—Regular Articles—

Effects of Propofol and Midazolam on Lipids, Glucose, and Plasma Osmolality during and in the Early Postoperative Period Following Coronary Artery Bypass Graft Surgery: A Randomized Trial

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(Received April 20, 2006; Accepted September 18, 2006)

It is not clear how levels of serum lipids and glucose and plasma osmolality change during propofol infusion in the pre- and postoperative period of coronary artery bypass graft surgery (CABG). This prospective, randomized, controlled trial evaluated changes in these parameters during propofol or midazolam infusion during and in the early postoperative period following surgery. Twenty patients undergoing CABG were randomized preoperatively into two groups: 10 patients received propofol (induction 1.5 mg/kg, maintenance 1.5 mg kg^{-1} h^{-1}) and 10 patients received midazolam (induction 0.5 mg/kg, maintenance 0.1 mg kg^{-1} h^{-1}). Both groups also received fentanyl (induction 20 μg/kg, maintenance 10 μg kg^{-1}). Serum lipids, glucose, and plasma osmolality were measured preinduction, precardiopulmonary bypass, at the end of cardiopulmonary bypass, at the end of surgery, and 4 and 24 h postoperatively. In the propofol group, we observed a significant increase in triglycerides and very low-density lipoprotein levels 4 h postoperatively. In the midazolam group, we observed a significant decrease in low-density lipoprotein, cholesterol at the end of cardiopulmonary bypass, end of surgery, and 4 and 24 h postoperatively and significant increase in osmolality at the end of cardiovascular bypass. Changes in glucose levels did not differ significantly different between the two groups. In patients with normal serum lipids, glucose, and plasma osmolality undergoing CABG, propofol infusion for maintenance anesthesia is not associated with dangerous changes in serum lipids, glucose, and plasma osmolality compared with midazolam. A propofol infusion technique for maintenance of anesthesia for cardiac surgery where serum lipids and glucose may be of concern could be recommended as an alternative to midazolam.

Key words——propofol; midazolam; fentanyl; serum lipids; glucose; plasma osmolality

INTRODUCTION

Propofol is formulated from yolk sac lecithin emulsion consisting of 0.1 g/ml of soybean oil; therefore it may increase serum lipid levels following continuous infusion. There are some published reports showing significant increases in serum triglyceride (TRG) concentrations secondary to long-term propofol infusion while using a formulation containing long-chain triglycerides (LCT) from soybean oil in the postoperative intensive care unit (ICU).[1—4] However, some research did not support this finding of hypertriglyceridemia.[5]

In recent years, propofol infusion has increasingly been recognized as the anesthetic agent of choice in cardiac surgery for patients with normal ventricular function.[6—8] The main advantage of propofol is the short preparation period and consequently, short duration of stay in the ICU.[9] In cardiac surgery, especially CABG surgery, perioperative myocardial ischemia and myocardial infarction are potential dangers and can adversely affect the outcome during the postoperative period.[10] Increased free fatty acids in the serum can increase myocardial ischemic injury and be artythmogenic.[11,12]

In this randomized study, we investigated the effects of propofol infusion on levels of serum lipids, blood glucose (GLU), and plasma osmolality (OSM) in patients with normal serum lipids, GLU, and OSM undergoing elective CABG with cardiopulmonary bypass (CPB) compared with the control midazolam infusion group during and in the early postoperative period. It was hypothesized that midazolam infusion would decrease serum lipid concentrations more than propofol infusion in cardiac surgery with CPB; propofol infusion would increase TRG, total

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cholesterol (CHL), and its fractions secondary to lipid content in patients with normal levels of serum lipids; and propofol infusion would not affect GLU levels and OSM.

METHODS

This study was designed as a prospective, randomized, controlled clinical trial. Before the initiation of the trial, approval was obtained from the Ethics Committee of Siyami Ersek Thoracic and Cardiovascular Surgery Hospital. Study participants and family members were informed about the study by the research team and informed consent was obtained from both the study participants and their family members.

Patients Twenty patients undergoing CABG with American Society of Anesthesiologists (ASA) class 2—3 and an ejection fraction greater than 40% were randomly assigned to the propofol group (Gp-P) or midazolam group (Gp-M). Patients with a history of hepatic disease, diabetes mellitus, and hyperlipidemia were excluded from the study.

Data Collection Initial data from patients' medical records and interviews with the family members were collected by the research nurse. Chemistry profiles including serum lipids, glucose, and plasma osmolality for preanesthesia care were obtained according to the American Society of Postanesthesia Nurses (ASPAN) standards of nursing practice and ASA.[13,14] The principal investigator was informed by the research nurse of patients with normal values (*see* all Tables and Figures) of serum lipids, GLU, and OSM prior to surgery to assess eligibility into the trial.

In the propofol arm, induction of general anesthesia was performed with fentanyl (15—18 μcg/kg), 1% propofol (1.4—1.6 mg/kg) and pancuronium (0.1 mg/kg) *i.v.* For maintenance of anesthesia, 1% propofol (1.4—1.6 mg/kg/h), and fentanyl (total 15—18 μcg/kg/h) infusion, pancuronium (0.03 mg/kg/h) *i.v.*, and isoflurane inhalation was used. In the midazolam arm, general anesthesia was induced with fentanyl (14—16 μcg/kg) and midazolam (0.1—0.25 mg/kg). For maintenance of anesthesia, midazolam (0.05—0.1 mg/kg/h) and fentanyl (total 14—16 μcg/kg/h) infusion, pancuronium (0.03 mg/kg/h) *i.v.*, and isoflurane (0.5—1%) inhalation was used. None of the patients received either propofol or midazolam during the postoperative period.

In both groups, serum lipids (mg/dl), TRG, CHL, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), GLU (mg/dl), and OSM [mOsm kg^{-1}] were measured prior to induction of anesthesia (PI), prior to the start of CPB (pre-CPB), at the end of CPB (E-CPB), at the end of operation (End-Op), 4 h postoperatively ($P^{4th\ h}$), and 24 h postoperatively ($P^{24th\ h}$). Data required for the initial and ongoing assessments were obtained and blood samples were obtained by the research nurse in the postoperative ICU, phase I and phase II according to ASPAN standards.[13]

Statistical Analysis Descriptive statistics (means, standard deviation) were used to summarize the data. Two-way ANOVA for repeated measures was used to examine differences between the two groups. Mauchly's test of sphericity was significant for all parameters, and therefore multivariate tests were used with consideration of Wilks' lambda. Paired *t*-tests were used for parameters where there was a significant interaction between trial group and time. The Bonferroni corrected paired *t*-test was used to examine paired comparisons within groups. Bonferroni corrected *t*-test was used to examine differences between groups. In multivariate comparisons between groups, the baseline (PI-control value) were taken into account to account for the baseline biological values.

RESULTS

Patient demographic profiles and anesthetic variables of the two groups are shown in Table 1. All patients in the Gp-P were men, whereas there were 2 women in the Gp-M. Mean age in Gp-P and Gp-M were 60.9 ($\pm$7.95) years and 60.7 ($\pm$9.76) years, respectively. Mean weight in Gp-P and Gp-M as 68.4 kg ($\pm$11.44) and 76.4 ($\pm$12.65) kg, respectively. Mean anesthesia duration in Gp-P was 526 ($\pm$30) minutes and in Gp-M 538 ($\pm$48) min. Operation duration, cardiac bypass duration, and aortic clamp duration were similar in both groups. There were no significant differences between the two groups (Table 1).

Results at PI were within normal limits. Both groups demonstrated significant changes in comparison with baseline levels. In Gp-P, TRG and VLDL levels were significantly different at $P^{4th\ h}$. TRG levels changed from PI (Gp-P: 112.90$\pm$44.55, Gp-M:

Table 1. Patient Characteristics

Characteristics	Group		Significance*
	Propofol	Midazolam	
Patient number (n)	10	10	
Male/female	10/0	8/2	$p=0.47$
Age (years)	60.9±7.95	60.7±9.76	$p=0.96$
Weight (kg)	68.4±11.44	76.4±12.65	$p=0.15$
Height (cm)	168.25±5.25	170.03±6.56	$p=0.51$
Duration of the drug infusion (min)	526±30	538±48	$p=0.51$
Duration of surgery	446±20	468±38	$p=0.12$
Duration of CPB	140±27	151±32	$p=0.41$
Duration of aortic clamping	92±15	87±12	$p=0.42$

CPB: Cardiopulmonary bypass, * Student's t-test.

136.10±64.38 mg/dl) to $P^{4th\ h}$ (Gp-P: 125±34.21, Gp-M: 93.70±39.28 mg/dl); changes from PI to $P^{4th\ h}$ were significantly different in the two groups ($p<0.05$); (Table 2 and Fig. 1).

VLDL levels also changed from PI (Gp-P: 22.56±8.83, Gp-M: 27.44±12.63 mg/dl) to $P^{4th\ h}$ (Gp-P: 24.44±6.79, Gp-M: 18.49±7.38 mg/dl) ($p<0.05$) (*See* Table 3 and Fig. 2). Gp-M demonstrated a more prominent decreases in CHL and LDL levels at E-CPB, End-OP, $P^{4th\ h}$ and $P^{24th\ h}$, ($p<0.05$). CHL levels had a significant univariate relationship between groups at PI (Gp-P: 130.30±41.78, Gp-M: 197.70±34.90 mg/dl), Pre-CPB, E-CPB, End -Op, $P^{4th\ h}$, and $P^{24th\ h}$ (Gp-P: 92.10±15.84, Gp-M: 85.30±7.70 mg/dl). Changes from PI to Pre CPB, E-CPB, End -Op, $P^{4th\ h}$, and $P^{24th\ h}$ were significant between the two groups ($p<0.05$) (Table 4 and Fig. 3). LDL also demonstrated a similar univariate pattern from PI (Gp-P: 74.54±34.06, Gp-M: 134.26±26.50 mg/dl) to Pre-CPB, E-CPB, End -Op, $P^{4th\ h}$, and $P^{24th\ h}$ (Gp-P: 47.03±15.95, Gp-M: 52.20±15.60 mg/dl), which was also significant ($p<0.05$) (Table 5 and Fig. 4).

OSM demonstrated significant increase at E-CPB (Gp-P: 282.60±11.09, Gp-M: 292.40±12.32 $mOsmkg^{-1}$) from PI (Gp-P: 284.40±10.32, Gp-M: 283.90±8.81 $mOsmkg^{-1}$) ($p<0.05$). This two-way interaction in OSM was also significantly different between the groups ($p<0.05$) (*See* Table 6 and Fig. 5).

Despite changes at different time points, levels of TRG, VLDL, CHL, and LDL remained normal; clinically significant changes were not observed. Changes in HDL and GLU levels were not significantly different between the two groups ($p>0.05$) (Figs. 6 and 7).

DISCUSSION

Among the potential adverse events following CABG, perioperative myocardial ischemia and infarction may lead to an unfavorable clinical outcome.[10] High free fatty acid levels may increase ischemic and arrhythmogenic insult to the myocardium.[11,12] The myocardium is dependent on the oxidative metabolism, unlike skeletal muscles. In fasting states, fatty acids predominate as the energy source of the myocardium. GLU is preferred during postprandial states, and lactate in addition to free fatty acids is utilized during exercise. A segmental or global anaerobic state in myocardial tissue results in changes in priority for those substrates, and reduced free fatty acid products accumulate. Severe ischemia and early infarction result in a rise in plasma catecholamine levels, which cause increased levels of free fatty acids and reduced secretion of insulin from pancreatic beta cells.[12] Appropriate presentation of energy sources during ischemic insult will prevent abnormal excitation of the membranes and the loss of contractility due to ischemia. This may minimize myocardial cell loss, ischemic arrhythmias, and low output states.[12]

Some researchers have shown that TRG increase significantly during the postoperative period after intraoperative propofol infusion at a rate of 4 to 9 mg $kg^{-1}\ h^{-1}$ in noncardiac surgery.[15] TRG and VLDL levels were stable due to exogenous triglycerides via propofol infusion. Increased levels of chylomicron formation lead to higher VLDL conversion. Increased levels of TRG in noncardiac studies are attributed to the absence of dilution effects with the CPB.[10,16] Other investigators have also concluded

Table 2. TRG Values during PI, Pre-CPB, E-CPB, End-Op, $P^{4th\,h}$, and $P^{24th\,h}$ Periods for Both Groups

Group	Factor	Mean	SD	Difference mean±SD*	95% CI (for mean)	
					Lower	Upper
Propofol	PI (level 1)	112.90	44.55		76.12	149.68
	Pre-CPB (level 2)	96.50	34.50	16.4±40.25	74.24	118.76
	E-CPB (level 3)	86.10	42.92	26.8±58.74	61.12	111.08
	End-Op (level 4)	93.90	39.34	19±54.23	60.44	127.36
	$P^{4th\,h}$ (level 5)	125.00	34.21	−12.1±42.23	100.53	149.47
	$P^{24th\,h}$ (level 6)	87.00	31.34	25.9±44.99	67.10	106.90
Midazolam	PI (level 1)	136.10	64.38		99.32	172.88
	Pre-CPB (level 2)	102.90	32.48	33.2±56.61	80.64	125.16
	E-CPB (level 3)	68.00	31.41	681±61.89	43.02	92.98
	End-Op (level 4)	80.90	59.37	55.2±61.47	47.44	114.36
	$P^{4th\,h}$ (level 5)	93.70	39.28	42.4±52.41	69.23	118.17
	$P^{24th\,h}$ (level 6)	77.20	28.50	58.9±57.80	57.30	97.10

Source	Factor	Type III sum of squares	df	Mean square	F	P
TRG	Level 2 vs. level 1	12300.80	1	12300.80	5.10	0.0366
	Level 3 vs. level 1	45030.05	1	45030.05	12.37	0.0025
	Level 4 vs. level 1	27528.20	1	27528.20	8.19	0.0104
	Level 5 vs. level 1	4590.45	1	4590.45	2.03	0.1717
	Level 6 vs. level 1	35955.20	1	35955.20	13.40	0.0018
TRG* groups	Level 2 vs. level 1	1411.20	1	1411.20	0.58	0.4544
	Level 3 vs. level 1	8528.45	1	8528.45	2.34	0.1433
	Level 4 vs. level 1	6552.20	1	6552.20	1.95	0.1796
	Level 5 vs. level 1	14851.25	1	14851.25	6.55	0.0197
	Level 6 vs. level 1	5445.00	1	5445.00	2.03	0.1714

Tests of between-patient effects

Source	Type III sum of squares	df	Mean square	F	P
Intercept	186953.34	1	186953.34	202.452	0.000
Group	252.05	1	252.05	0.273	0.608

* According to PI (level 1). TRG: Triglyceride, PI: prior to induction of anesthesia, Pre CPB: prior to the start of CPB, E CPB: at the end of CPB, End Op: at the end of operation, $P^{4th\,h}$: at 4th hour postoperatively, $P^{24th\,h}$: at postoperative 24th hour.

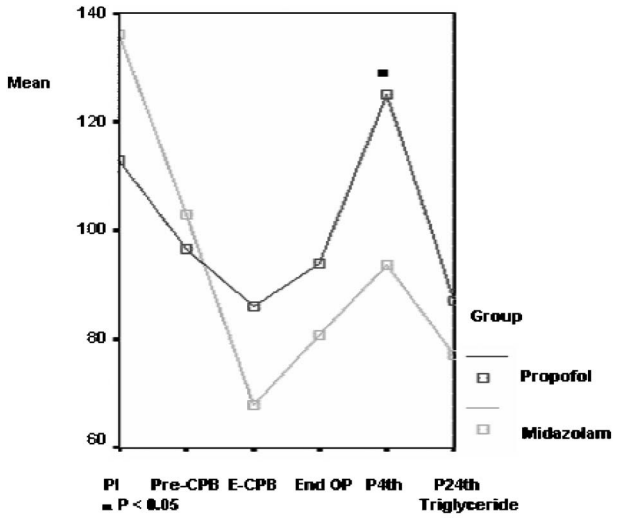

Fig. 1. Mean TRG Levels (mg/dl) at Different Time Points Prior to and Following CABG

that propofol administration at standard doses might have a significant effect on serum TRG levels.[3,17] In the present study, we observed a significant increase in TRG and VLDL levels at P^{4th} in the Gp-P. This was almost certainly because of the low dose of intraoperative propofol infusion ($1.5\ mg\ kg^{-1}\ h^{-1}$) which are sufficient for the maintenance of general anesthesia in our patients with stable hemodynamic status. The increase in TRG level is dependent on the added TRG from the propofol infusion (exogenous TRG).[18] Some researchers[18] showed that there was no change in serum TRG during and after CPB, depending on the hemodilution with CPB. Others[19] also found similar results. In the present study, we demonstrated that there were no significant changes in TRG and VLDL levels between the two groups during CPB and at $P^{24th\,h}$. However, there were significant differences in TRG and VLDL between PI and $P^{4th\,h}$ in the Gp-P

Table 3. VLDL Levels during PI, Pre-CPB, E-CPB, End -Op, $P^{4th\ h}$, and $P^{24th\ h}$ Periods for Both Groups

Group	Factor	Mean	SD	Difference mean±SD*	95% CI (for mean)	
					Lower	Upper
Propofol	PI (level 1)	22.56	8.83		15.32	29.80
	Pre-CPB (level 2)	19.52	6.89	3.04±7.44	15.05	23.99
	E-CPB (level 3)	17.30	8.57	5.26±11.66	12.31	22.29
	End-Op (level 4)	18.94	7.85	3.62±10.73	12.25	25.63
	$P^{4th\ h}$ (level 5)	24.44	6.79	−1.88±9.19	19.73	29.15
	$P^{24th\ h}$ (level 6)	17.98	7.38	4.58±8.91	13.48	22.48
Midazolam	PI (level 1)	27.44	12.63		20.20	34.68
	Pre-CPB (level 2)	20.56	6.56	6.88±10.83	16.09	25.03
	E-CPB (level 3)	13.60	6.28	13.84±12.22	8.61	18.59
	End-Op (level 4)	15.58	11.89	11.86±12.89	8.89	22.27
	$P^{4th\ h}$ (level 5)	18.49	7.38	8.95±10.22	13.78	23.20
	$P^{24th\ h}$ (level 6)	15.90	6.09	11.54±10.89	11.40	20.40

Tests of within-patient effect

Source	Factor	Type III sum of squares	df	Mean square	F	P
VLDL	Level 2 vs. level 1	492.03	1	492.03	5.69	0.0282
	Level 3 vs. level 1	1824.05	1	1824.05	12.78	0.0022
	Level 4 vs. level 1	1198.15	1	1198.15	8.51	0.0092
	Level 5 vs. level 1	249.92	1	249.92	2.64	0.1215
	Level 6 vs. level 1	1299.27	1	1299.27	13.12	0.0019
VLDL* groups	Level 2 vs. level 1	73.73	1	73.73	0.85	0.3679
	Level 3 vs. level 1	368.08	1	368.08	2.58	0.1258
	Level 4 vs. level 1	339.49	1	339.49	2.41	0.1378
	Level 5 vs. level 1	586.44	1	586.44	6.20	0.0228
	Level 6 vs. level 1	242.21	1	242.21	2.45	0.1352

Tests of between-patient effects

Source	Type III sum of squares	df	Mean square	F	P
Intercept	7495.55	1	7495.55	200.22	0.0000
Group	11.68	1	11.68	0.31	0.5834

* According to PI (level 1).

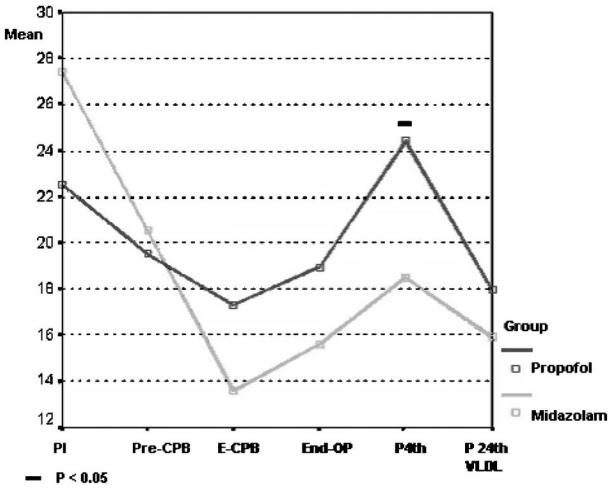

Fig. 2. Mean VLDL Levels (mg/dl) at Different Time Points Prior to and Following CABG

($p<0.05$). This was likely because of the added TRG-rich lipoproteins from propofol and dependent on the effects of serum lipids in the protein of propofol.[20] In addition, it has been reported in non-cardiac studies that an increase in TRG levels seen with propofol infusion is due to the absence of the dilution effect during CPB.[10,16,21] In the present study, we used 1% propofol. In the literature, it was shown that mean TRG concentrations were higher in the propofol 10 mg ml^{-1} group compared with the propofol 60 mg ml^{-1} group for long-term sedation in critically ill patients.[22] Knibbe et al. concluded that sedation with propofol 60 mg ml^{-1} reduces the fat and volume load, which reduces the risk of hypertriglyceridemia.[22] They also pointed out there were no differences in pharmacokinetic and phar-

Table 4. CHL Values during PI, Pre-CPB, E-CPB, End-Op, $P^{4th\ h}$, and $P^{24th\ h}$ Periods for Both Groups

Group	Factor	Mean	SD	Difference mean±SD*	95% CI (for mean)	
					Lower	Upper
Propofol	PI (level 1)	130.30	41.78		104.73	155.87
	Pre-CPB (level 2)	124.90	49.62	5.4±56.56	97.10	152.70
	E-CPB (level 3)	117.00	72.67	13.3±66.13	82.18	151.82
	End-Op (level 4)	104.40	35.37	25.9±49.93	83.01	125.79
	$P^{4th\ h}$ (level 5)	103.20	24.09	27.1±49.30	87.88	118.52
	$P^{24th\ h}$ (level 6)	92.10	15.84	38.2±48.83	83.83	100.37
Midazolam	PI (level 1)	197.70	34.90		172.13	223.27
	Pre-CPB (level 2)	180.20	32.27	17.5±33.34	152.40	208.00
	E-CPB (level 3)	111.30	14.59	86.4±30.63	76.48	146.12
	End-Op (level 4)	106.20	28.69	91.5±42.26	84.81	127.59
	$P^{4th\ h}$ (level 5)	105.00	21.97	92.7±34.93	89.68	120.32
	$P^{24th\ h}$ (level 6)	85.30	7.70	112.4±39.94	77.03	93.57

Tests of within-patient effects

Source	Factor	Type III sum of squares	df	Mean square	F	P
CHL	Level 2 vs. level 1	2622.05	1	2622.05	1.22	0.2846
	Level 3 vs. level 1	49700.45	1	49700.45	18.71	0.0004
	Level 4 vs. level 1	68913.8	1	68913.80	32.20	0.0000
	Level 5 vs. level 1	71760.2	1	71760.20	39.31	0.0000
	Level 6 vs. level 1	113401.8	1	113401.80	56.98	0.0000
CHL* groups	Level 2 vs. level 1	732.05	1	732.05	0.34	0.5673
	Level 3 vs. level 1	26718.05	1	26718.05	10.06	0.0053
	Level 4 vs. level 1	21516.8	1	21516.80	10.05	0.0053
	Level 5 vs. level 1	21516.8	1	21516.80	11.79	0.0030
	Level 6 vs. level 1	27528.2	1	27528.20	13.83	0.0016

Tests of between-patients effect.

Source	Type III sum of squares	df	Mean square	F	P
Intercept	295083.02	1	295083.02	809.35	0.0000
Group	1798.67	1	1798.67	4.93	0.0394

* According to PI (level 1).

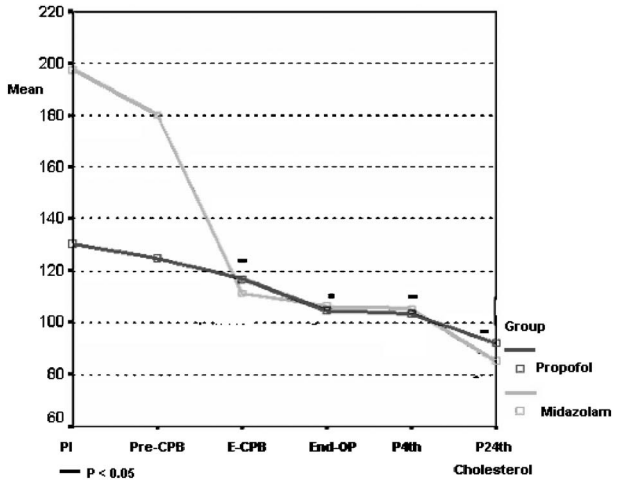

Fig. 3. Mean CHL Values (mg/dl) at Different Time Points Prior to and Following CABG

CHL: Total cholesterol, PI: Prior to induction of anaesthesia, Pre-CPB: Prior to the start of CPB, E-CPB: At the end of CPB, End-Op: At the end of operation, $P^{4th\ h}$: At postoperative 4th hour, $P^{24th\ h}$: At postoperative 24th hour.

macodynamics between 6% propofol and 1% propofol. In an earlier study, Knibbe et al. found that TRG level and relative body temperature appeared to be significant covariates for elimination clearance.[23]

Studies have shown that heparin activates lipoprotein lipase and therefore results in a rapid and significant decrease in TRG immediately after heparinization; this results in an increase in circulating glycerol and free fatty acids.[24—26] Similar results were seen in TRG during CPB in the present study. On the other hand, after heparinization TRG, HDL, and VLDL values decreased at the E-CPB. There was a decrease in serum CHL, including HDL and LDL, after induction of anesthesia in the two groups. This was almost certainly a dilution effect of rapid crystalloid infusion to maintain filling pressure. There was a further decrease during CPB, probably secondary to dilution with the CPB prime as reported earlier.[18,19]

Table 5. LDL Levels during PI, Pre-CPB, E-CPB, End-Op, $P^{4th\ h}$, and $P^{24th\ h}$ Periods for Both Groups

Group	Factor	Mean	SD	Difference mean±SD*	95% CI (for mean)	
					Lower	Upper
Propofol	PI (level1)	74.54	34.06		54.26	94.82
	Pre-CPB (level 2)	67.54	35.40	7±35.54	46.64	88.44
	E-CPB (level 3)	77.38	68.05	−2.84±59.39	44.52	110.24
	End-Op (level 4)	61.02	25.33	13.52±33.91	45.30	76.74
	$P^{4th\ h}$ (level 5)	55.49	17.70	19.05±35.27	44.29	66.69
	$P^{24th\ h}$ (level 6)	47.03	15.95	27.507±35.64	36.55	57.51
Midazolam	PI (Level 1)	134.26	26.50		113.98	154.53
	Pre-CPB (level 2)	129.45	26.94	4.809±23.50	108.55	150.35
	E-CPB (level 3)	74.38	16.15	59.877±26.28	41.52	107.24
	End-Op (level 4)	70.42	21.87	63.837±35.65	54.70	86.14
	$P^{4th\ h}$ (level 5)	67.18	15.98	67.077±27.91	55.98	78.38
	$P^{24th\ h}$ (level 6)	52.20	15.60	82.057±31.82	41.72	62.68

Tests of within-patient effects

Source	Factor	Type III sum of squares	df	Mean square	F	P
LDL	Level 2 vs. level 1	697.26	1	697.26	0.77	0.3924
	Level 3 vs. level 1	16266.10	1	16266.10	7.71	0.0124
	Level 4 vs. level 1	29920.53	1	29920.53	25.45	0.0001
	Level 5 vs. level 1	37089.30	1	37089.30	36.67	0.0000
	Level 6 vs. level 1	60021.35	1	60021.35	52.60	0.0000
LDL* groups	Level 2 vs. level 1	24.00	1	24.00	0.03	0.8726
	Level 3 vs. level 1	19667.11	1	19667.11	9.33	0.0068
	Level 4 vs. level 1	12659.00	1	12659.00	10.77	0.0041
	Level 5 vs. level 1	11532.96	1	11532.96	11.40	0.0034
	Level 6 vs. level 1	14878.51	1	14878.51	13.04	0.0020

Tests of between-patient effects

Source	Type III sum of squares	df	Mean square	F	P
Intercept	115238.47	1	115238.47	360.85	0.0000
Group	2915.39	1	2915.39	9.13	0.0073

* According to PI (level 1).

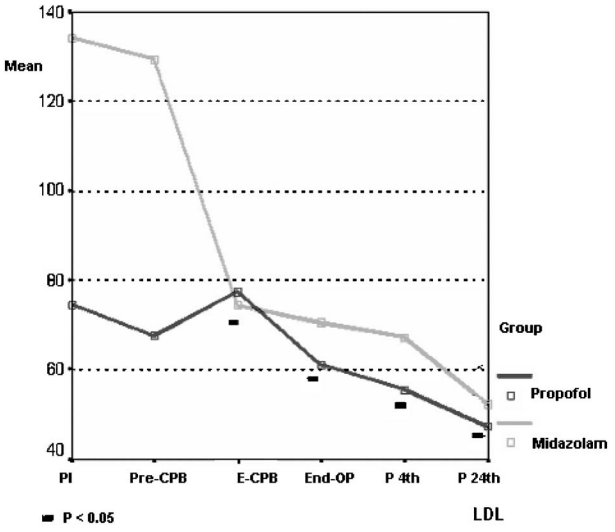

Fig. 4. Mean LDL Levels (mg/dl) at Different Time Points Prior to and Following CABG

The significant decreases in CHL and LDL in GP-M in the present study are similar to the results of previous studies.[18] This was attributed to low CHL in the fat emulsion of propofol[18] and observed even in non-cardiac studies.[10,16] It can thus be concluded that propofol infusion does not result in dangerous elevation of serum lipids during cardiac surgery.

Although our patients had no history of diabetes, there were increases in GLU levels at the E-CPB and then GLU levels in the two groups remained stable. This has been described previously in a study of glucose based cardioplegia solutions and the ''neurohumoral stress response'' of cardiac surgery and CPB.[25] Carbohydrate metabolism is regulated by insulin, glucagon, cortisol, growth hormone, and epinephrine levels, which are expected to change as a

Table 6. OSM Values during PI, Pre-CPB, E-CPB, End -Op, $P^{4th\,h}$, and $P^{24th\,h}$ Periods for Both Groups

Group	Factor	Mean	SD	Difference mean±SD*	95% CI (for mean)	
					Lower	Upper
Propofol	PI (level 1)	284.40	10.32		278.03	290.77
	Pre-CPB (level 2)	277.80	9.46	6.6±9.20	272.35	283.25
	E-CPB (level 3)	282.60	11.09	1.8±12.67	274.81	290.39
	End-Op (level 4)	283.00	8.03	1.4±8.50	275.16	290.84
	$P^{4th\,h}$ (level 5)	290.20	7.76	−5.8±11.59	284.22	296.18
	$P^{24th\,h}$ (level 6)	286.00	8.77	−1.6±14.24	278.91	293.09
Midazolam	PI (level 1)	283.90	8.81		277.53	290.27
	Pre-CPB (level 2)	283.00	6.70	0.9±5.85	277.55	288.45
	E-CPB (level 3)	292.40	12.32	−8.5±8.69	284.61	300.19
	End-Op (level 4)	290.00	14.64	−6.1±13.05	282.16	297.84
	$P^{4th\,h}$ (level 5)	294.90	10.10	−11±14.10	288.92	300.88
	$P^{24th\,h}$ (level 6)	291.50	12.29	−7.6±14.47	284.41	298.59

Tests of within-patient effects

Source	Factor	Type III sum of squares	df	Mean square	F	P
OSM	Level 2 vs. level 1	281.25	1	281.25	4.73	0.0433
	Level 3 vs. level 1	224.45	1	224.45	1.90	0.1849
	Level 4 vs. level 1	110.45	1	110.45	0.91	0.3528
	Level 5 vs. level 1	1411.2	1	1411.2	8.47	0.0093
	Level 6 vs. level 1	423.2	1	423.2	2.05	0.1692
OSM* groups	Level 2 vs. level 1	162.45	1	162.45	2.73	0.1158
	Level 3 vs. level 1	530.45	1	530.45	4.49	0.0482
	Level 4 vs. level 1	281.25	1	281.25	2.32	0.1454
	Level 5 vs. level 1	135.2	1	135.2	0.81	0.3796
	Level 6 vs. level 1	180	1	180	0.87	0.3626

Tests of between-patient effects

Source	Type III sum of squares	df	Mean square	F	P
Intercept	1643268.90	1	1643268.90	48361.95	0.0000
Group	139.57	1	139.57	4.11	0.0578

* According to PI (level 1).

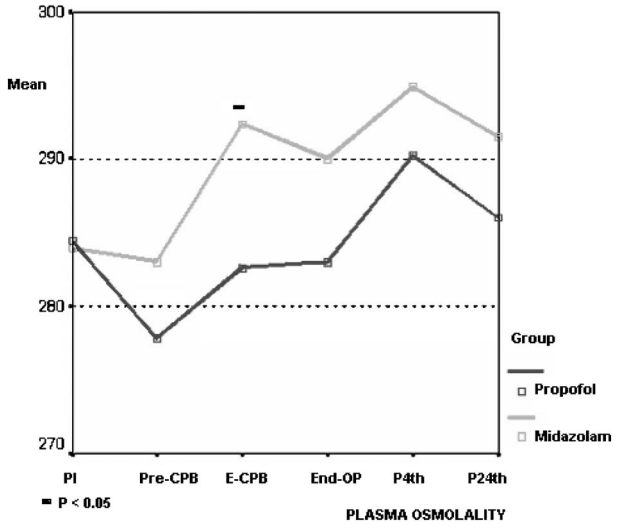

Fig. 5. Mean OSM Levels [$mOsmkg^{-1}$] at Different Time Points Prior to and Following CABG

OSM: Plasma osmolality, PI: Prior to induction of anaesthesia, Pre-CPB: Prior to the start of CPB, E-CPB: At the end of CPB, End-Op: At the end of operation, $P^{4th\,h}$: At postoperative 4th hour, $P^{24th\,h}$: At postoperative 24th hour.

result of CPB. Following the onset of CPB, plasma GLU levels are significantly increased.[27—29] Nevertheless, nonpulsatile hypothermic CPB results in a hypoinsulinemic state and an increased exogenic insulin demand due to increased insulin resistance.[27—29] It is not possible to conclude from our study which effect predominates in the perioperative hyperglycemic state. However, propofol and midazolam infusions did not result in significant effects on GLU levels in our study.

Osmolality is related to GLU and sodium levels.[30] In the present study, there was a significant increase in OSM at the E-CPB based on PI in Gp-M ($p<0.05$). However, these changes at the E-CPB in both groups were in the normal range (292.40 ± 12.32 $mOsmkg^{-1}$); (normal range, 285—308 $mOsmkg^{-1}$). We did not add any GLU or electrolyte solution in either group. Plasmalyte A and Haemaccel (polyge-

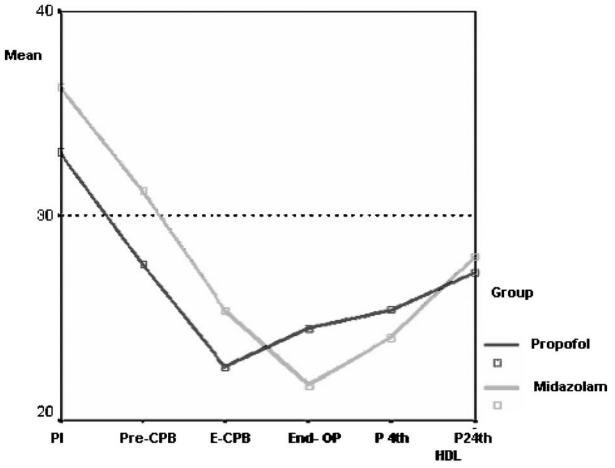

Fig. 6. Mean HDL Levels (mg/dl) at Different Time Points Prior to and Following CABG

HDL: High Density Lipoprotein, PI: Prior to induction of anaesthesia, Pre-CPB: Prior to the start of CPB, E-CPB: At the end of CPB, End-Op: At the end of operation, $P^{4th\ h}$: At postoperative 4th hour, $P^{24th\ h}$: At postoperative 24th hour.

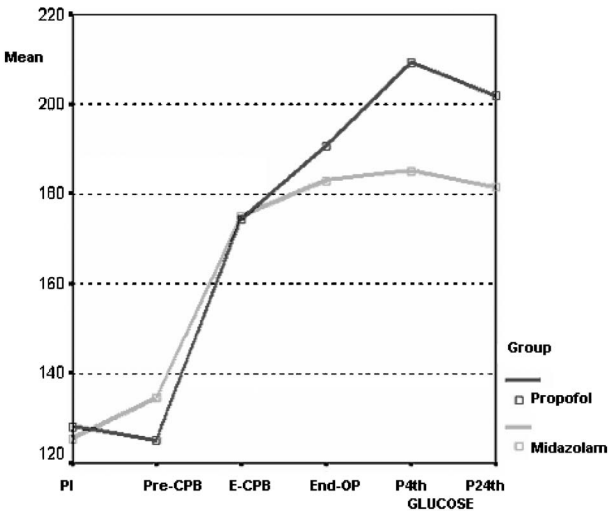

Fig. 7. Mean GLU Levels (mg/dl) at Different Time Points Prior to and Following CABG

line colloid) solutions were used in all patients. This increase during CPB in Gp-M should be investigated in a large cohort.

Monitoring patients for changes in serum lipids, GLU, and OSM is essential during preanesthesia care and baseline values should be recorded before cardiac surgery, continuous monitoring of laboratory tests should be performed during CABG, changes should be reported to the anesthesiologist, and patients should be evaluated at the end of CABG surgery by the perioperative nurse.

In conclusion, propofol infusion for maintenance of anesthesia for cardiac surgery when serum lipid and GLU levels may be of concern can be recommended as an alternative to midazolam.

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