 2010; 13: 217-23.
2. Iribarren JL, Jiménez JJ, Hernández D, Lorenzo L, Brouard M, Milena A, et al. Relative adrenal insufficiency and hemodynamic status in cardiopulmonary bypass surgery patients. A prospective cohort study. J Cardiothorac Surg 2010; 5: 26.
3. Albert SG, Ariyan S, Rather A. The effect of etomidate on adrenal function in critical illness: a systematic review. Intensive Care Med 2011; 37: 901-10.
4. Hildreth AN, Mejia VA, Maxwell RA, Smith PW, Dart BW, Barker DE. Adrenal suppression following a single dose of etomidate for rapid sequence induction: a prospective randomized study. J Trauma 2008; 65: 573-9.
5. Absalom A, Pledger D, Kong A. Adrenocortical function in critically ill patients 24 h after a single dose of etomidate. Anaesthesia 1999; 54: 861-7.
6. Bornstein SR. Predisposing factors for adrenal insufficiency. N Engl J Med 2009; 360: 2328-39.
7. Bergen JM, Smith DC. A review of etomidate for rapid sequence intubation in the emergency department. J Emerg Med 1997; 15: 221-30.
8. Velissaris T, Tang AT, Murray M, Mehta RL, Wood PJ, Hett DA, et al. A prospective randomized study to evaluate stress response during beating-heart and conventional coronary revascularization. Ann Thorac Surg 2004; 78: 506-12.
9. Maggio M, Ceda GP, De Cicco G, Cattadori E, Visioli S, Ablondi F, et al. Acute changes in circulating hormones in older patients with impaired ventricular function undergoing on-pump coronary artery bypass grafting. J Endocrinol Invest 2005; 28: 711-9.
10. Hoda MR, El Achkar H, Schmitz E, Scheffold T, Vetter HO, De Simone R. Systemic stress hormone response in patients undergoing open heart surgery with or without cardiopulmonary bypass. Ann Thorac Surg 2006; 82: 2179-86.
11. Finfer S, Chittock DR, Su SY, Blair D, Foster D, Dhingra V, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med 2009; 360: 1283-97.
12. Marik PE, Pastores SM, Annane D, Meduri GU, Sprung CL, Arlt W, et al. Recommendations for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients: consensus statements from an international task force by the American College of Critical Care Medicine. Crit Care Med 2008; 36: 1937-49.
13. Christ-Crain M, Jutla S, Widmer I, Couppis O, Konig C, Pargger H, et al. Measurement of serum free cortisol shows discordant responsivity to stress and dynamic evaluation. J Clin Endocrinol Metab 2007; 92: 1729-35.
14. Hohl CM, Kelly-Smith CH, Yeung TC, Sweet DD, Doyle-Waters MM, Schulzer M. The effect of

a bolus dose of etomidate on cortisol levels, mortality, and health services utilization: a systematic review. Ann Emerg Med 2010; 56: 105-13.
15. Marik PE. Mechanisms and clinical consequences of critical illness associated adrenal insufficiency. Curr Opin Crit Care 2007; 13: 363-9.
16. Morel J, Salard M, Castelain C, Bayon MC, Lambert P, Vola M, et al. Haemodynamic consequences of etomidate administration in elective cardiac surgery: a randomized double-blinded study. Br J Anaesth 2011; 107: 503-9.
17. Henzen C, Kobza R, Schwaller-Protzmann B, Stulz P, Briner VA. Adrenal function during coronary artery bypass grafting. Eur J Endocrinol 2003; 148: 663-8.
18. Payen JF, Dupuis C, Trouve-Buisson T, Vinclair M, Broux C, Bouzat P, et al. Corticosteroid after etomidate in critically ill patients: a randomized controlled trial. Crit Care Med 2012; 40: 29-35.
19. Wagner CE, Bick JS, Johnson D, Ahmad R, Han X, Ehrenfeld JM, et al. Etomidate use and postoperative outcomes among cardiac surgery patients. Anesthesiology 2014; 120: 579-89.

การเปลี่ยนแปลงของระดับฮอร์โมนคอร์ติซอลระหว่างการผ่าตัดหัวใจ: การศึกษาเปรียบเทียบระหว่างการได้รับยานำสลบสองชนิดอีโตมิเดตกับธัยโอเพนทอล

มานี รักษาเกียรติศักดิ์, ชุติมาศ งามละเมียด, ฐิติกัญญา ดวงรัตน์, สุวิทย์ สุนทรินคะ, กษณา รักษมณี

วัตถุประสงค์: *เพื่อศึกษาการเปลี่ยนแปลงของระดับฮอร์โมนคอร์ติซอลก่อน ระหว่างและหลังการผ่าตัดหัวใจในผู้ป่วยสองกลุ่มที่ได้รับยานำสลบอีโตมิเดตหรือธัยโอเพนทอลและผลที่เกิดกับผู้ป่วย*

วัสดุและวิธีการ: *การศึกษาแบบไปข้างหน้าในผู้ป่วย 26 ราย โดยแบ่งผู้ป่วยโดยการสุ่มเป็น 2 กลุ่ม ๆ ละ 13 ราย ที่มารับการผ่าตัดหัวใจแบบไม่ฉุกเฉิน โดยจะได้รับยานำสลบอีโตมิเดตหรือธัยโอเพนทอล โดยมีการวัดระดับฮอร์โมนคอร์ติซอลตั้งแต่ก่อนการนำสลบ ที่ 2, 4, 8, 24 ชั่วโมงต่อมา รวมถึงการศึกษาข้อมูลทั่วไปของผู้ป่วย การรักษาที่ได้รับ และผลการรักษา*

ผลการศึกษา: *ไม่มีความแตกต่างของผู้ป่วยทั้ง 2 กลุ่ม ในแง่ข้อมูลทั่วไป ผู้ป่วยทั้งสองกลุ่มมีค่าคอร์ติซอลที่เริ่มต้นใกล้เคียงกัน คือ ในกลุ่มอีโตมิเดตได้ค่าคอร์ติซอลเฉลี่ย 11.7±7.5 ไมโครกรัม/เดซิลิตร ในกลุ่มธัยโอเพนทอลได้ค่าคอร์ติซอลเฉลี่ย 12.0±8.2 ไมโครกรัม/เดซิลิตร ระหว่างการผ่าตัดทั้งสองกลุ่มระดับคอร์ติซอลสูงขึ้นกว่าเดิมและสูงที่สุดในช่วง 4-8 ชั่วโมง ซึ่งสัมพันธ์กับภาวะเครียดจากการผ่าตัด (surgical stress) โดยกลุ่มอีโตมิเดตได้ค่าเฉลี่ยที่ต่ำกว่าทุกช่วงเวลาและ ที่ 8 ชั่วโมง ในกลุ่มอีโตมิเดตได้ค่าคอร์ติซอลเฉลี่ยที่ต่ำกว่ามากอย่างมีนัยสำคัญทางสถิติ (39.9±14.2 vs. 65.9±20.0 ไมโครกรัม/เดซิลิตร ที่ 24 ชั่วโมง ทั้งสองกลุ่มค่าคอร์ติซอลเฉลี่ยมีระดับที่เริ่มลดต่ำลงแต่ยังคงสูงกว่าค่าปกติ ไม่มีความแตกต่างของการใช้ยาช่วยการบีบตัวของหัวใจ ระยะเวลาของการอยู่ไอซียูแต่กลุ่มที่ได้รับยานำสลบอีโตมิเดตอยู่โรงพยาบาลในช่วงที่สั้นกว่า*

สรุป: *การใช้ยานำสลบอีโตมิเดตในผู้ป่วยที่มารับการผ่าตัดหัวใจมีผลยับยั้งการสร้างฮอร์โมนคอร์ติซอลอบางส่วนอย่างน้อย 24 ชั่วโมง*