PROPOFOL - REMIFENTANIL VERSUS MIDAZOLAM - FENTANYL IN CORONARY ARTERY BYPASS GRAFT SURGERY AND INTENSIVE CARE UNIT

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Submitted 3/1/2017; accepted 28/2/2017

ABSTRACT

Background: In this study, we aim to identify the efficiency of propofol-remifentanil anesthesia in reducing the postoperative intensive-care unit stay in patients undergoing cardiac surgery in our center, without compromising the hemodynamic stability.

Subject and Methods: Two hundred patients undergoing first time elective coronary artery bypass graft surgery were recruited in this single-centered, single-blinded, prospective and controlled study. Study patients were randomized into two treatment groups: group 1 (P-R; Propofol-Remifentanil) (n=100 patients) and group 2 (M-F; Midazolam-Fentanyl) (n=100 Patients). Clinical measurement of Mean arterial blood pressure and heart rate for each patient were recorded before (T1) and after (T2) induction of anesthesia; after sternotomy (T3) and before cardiopulmonary bypass (CPB) (T4). Time from cessation of anesthesia to tracheal extubation was also recorded (T5).

Results: Comparing the hemodynamic parameters between the two groups at T1, T2, T3 and T4 set points revealed statistically significant difference ($P < 0.5$) in hemodynamic variables in all parameters measured apart from HR at T3. The mean recorded times from cessation of anesthesia to tracheal extubation (T5) were 99.32 minutes and 183.33 minutes in group 1 and 2, respectively. A statistically significant difference was noted between T5 in both groups (P value = 0.003).

Conclusions: Our study has shown that Propofol-Remifentanil anesthesia helps to reduce the time interval between cessation of anesthesia and extubation and, by doing so, it can potentially reduce the postoperative ICU stay, without compromising hemodynamic stability.

Duhok Med J 2017; 11 (1): 39-47.

Keywords: Cardiac anesthesia, Propofol, Remifentanil, Midazolam, Fentanyl, elective CABG surgery, hemodynamics, depth of anesthesia, ICU.

Cardiovascular stability is an essential prerequisite for cardiac anesthesia, where myocardial protection is vital in patients who already have compromised cardiovascular function. Traditionally, profound intraoperative analgesia has been provided by using high doses of opioids to suppress hormonal and metabolic stress responses to surgical stimuli. This regimen resulted in reduced morbidity and mortality after cardiac surgery[1]. However high doses or prolonged administration of conventional opioids can result in their accumulation, leading to postoperative

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respiratory depression and prolonged Intensive Care Unit (ICU) stay[2].

Due to economic considerations, many centers adopts cardiac anesthesia regimens using intermittent low- to medium-dose opioids to reduce time to extubation and postoperative ICU and hospital stay. Such regimens have been shown to allow reduction in extubation time and hospital stay with no significant postoperative sequelae in low-risk cardiac patients[3].

Goals of anesthesia for coronary artery bypass graft (CABG) surgery include hypnosis, hemodynamic stability, neurohumoral stress ablation[4] and may include early tracheal extubation[5]. Fast-track cardiac surgery is partly dependent on smaller-dose opioid regimens and although these may be associated with increased hemodynamic responses during surgery, there is no apparent increased risk of complications[5].

Propofol in combination with opioids is widely used in cardiac surgery providing the benefit of early extubation[6,7]. This may help to reduce costs by reducing the postoperative ICU stay[8].

In this study, we aim to identify the efficiency of propofol-remifentanil anesthesia in reducing the postoperative ICU stay in patients undergoing cardiac surgery in our centre, without compromising the hemodynamic stability.

PATIENTS AND METHODS

Two hundred patients undergoing first time elective CABG surgery were recruited in this single-centered, single-blinded, prospective and controlled study. Inclusion criteria for the study were patients with good or only slightly reduced left ventricular function (left ventricular ejection fraction (LVEF) of more than 40%) and younger than 82 years old. Exclusion criteria included weight of more than 100 kilograms (kg), confirmed diagnosis of uncontrolled hyper- and / or hypotension, congestive cardiac failure, atrioventricular or left bundle branch block detected on their preoperative electrocardiogram (ECG), valvular heart disease and patients with severe hepatic or renal insufficiency, pacemaker in situ, previous coronary artery bypass grafting (CABG) surgery, previous alcohol misuse and / or hypersensitivity to opioids or Propofol-lipid emulsion.

Study patients were randomized into two treatment groups: group 1 (P-R; Propofol-Remifentanil) (n=100 patients) and group 2 (M-F; Midazolam-Fentanyl) (n=100 Patients). Out of 200 patients, 8 patients were excluded (4 patients developed bleeding less than an hour after admission to ICU and 4 patients developed intraoperative congestive heart failure). Patients' regular prescribed medications were continued until the time of operation.

In both groups, the dose of the anesthetic medications was adapted to ensure optimal anesthetic and surgical conditions, whilst maintaining hemodynamic stability. The dose of Propofol-Remifentanil or Midazolam-Fentanyl was increased when heart rate (HR) and / or systolic blood pressure increased by 20% from baseline values and when sweating or lacrimation was observed.

In group 1, induction of anesthesia was achieved using a continuous infusion of Remifentanil (1 microgram / kg / minute) and Propofol (1-1.5 milligram / kg / minute) with Isoflurane (1-1.5 MAC). Five minutes later, Atracurium (0.4 milligram /

 https://doi.org/10.31386/dmj.2017.11.5

kg) was given as a bolus intravenous injection followed by endotracheal intubation. Mechanical ventilation was secured using with a tidal volume of 7 milliliters / kg, respiratory rate of 10 cycles / minute and an Inspiration: Expiration (I:E) ratio of 1:2 (GE Datex-Ohmeda anesthesia machine).

Maintenance of anesthesia was achieved by continuous infusion of a reduced dose of Remifentanil (0.2-0.5 micrograms / kg / minute) and Propofol which was run by increments of 50 micrograms / kg / minute (infusion between 100 and 250 micrograms / kg / minute).

In group 2, patients were induced by bolus intravenous dose of Midazolam (0.07 milligrams / kg) and Fentanyl (5-10 micrograms / kg). Tracheal intubation was performed in the similar fashion to group 1. After intubation, intermittent bolus doses of Fentanyl (5-10 micrograms / kg) were administered. Further doses of Midazolam were given as an intravenous bolus (0.03-0.07 milligrams / kg), as indicated by the attending anesthesiologist. Mechanical ventilation and muscle relaxation were performed as in group 1.

Clinical measurement of arterial blood pressure and heart rate for each patient were recorded before (T1) and after (T2) induction of anesthesia; after sternotomy (T3) and before cardiopulmonary bypass (CPB) (T4), using GE Healthcare Carescape B650 compact patient monitor. Time from cessation of anesthesia to tracheal extubation was also recorded (T5). Patient monitoring consisted of five-lead ECG. Correct ECG ST Segment monitoring was confirmed (with definition of isoelectric line and J point), pulse oximetry, capnography and invasive arterial pressure. Intravascular catheters were inserted after induction of anesthesia. Continuous three-lead (II, aVL, V5) automated ST segment analysis was used to detect intraoperative myocardial ischemia.

Following surgery, analgesia consisted of Morphine intravenous infusion of 1–2 milligrams / hour. Patients' remained intubated and mechanically ventilated whilst being transferred to ICU. As soon as patients' responded to verbal stimuli, were normothermic and hemodynamically-stable and their estimated blood loss were within the acceptable level (less than l00 milliliters / hour), patients were weaned off mechanical ventilation. Tracheal extubation was achieved when the patient was awake and cooperative, with a respiratory rate of 10-20 breaths / min and had satisfactory arterial blood gas analyses.

The data were analyzed using statistical package of social science SPSS Version 18. Statistical T test was used to analyze the difference in the variables of both group. A P value of ≤ 0.05 was considered statistically significant.

RESULTS

One hundred ninety two patients aged 40-82 years (145 males and 47 females; with a Male: Female ratio of 3:1) completed our study (Table 1). Out of 192, 66 (34.4%) patients had hypertension well controlled on regular medication(s) and 41 (21.3%) patients were known diabetic.

Table 1: Gender frequency

Gender	Frequency	Percentage (%)
Female	47	24.4
Male	145	75.5
Total	192	100

MABP showed slight drop after induction of anesthesia followed by mild rise during sternotomy in both groups as shown in Figure 1. Changes in mean HR during the study are illustrated in Figure 2. Before going on CPB, a further drop in MABP was noticed without a significant change in HR (Figures 1 and 2).

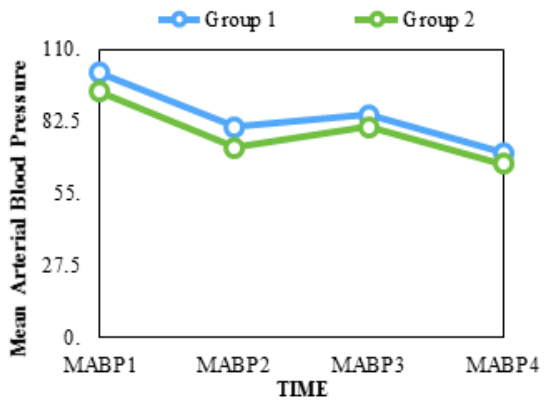

Figure 1. Changes in mean arterial blood pressure measurement according to time sets in group 1 (blue) and 2 (Green).

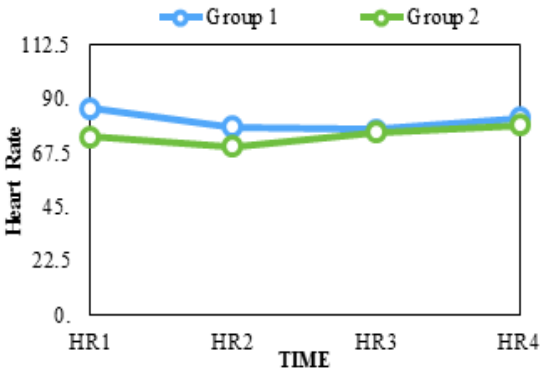

Figure 2. Changes in heart rate measurement according to time sets in group 1 (Blue) and 2 (Green).

Comparing MABP and HR between the two groups at T1, T2, T3 and T4 set points revealed statistically significant difference ($P < 0.5$) in hemodynamic variables in all parameters measured apart from HR at T3 detailed in (Table 2 and 3).

Table 2: The difference in mean arterial blood pressure measurement (MABP) between the two groups.

Regimen of anesthesia		MABP			
		T1	T2	T3	T4
R-P group (n=93)	Mean	101.2	80.5	85	70.5
	Std. Deviation	16.5	11.5	13.5	11.4
M-F group (n=99)	Mean	94	72.5	80.3	66.1
	Std. Deviation	20.2	10.9	14.7	13.9
P-value		0.15	0.008	0.21	0.2

Table 3: The difference in heart rate measurement (HR) between the two groups.

Regimen of anesthesia		HR			
		T1	T2	T3	T4
R-P group (n=93)	Mean	86.3	78.5	77.44	82.2
	Std. Deviation	19.5	15.1	25.1	17
M-F group (n=99)	Mean	74.3	70.3	76.1	79.1
	Std. Deviation	13.7	13.5	12.6	14.8
P-value		0.007	0.33	0.79	0.44

The mean recorded times from cessation of anesthesia to tracheal extubation (T5) were 99.32 minutes and 183.33 minutes in

https://doi.org/10.31386/dmj.2017.11.5

group 1 and 2, respectively. A statistically significant difference was noted between T5 in both groups (P value = 0.003; Figure3).

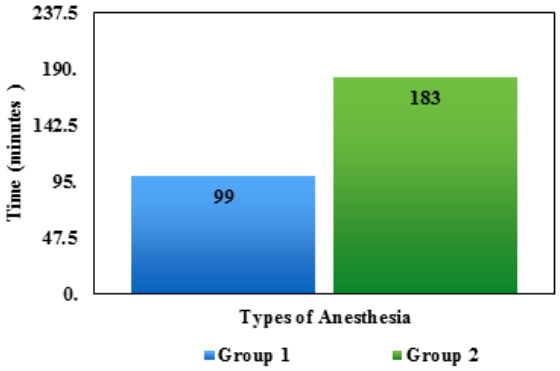

Figure (3). The difference in the meantime from cessation of anesthesia to tracheal extubation between the two groups, in minutes.

DISCUSSION

In this prospective single-blinded, randomized and controlled study, we analyzed the hemodynamic effects of Remifentanil – Propofol compared with Fentanyl – Midazolam regimens in patients undergoing CABG surgery aiming to identify the efficiency of propofol-remifentanil anesthesia in achieving early tracheal extubation and reducing the postoperative ICU stay without compromising the hemodynamic stability throughout surgery.

Given the possible relationship between the neurohumoral stress response and postoperative myocardial ischemia, large-dose opioid use have been the preferred technique in many centers[9]. Our study suggests that Remifentanil can provide this effect without prolonging recovery times.

Comparing the hemodynamic results from group 1 in our study to those from another study performed by Lehmann and colleagues in Germany in 2000, we identified a higher MABP after induction of anesthesia and during sternotomy in our patients. The former study pre-medicated their patients orally with 1-2mg Flunitrazepam and used Propofol as target-controlled infusion with calculated plasma concentration of 3 micrograms / milliliters. Also, the change in HR in our P-R group after induction of anesthesia were nearly similar to those from Lehmann et al study. However, after sternotomy the changes in HR in our study P-R group were with higher standard deviation compared to Lehmann et al study[8].

This can be explained by the fact that a significant number of our patients had an increase in HR after sternotomy, shifting the calculated standard deviation. Having said that, the overall mean HR in our study P-R group was more stable than those related to M-F group, showing the superiority of propofol–remifentanil group in maintaining hemodynamic stability during CABG.

It has been shown that adjustment of the dose of Remifentanil helps to control hemodynamics by reducing its dose when MABP is decreased or increasing the dose before potential major surgical stress events without significantly prolonging recovery time[10]. Also, Remifentanil, compared to Fentanyl, has a more pronounced sympathoadrenergic stimulatory effect in the early postoperative period[11]. On the other hand, Propofol in combination with an opioid is already in use in cardiac surgery[12].

Early extubation is shown to be the main advantage of Propofol anesthesia in cardiac surgery potentially leading to cost reduction by reducing the length of ICU stay[11,12]. Consistent results are obtained from our study as patients in group 1 were

generally able to be extubated earlier than those in Group 2.

Our study shows that both Propofol-Remifentanil and Midazolam-Fentanyl regimens in patients undergoing CABG surgery were safe and showed stable hemodynamics.

More importantly, we have shown that Propofol-Remifenatnil anesthesia helps to reduce the time interval between cessation of anesthesia and extubation and, by doing so, it can potentially reduce the postoperative ICU stay, without compromising hemodynamic stability.

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ثوختة

ثرِوَثوَفوَل - رِيَمى فنتانيل بةرامبةر بة ميَدازولام – فنتانيل لة نةشتةرطةرى ثةيوةندكردنى تيَثةرِينى خويَنبةرى تاجى دلَ و بةشى ضاوديرى ضرِ

پ‌ي‌ش‌ه‌ك‌ى و ئارمانج: لةم تويَذينةوةيةدا ، ئامانجمان ديارى كردنى توانستى بةكارهيَنانى ثرِوَثوَفوَل – رِيَمى فنتانيل بوَ كةم كردنةوةى ئةطةرى مانةوةى نةخوَشةكان لة بةشى ضاوديرى ضر دواى نةشتةرطةرى ، لةو نةخوَشانةى كة نةشتةرطةرى دلَيان بؤ ئةنجام دةدريَت لة سةنتةرةكةمان ، بةبىَ تيَكضوونى بارى ديناميكى خويَن.

ر‌ێ‌ك‌ا‌ر‌ى ق‌ه‌ك‌و‌ل‌ى‌ن‌ى: دوو سةد نةخوش بوَ جارى يةكةم نةشتةرطةرى ساردى ثةيوةندكردنى تيَثةرِينى خويَنبةرى تاجى دلَيان بوَ كرا ؛ ئينجا ضاوديَرى كران لة تويَذينةوةيةكى تاكى،ناوةندى،ضاوةرِوان كراوى،هةرِةمةكى ،نابينايى،بةراوردكارى كوَنترِوَلَ كردوو . دواتر بة هةرِةمةكى دابةش كران بؤ دوو طرووثى ضارةسةركردن: طرووثى 1 (ثرِوَثوَفوَل – رِيَمى فنتانيل)،(ذ=سةد نةخوَش)،،،طرووثى 2 (ميَدازولام – فنتانيل)،(ذ=سةد نةخوَش) ناوةندى ثةستانى خويَن و ترثةى دلَى نةخوَشةكان بة شيَوةيةكى سةريرى وةرطيرا ، ئينجا زانيارييةكان وةرطيران ثيَش ثيَدانى ماددة سرِكةرةكان(كات1)،وةدواى ثيَدانى ماددة سرِكةرةكان(كات2)،دواى كردنةوةى قةفةزةى سنط(كات3)،ثيَش ئةنجامدانى ثةيوةندكردنى تيَثةرِينى خويَنبةرى تاجى(كات4)، كاتى خايةندراو لةنيَوان رِاطرتنى ماددة سرِكةرةكان تاوةكو دةرهيَنانى سوَندةى بوَرى هةناسة(كات5).

ئ‌ه‌ن‌ج‌ام: بةبةراوردكردنى ثيَوةرةكانى تايبةت بة بارى ديناميكى خويَن لةنيَوان دوو طرووثةكةدا لة كات (1،2،3،4) ئةوةى ئاشكرا كرد جياوازيةكى هةذمارى بةرضاو (لةستر بنةماى رِيَذةيى كةمتر لة 0.5)دةبينريَت لة بارى ديناميكى خويَن لة هةموو ثيَوةرةكاندا تةنها لة ثيَوةرى ترثةى دلَ (كات3) نةبيَت ، ناوةندى كاتى خايةندراو لةكاتى رِاطرتنى ماددة سرِكةرةكان تاوةكو دةرهيَنانى سوَندةى بوَرى هةناسة(كات5) بريتى بوو لة 99.32 خولةك بؤ طرووثى 1 وة 183.33 خولةك بؤ طرووثى 2 ،، جياوازيةكى هةذمارى بةرضاو بينرا لةنيَوان دوو طرووثةكةدا لة كات 5 (رِيَذةى بةراوردى 0.003).

د‌ه‌ر‌ئ‌ه‌ن‌ج‌ام: ئةم تويَذينةوةية ئةوةمان بؤ دةردةخات كة ثرِوَثوَفوَل – رِيَمى فنتانيل يارمةتى كةم كردنةوةى كاتى خايةندراو دةدات لةنيَوان رِاطرتنى ماددة سرِكةرةكان تاوةكو دةرهيَنانى سوَندةى بوَرى هةناسة ، بةم شيَوةية رِيَذةى مانةوة لة بةشى ضاوديَرى ضرِ كةم دةكاتةوة بةبىَ تيَكضوونى بارى ديناميكى خويَن.

 https://doi.org/10.31386/dmj.2017.11.5

الخلاصة

بروبوفول – ريميفينتانيل مقارنة ب ميدازولام – فينتانيل في عمليات زرع الشرايين التاجية والعناية المركزة

خلفية وأهداف البحث: في هذه الدراسة، هدفنا هو ايجاد فعالية دواء البروبوفول– ريميفينتانيل لغرض تقليص وقت بقاء المريض في العناية القلبية بعد العملية لمرضى عمليات زرع الشرايين التاجية في مركزنا، دون التأثير على استقرار الفعاليات الحيوية.

طرائق البحث: مائتين مريض تجرى لهم عملية زرع شرايين تاجية لاول مرة. مئة من المرضى اعطوا تخدير البروبوفول مع الريميفينتانيل ومائة مريض اعطوا تخدير الميدازولام مع الفينتانيل. المعلومات جمعت قبل اعطاء التخدير (ت١)، بعد اعطاء التخدير (ت٢)، بعد فتح عظم القص (ت٣)، قبل عمل جهاز القلب الصناعي (ت٤).(ت٥) كان الوقت بين ايقاف التخدير لحين اخراج انبوبة القصبة الهوائية. تمت المقارنة بين المجاميع للمعلومات التي جمعت.

النتائج: كان هناك فرق واضح في قراءات الدورة الدموية في ت١، ت٢، ت٣ و ت٤ بين المجموعتين.

الاستنتاج: بالنسبة للوقت من قطع التخدير ولغاية اخراج انبوب القصبة الهوائية كان اقصر لمجموعة البروبوفول مع الريميفينتانيل وكان وقت اخراج الانبوبة اقصر. المجموعتين من الادوية كانت امينة ومستقرة فيها فعاليات الدورة الدموية اثناء عملية زرع الشرايين التاجية.