

Tanaffos (2007) 6(4), 31-36

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Comparison of Propofol and Remifentanil Administration on Lipid Profile

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ABSTRACT

Background: This study aimed to investigate the serum level of triglyceride, cholesterol, high density lipoprotein, low density lipoprotein, and very low density lipoprotein during administration of propofol and comparing it with infusion of remifentanil in patients undergoing sedation in ICU of Masih Daneshvari Hospital during 2005-2007.

Materials and Methods: All patients with pulmonary disease, undergoing intubation and mechanical ventilation were enrolled in our study. The patients were randomly divided into two groups, first receiving propofol and second receiving remifentanil as the sedative agent. Lipid profile (triglyceride, cholesterol, high density lipoprotein, low density lipoprotein, and very low density lipoprotein) was checked before, immediately after, and the day after drug administration.

Results: A total of 40 patients were enrolled in this study, 20 of which took propofol and the remaining took remifentanil. The mean age of the patients was 58.67 ± 18.57 yrs. Triglyceride and very low density lipoprotein (VLDL) were the two factors with statistically significant rise after infusion of propofol ($p < 0.002$). Such a change was not detected in the remifentanil group. The other understudy factors did not show similar changes.

Conclusion: Propofol infusion can induce dramatic rises in triglyceride and VLDL concentration even after low dose infusions and therefore special attention must be paid to patients prone to hyper-triglyceridemia and pancreatitis. (*Tanaffos* 2007; 6(4): 31-36)

Key words: Propofol, Lipid profile, Triglyceride, Cholesterol, Remifentanil

INTRODUCTION

Propofol is an intravenous anesthetic drug used for clinical purposes. It is slightly soluble in water and is presented in emulsion formulation.

Propofol is an alkyl phenol with sedative-hypnotic effects. Alkyl phenols are oily at room temperature and are insoluble in water but are very soluble in oil. The commercially available preparations of propofol contain 1% propofol, 10% soya bean oil 2.25% glycerol and 1.2% egg lecithin (1).

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Received: 9 July 2007

Accepted: 9 Dec 2007

Since this drug contains oil microspheres extracted from soy bean oil, it can increase serum lipid concentrations of the patients in long infusions of drug during surgical procedures or in the critical care settings (ICU).

Several studies have been performed in this respect but there is no definite consensus regarding the effect of this drug on the body's lipid metabolism. Gottardis (2) in his study stated that the 3-day infusion of this drug in ICU patients did not change serum lipid concentrations while Kimura (3) and Eddleston (4) reported that the serum triglyceride level can considerably increase after anesthesia with propofol or during long infusions of this drug in the ICU. Inoue (5) and Myles (6) in a study performed on patients undergoing cardiopulmonary bypass and cardiac surgery receiving propofol stated that administration of this drug resulted in no complication in patients with heart problems and did not cause significant changes in serum lipid concentration. Therefore, considering the optimal anesthetic effects of this drug, its rapid effect and short-acting nature, it seems that propofol is a suitable drug for induction and maintenance of anesthesia in different surgical operations. However, the effect of this drug on patients' lipid metabolism especially in long-term infusions in ICU is not known and extensive research is required in this regard. This study aimed to compare the effect of propofol and remifentanil on serum lipid concentrations in intubated and mechanically ventilated patients with pulmonary diseases who had been under 48- hour infusion of the afore-mentioned drugs in the ICU of Masih Daneshvari Hospital during 2005- 2007.

MATERIALS AND METHODS

All mechanically-ventilated patients with pulmonary diseases requiring sedation in the ICU of

Masih Daneshvari Hospital were randomly divided into two groups, one receiving propofol and the other remifentanil.

All patients had been recently hospitalized and undergone mechanical ventilation and therefore were NPO during the study and were not receiving total parenteral nutrition (NTP) either.

None of the patients had underlying hepatic disease interfering with the metabolism of propofol and neither of them developed hypoxemia during the study period. None of the patients were drug addicts and none required extradoses of opioids. Prior to drug infusion, serum concentrations of cholesterol, LDL, HDL, VLDL and TG were measured in all patients. The above-mentioned factors were measured 48 and 72 hours post-anesthesia. Patients' blood samples were taken by the nurses and sent to the laboratory. These samples were first centrifuged and the obtained sera were kept at - 4°C to be evaluated as a whole every 6 months. In this way, the laboratory conditions were the same in every assessment. Only the researcher and the nurses were aware of the classification of patients and the laboratory personnel had no awareness in this respect (single blind randomized controlled trial). Intubated patients were connected to the ventilator. To tolerate the ventilator, optimal sedation had to be induced. Therefore, patients were randomly divided into two groups of case and control. The cases received minimal dose of remifentanil 0.05/μg/ kg/min as IV infusion while the controls received minimal dose of propofol 10 μg/kg/min intravenously. It should be mentioned that none of the patients received bolus dose for induction of sedation and except for the above-mentioned drugs, no other sedatives were used.

Level of sedation in patients was controlled by using the Ramsey scale and the dosage required to reach level 3-4 of this scale was calculated. In case of failure to reach this level by using minimal doses of

remifentanyl and propofol, the dosage was increased every 5 minutes as titrated to reach the desired level of sedation.

After collecting the patient's demographic data and performing serum lipid concentration tests by the laboratory, data were statistically analyzed and compared between the two groups. The mean was calculated for each variable and the difference between the means of the 2 groups. Statistical analysis was performed using SPSS ver.11 software. Mean \pm SD was used for analyzing the distribution of variables and t-student test was used for the comparison of quantitative variables.

RESULTS

A total of 40 patients with pulmonary diseases including COPD (18%), pneumonia (10.3%), malignancies (10.3%), ARDS (5.7%), IPF (7.7%) and others (48%) were studied. These patients were randomly divided into two groups of remifentanyl and propofol each containing 20 patients.

The mean age of total patients was 58.67 \pm 18.57 yrs. The mean age of patients in the remifentanyl and propofol groups was 56 \pm 21.48 yrs and 61.20 \pm 15.26 yrs. respectively.

There were 27 (67.5%) males and 13(32.5%) females in this study out of which 11 males (55%) and 9 females (45%) were in the remifentanyl and 16(80%) males and 4(20%) females were in the propofol group.

Patients' blood was tested 3 times to find lipid concentration changes (Tables 1 and 2). Results indicated that serum triglyceride level did not change considerably in the remifentanyl group but it was significantly higher in the second measurement compared to the first in the propofol group (Tables 1 and 2 and Figure 1).

Measurement of serum cholesterol level indicated that in the remifentanyl group significant increase was detected in all 3 measurements and the

difference was not statistically significant (Table 1 and Figure 2). In the propofol group, this level increased in the 2nd and 3rd phases but the differences were not statistically significant (Table 2 and Figure 2).

Serum VLDL concentration gradually increased in the remifentanyl group, but in the propofol group it initially increased and decreased afterwards. The difference in this regard between the first and the 2nd phases was statistically significant in the propofol group (Tables 1 and 2 Figure 3).

Alterations of the LDL level were different from those of other variables as in the remifentanyl group serum LDL level had a decreasing trend but with no significant difference and in the propofol group it decreased at first but considerably elevated afterwards. This increase was statistically significant (Tables 1 and 2 and Figure 4).

Changes in the HDL level were similar to those of LDL; HDL concentration relatively decreased at first but increased afterwards. However, these differences were not statistically significant (Table 1 and 2 and Figure 5).

Table 1. The concentrations of serum lipid indices and comparison of serum lipid concentrations between the 1st and 2nd, and 2nd and 3rd measurements in the remifentanyl group.

Variable	Before infusion *	Immediately following discontinuation of infusion *	The day after infusion *	Statistical difference between the phases 1 and 2 **	Statistical difference between the phases 2 and 3 **
TG **	167.58 \pm 84.53	157.11 \pm 87.53	168.40 \pm 97.22	0.433	0.684
Chol **	157.52 \pm 71.23	151.82 \pm 53.71	149.73 \pm 46.92	0.585	0.358
LDL **	90.00 \pm 58.05	80.71 \pm 36.26	81.20 \pm 36.04	0.522	0.982
HDL **	34.64 \pm 9.20	34.85 \pm 11.31	35.80 \pm 9.93	0.938	0.96
VLDL **	32.09 \pm 17.41	32.78 \pm 18.46	36.26 \pm 20.63	0.762	0.788

* Mean \pm SD

** mg/dl

***p-value

Table 2. The concentrations of serum lipid indices and comparison of serum lipid concentration between the 1st and 2nd, and 2nd and 3rd measurements in the propofol group.

Variable	Before infusion *	Immediately following discontinuation of infusion *	The day after infusion *	Statistical difference between the phases 1 and 2 **	Statistical difference between the phases 2 and 3 ***
TG **	145.26±48.16	194.66±67.60	160.20±33.57	0.002.	0.151
Chol **	159.00±52.35	166.06±46.66	173.80±50.30	0.552.	0.237
LDL **	91.64±45.81	82.35±36.92	100.33±38.82	0.169.	0.04
HDL **	37.46±14.42	37.20±19.48	39.60±20.21	0.904.	0.21
VLDL **	29.51±9.65	39.71±13.62	33.00±6.63	0.004	0.234

* Mean±SD

** mg/dl

***p-value

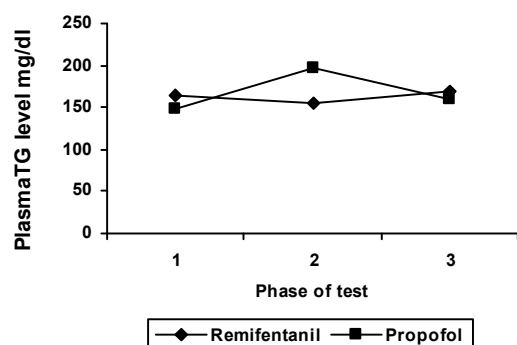


Figure 1. Comparison between plasma TG levels in three phases

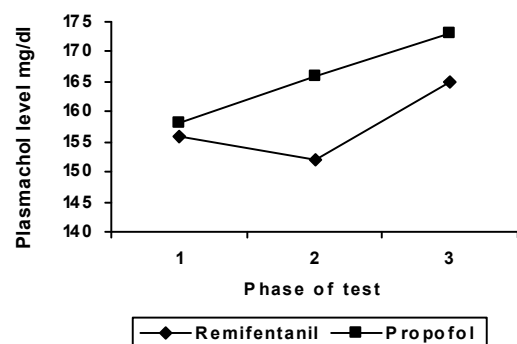


Figure 2. Comparison between cholesterol levels in three phases.

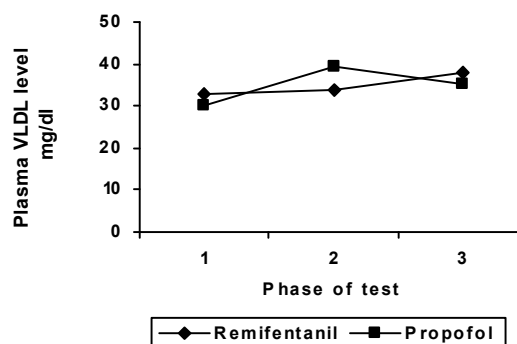


Figure 3. Comparison between plasma VLDL levels in three phases.

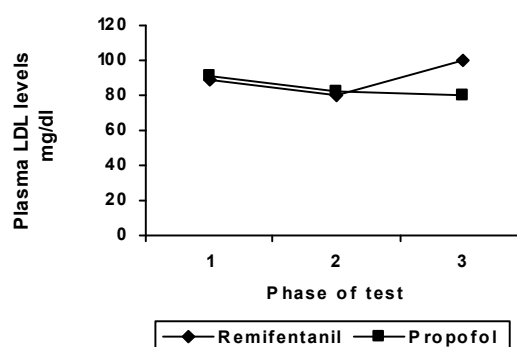


Figure 4. Comparison between plasma LDL levels in three phases.

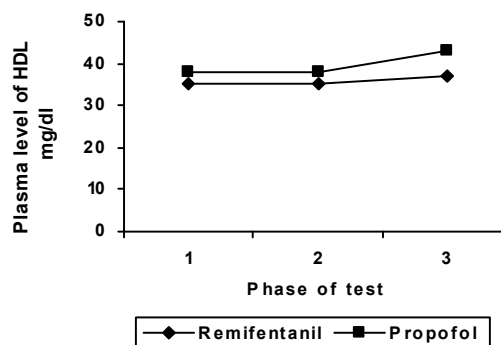


Figure 5. Comparison between plasma levels of HDL in three phases.

DISCUSSION

This study demonstrated that the serum concentrations of TG and VLDL considerably increased during the infusion of propofol in the ICU.

Today, propofol as a sedative and hypnotic drug is widely used for induction of anesthesia in the

operating room and ICU. It is soluble in oil and is prepared as an emulsion containing soy bean oil, glycerol and egg. Therefore, during its infusion, especially for long periods, there is a risk of increase in serum lipid concentration and consequent complications such as pancreatitis (7).

Several studies performed in this regard have shown a wide range of different results. In a study conducted by Carrasco and colleagues (8), serum triglyceride level of patients receiving propofol in ICU showed a statistically significant increase compared to that of controls; whereas, in studies performed by Gottardis (2) and colleagues and McLeod (9) and coworkers, it was just the contrary. In a study by Eddleston (4) and colleagues one case of dramatic increase in triglyceride following a 10-day use of propofol in the ICU was reported which was not accompanied by dramatic elevation of cholesterol level. All of the above-mentioned studies were conducted in ICU confirming the effect of long-term use of this drug. Inoue (5), Myles (6) Kimura (3) and colleagues studied the effect of using this drug in operating room for surgical procedures and all confirmed the resultant increase in serum triglyceride concentration of patients. However, these studies were mostly conducted on cardiac patients and during long-term procedures and therefore, many confounding factors can be expected.

In this study, we tried to eliminate the confounding factors by selecting patients with pulmonary diseases requiring intubation and mechanical ventilation and creating similar conditions, making sure that the patients' underlying diseases are being managed preventing hypoxemia during the study period.

Our results indicated that the serum triglyceride level increased significantly following the infusion of very low doses of propofol for sedation and considerably decreased after discontinuation. Such alterations did not occur in the remifentanyl group.

Since the conditions were similar in both groups, it is concluded that the infusion of propofol caused such alterations.

Tsubokawa and colleagues (10) in their study evaluated the role of hypoxemia during operation in increasing the level of TG and VLDL and demonstrated that occurrence of hypoxemia increases TG and VLDL concentrations.

In our study, hypoxemia did not occur during infusion in any of the patients. However, serum lipid concentrations increased in the propofol group which can be considered as a direct effect of propofol. Range of alterations in cholesterol, HDL and LDL concentrations was different. Concentration of cholesterol increased in the propofol group which was not significant. On the contrary, its concentration decreased in the remifentanyl group. HDL and LDL concentrations did not show a considerable change at first but significantly increased after discontinuation of drug.

Alterations in VLDL concentration were almost similar to those of triglyceride and in the propofol group, was significantly elevated following infusion. However, in the remifentanyl group it decreased gradually (almost similar to TG). The abovementioned changes are predictable and completely anticipated considering the characteristics of the administered drugs. However, it is noteworthy that administration of even minimal doses of this drug (which was used in this study) can increase serum lipid concentration of patients whereas all patients had been recently admitted to the ICU, all were NPO and TPN had not been initiated for any of them. Therefore, it is necessary to pay special attention to patients' nutrition and subtract the amount of lipid entering the body through infusion of propofol from the total lipid entering the body via gavage and TPN and in this way prevent the elevation of lipid concentration in patients.

CONCLUSION

Infusion of propofol in pulmonary patients requiring sedation in the ICU can play a major role in acute elevation of triglyceride and VLDL serum concentration. However, this increase is compensated by a following decrease.

This increase was also detected in cholesterol level but was not statistically significant. Therefore, it is recommended that in patients suffering from hyperlipidemia especially hypertriglyceridemia, serum lipid concentration be checked during the infusion of propofol. Also, these patients should be evaluated for possible complications.

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