Original Article

Changes in blood glucose level during and after light sedations using propofol-fentanyl and midazolam-fentanyl in diabetic patients who underwent cataract surgery

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Abstract

Background: Surgeries may trigger the stress response which leads to changes in blood glucose level, and studies suggest that different sedation and anesthesia methods have different effects on blood glucose level. The aim of this study was to investigate changes of blood glucose levels in diabetic patients and compare them in two sedation methods of propofol + fentanyl and midazolam + fentanyl.

Materials and Methods: Totally, 80 diabetic candidates for cataract surgery who had all the inclusion criteria, underwent cataract surgery using two methods of propofol (1 mg/kg/h) + fentanyl (2 μg/kg) (Group P) and midazolam (0.03 mg/kg) + fentanyl (2 μg/kg) (Group M) for light sedation. In the end, 70 patients (Group P $n = 35$ and Group M $n = 35$) remained in the study. Patients' blood glucose levels, vital signs, and hemodynamic data were assessed 30 min prior to the surgery, each 15 min during surgery and at the end of surgery.

Results: Hemodynamic parameters did not have a statistically significant difference between the two groups mean blood glucose level in Group M was 149.15 mg/dl and in Group P was 149.2 mg/dl, and based on repeated measures analysis of variance test, significant differences were not observed between the two groups ($P = 0.99$). *T*-test showed no significant differences in the blood glucose level at any time of the study between the two groups.

Conclusions: Light sedation methods of propofol + fentanyl and midazolam + fentanyl did not have any differences in alteration of blood glucose level.

Key Words: Blood glucose, diabetes mellitus, fentanyl, midazolam, propofol

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Received: 29.01.2015, **Accepted:** 08.02.2015

INTRODUCTION

It is expected that the worldwide prevalence of diabetes mellitus (DM) will increase from 382 million people in 2013 to 592 million people in 2035.[1] The prevalence of DM in hospitalized patients is up to 40%,[2] thus the anesthesiologist will encounter a patient with DM in the operating room on a daily basis.

The effect of preoperative, intraoperative, and postoperative diabetes management and the effect of perioperative hypoglycemia and hyperglycemia in the long-term and short-term operative outcomes remains a notable clinical dilemma without a universally accepted solution.[3] Studies indicate that even the

Access this article online	
Quick Response Code:	Website: www.advbiores.net
	DOI: 10.4103/2277-9175.166645

How to cite this article: Khalighinejad P, Rahimi M, Naghibi K, Niknam N. Changes in blood glucose level during and after light sedations using propofol-fentanyl and midazolam-fentanyl in diabetic patients who underwent cataract surgery. Adv Biomed Res 2015;4:222.

fairly loose glucose target of 70–180 mg/dl is achieved consistently in only a few patients.[4]

Surgeries may trigger the stress response.[5] This response includes hemodynamic, metabolic, and hormonal changes which may alter the blood glucose level.[6,7] Studies suggest that different sedation and anesthesia methods have different effects on blood glucose level.[8,9]

Thus, in order to minimize complications related to hyperglycemia or hypoglycemia in surgeries, it is vital to minimize effects of anesthetics on blood glucose level. The aim of this study was to investigate changes of blood glucose levels in diabetic patients and compare them in two sedation methods of propofol + fentanyl and midazolam + fentanyl. Currently, there are no studies comparing effects of these two sedation methods on blood glucose level.

MATERIALS AND METHODS

Study design and data collection

From August 2013 to February 2014, this clinical trial was performed in Feiz Hospital, Isfahan, Iran. 80 diabetic candidates for cataract surgery, who had all the inclusion criteria, underwent cataract surgery using two methods of propofol + fentanyl and midazolam + fentanyl for light sedation by the same anesthesiologist (M.R.), and completed their follow-up. Data were collected prospectively. Inclusion criteria were as follows: Age of older than 35 years old, having diabetes type 2 for at least a year, being a candidate for Phacoemulsification surgery and having consent for joining the study. Exclusion criteria were as follows: Becoming hemodynamically unstable (need for vasopressors), patient's death before completion of the study, new occurrence of clotting and bleeding disorders and the condition that needed changing light sedation method to general anesthesia.

The Committee of Ethics approved the protocol and patients signed an informed consent before the operation.

Using computer software, patients were randomly and equally enrolled into two groups of P and M. Sample size of 40 patients in each group was determined in order to achieve 80% power. In Group P (n = 40), propofol (1 mg/kg/h) and fentanyl (2 μg/kg) were used as anesthetic agents to sedate the patients and in Group M (n = 40), midazolam (0.03 mg/kg) and fentanyl (2 μg/kg) were used. Exclusion criteria and CONSORT flow diagram are stated in Figure 1. In the end, 70 patients (Group P n = 35 and Group M n = 35) remained in the study.

Patients' blood glucose levels were assessed 30 min prior to the surgery, each 15 min during surgery and at the end of surgery using a glucometer (Beurer GmbH GL40 Blood Glucose Monitor). In the event of a rise in blood glucose level, 10 units of regular insulin was injected subcutaneously for each 100 mg/dl rise in blood glucose level higher than 150 mg/dl, in order to achieve a moderate glycemic control (90–150 mg/dl).[10] Furthermore, two vials of 50% hypertonic glucose were administrated for patients whose blood glucose level dropped below 70 mg/dl.

Vital signs and hemodynamic data including blood pressure, heart rate, respiratory rate (RR), and blood O_2 saturation level were noted in the respectively explained timetable. Patients' demographic data including age, gender, duration of suffering from diabetes, duration of surgery, duration of anesthesia, and duration of recovery were also noted and are shown in Table 1.

Duration of surgery was defined as the time period starting from the first incision to bandaging the eye. Duration of anesthesia was defined as the time period starting from the injection of sedation agent to being fully awaked. Duration of recovery was defined as the time period starting from admission in the recovery to discharging from recovery.

Each 15 min during the surgery, respiratory complications including apnea, fighting, and coughs were noted. Also each 15 min during the surgery and at the end of the surgery, drug side effects (agitation, anxiety, weakness, headache, vertigo, tachycardia, bradycardia, nausea, vomiting, diuresis, respiratory distress, cardiac distress, etc.,) were noted.

Since this study was a two-sided blind-fold trial, the anesthesiologist who administered the drugs and the

Table 1: Demographic data of patients

Group variable	Group M*	Group P**	*P*
Age (years)	66.8±6.6	67.4±4.6	0.66
Gender (%)			
Male	25 (71.4)	27 (77.1)	0.58
Female	10 (28.6)	8 (22.9)	
Weight (kg)	64.4±5.6	65±6.1	0.7
Duration of diabetes (years)	10.26±3.4	10.26±3	0.99
ASA (%)			
I	3 (8.6)	0 (0)	0.36
II	24 (68.6)	27 (77.1)	
III	8 (22.8)	8 (22.9)	
Duration of operation (min)	35.6±7.4	39±9.8	0.1
Duration of anesthesia (min)	48.4±6.4	48.9±9.2	0.82
Duration of recovery (min)	53.1±12.3	55.6±12.2	0.41

Data shown in this table are mean values and their SD. *Group M: Patients who received midazolam+fentanyl, **Group P: Patients who received propofol+fentanyl. SD: Standard deviation, ASA: American Society of Anesthesiologists

data collector did not know which group the patients belonged to.

Data analysis

Descriptive statistics was conducted on the variables. We used independent *t*-test, Chi-square test, Fisher's exact test and repeated measures analysis of variance (ANOVA) to determine the difference between groups in measured variables, with $P < 0.05$ considered statistically significant. Data were analyzed using the Windows release 20.0.0 of The Statistical Package for the Social Sciences (SPSS), PC program.

RESULTS

Demographic characteristics of patients are shown in Table 1.

Using *t*-test, mean age, weight, and duration of having diabetes did not have a statistically significant difference. Furthermore, the two groups did not differ in sex and American Society of Anesthesiologists using Chi-square test and Fisher's exact test. Moreover, using *t*-test showed no significant difference in duration of surgery, anesthesia and recovery in the two groups.

In Table 2, blood glucose changes of the two groups are shown from prior to the operation to the end of it. *t*-test showed no significant differences in the mean blood glucose level at any time of the study between the two groups. Mean blood glucose level in Group M was 149.15 mg/dl and in Group P was 149.2 mg/dl, and based on repeated measures ANOVA test, significant differences were not observed between the two groups ($P = 0.99$).

In Figures 2 and 3, changes in hemodynamic parameters of the two groups are shown from prior to the operation to the end of it. Mean systolic blood pressure ($P = 0.99$)

Table 2: Blood glucose changes in different time intervals

Timing of blood glucose measurement	Groups		*P*
	Group M*	Group P**	
Prior to induction	150.1±36.3	147.3±37.2	0.75
15th min	158.2±30.2	157.2±38.3	0.9
30th min	157.2±28.4	155.2±30.3	0.78
45th min	150.6±27.2	151.5±27	0.9
60th min	142.4±27.6	145.6±24.4	0.61
At the end of operation	136.7±25.9	138.1±25.3	0.81

Data shown in this table are mean values and their SD. *Group M: Patients who received midazolam+fentanyl, **Group P: Patients who received propofol+fentanyl. SD: Standard deviation

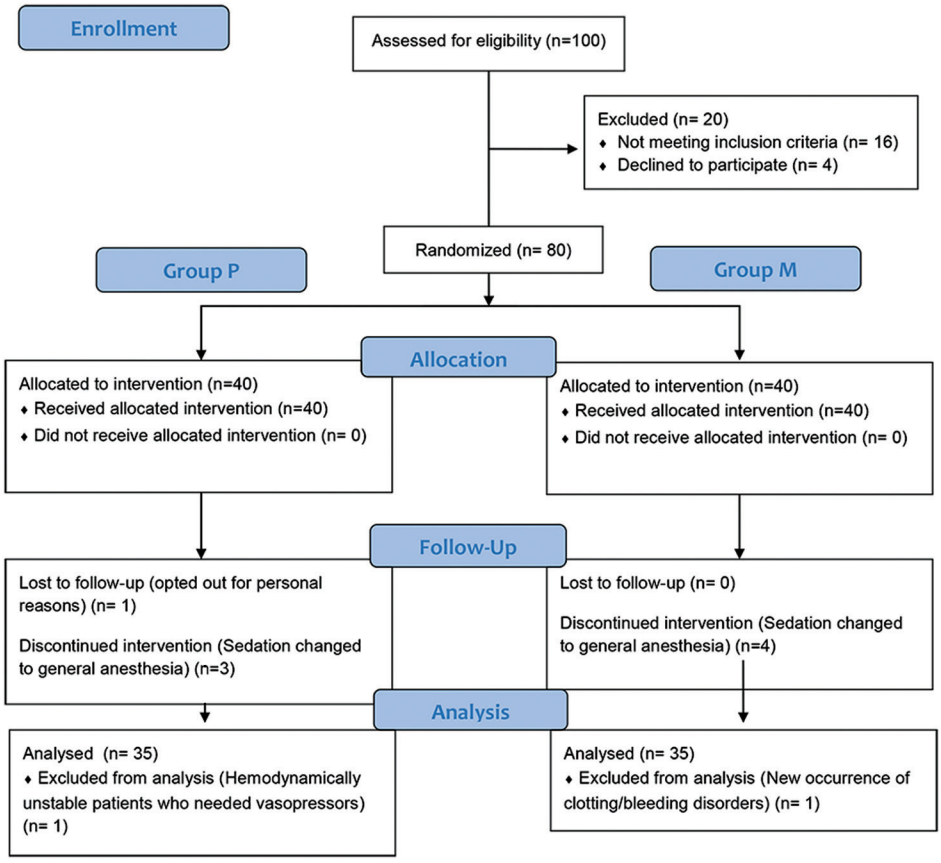

Figure 1: Flow diagram of randomizing patients (*Group P: Patients who received propofol + fentanyl, **Group M: Patients who received midazolam + fentanyl)

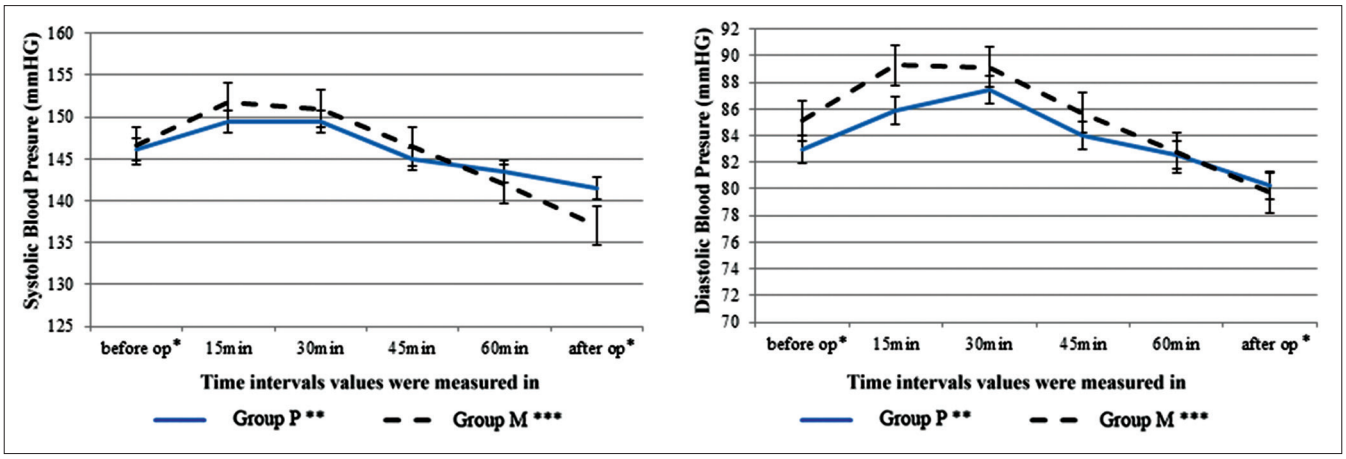

Figure 2: Changes of systolic blood pressure and diastolic blood pressure in the two groups (Data illustrated in this figure are mean values and their standard deviation. *OP: Operation. Before operation is the means the time interval of 30 min prior to the operation and after operation means at the end of the surgery, **Group P: Patients who received propofol + fentanyl, ***Group M: Patients who received midazolam + fentanyl)

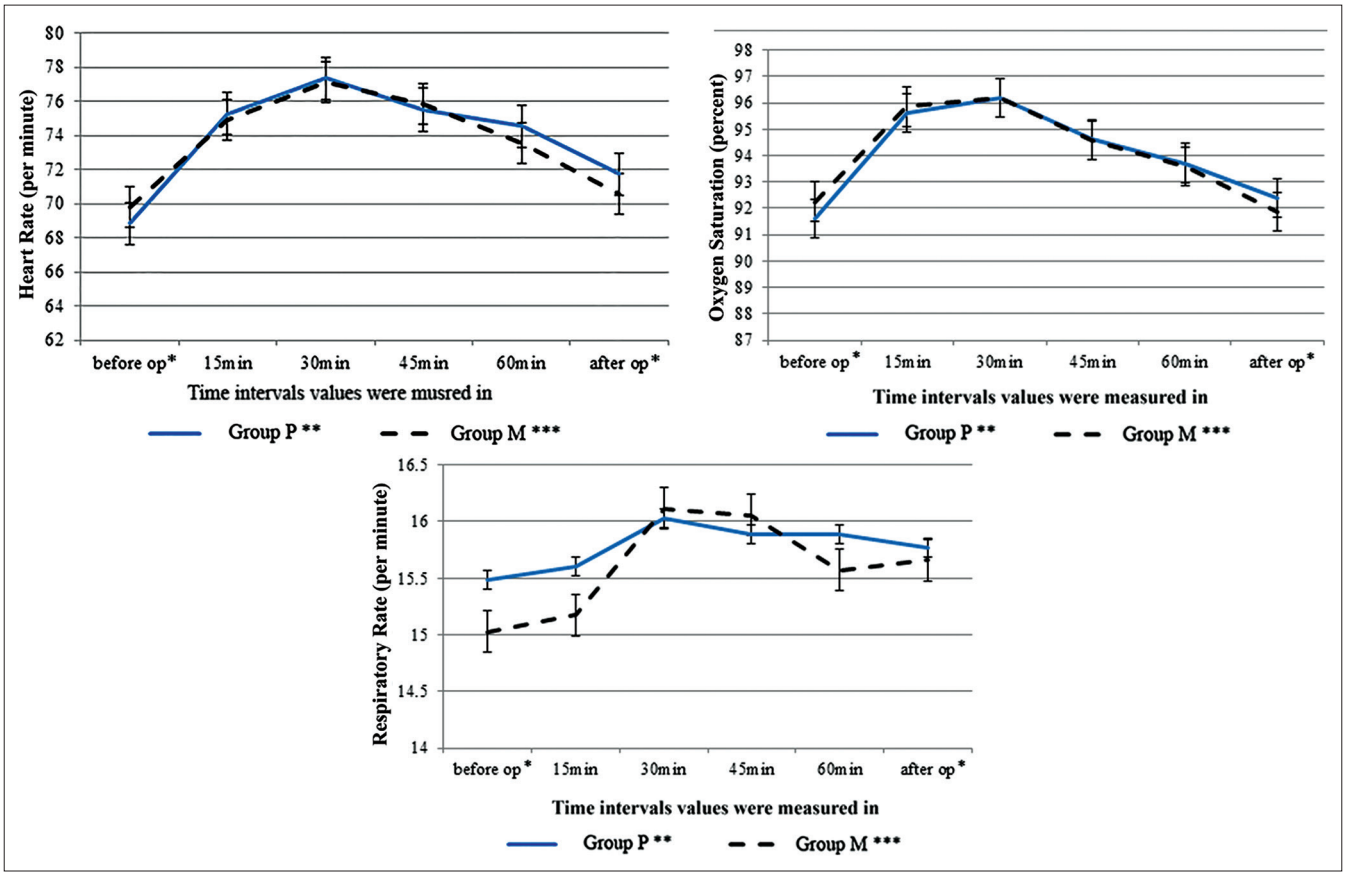

Figure 3: Changes of heart rate, respiratory rate, and oxygen saturation in the two groups (Data illustrated in this figure are mean values and their standard deviation. *OP: Operation. Before operation is the means the time interval of 30 min prior to the operation and after operation means at the end of the surgery, **Group P: Patients who received propofol + fentanyl, ***Group M: Patients who received midazolam + fentanyl)

and mean diastolic blood pressure ($P = 0.4$) in Groups P and M did not have statistically meaningful differences. Mean heart rate ($P = 0.88$), mean RR ($P = 0.04$), and mean O_2 saturation ($P = 0.92$) of the two groups did not have statistically significant differences too. By using repeated measures ANOVA, changes were not statistically significant in the listed parameters between the two groups, except RR. *T*-test showed a statistically significant difference in RR prior to the surgery ($P = 0.045$) as patients in Group P had higher RR, but at other time periods, there were no significant differences ($P > 0.05$).

Evaluation of the respiratory complications during the study, showed 4 patients (11.4%) of Group P and also 4 patients (11.4%) of Group M faced the complications and there was no statistically significant difference between the two groups. The frequency of postoperative complications in both groups was also evaluated, whereby, nausea and bradycardia were the most common complications observed in both groups and according to Fisher's exact test, frequency of postoperative complications in the two groups showed no significant difference ($P = 0.87$).

DISCUSSION

As mentioned earlier, an ideal perioperative diabetes management is controversial and out of reach. Studies indicate that even the fairly loose glucose target of 70–180 mg/dl is achieved consistently in only a few patients.[4]

Surgeries may trigger the stress response,[5] resulting in hemodynamic, metabolic, and hormonal changes which may alter the blood glucose level.[6,7] In order to avoid complications related to hyperglycemia or hypoglycemia in surgeries, it seems necessary to minimize effects of anesthetics on blood glucose level. This study was performed to compare the effects of different sedation methods (propofol + fentanyl and midazolam + fentanyl) on blood glucose level as some previous studies suggested that different sedation and anesthesia methods have different effects on it.[8,9]

Nascimento *et al*. suggested that there is no influence of the preoperative serum glucose level on perioperative clinical complications or visual acuity outcome in cataract surgeries.[11] Therefore, phacoemulsification surgery seemed to be the ideal surgery for this study.

In a study performed by Cok *et al*.,[9] it was presented that the combination of propofol + remifentanil resulted in greater levels of blood glucose compared to isoflurane + remifentanil. In another study, Kitamura *et al*.[8] suggested that the effect on glucose metabolism of propofol is much less than that of sevoflurane.

In the current study, effects of two common methods of light sedation on glucose were evaluated: Propofol + midazolam and fentanyl + midazolam. Vital signs and drug complications were evaluated as well.

Statistical analysis of the data revealed that there is no statistically significant difference in the blood glucose level during and after light sedations using propofol + midazolam and fentanyl + midazolam.

It is also implied that postoperative complications of these two methods have no significant difference in frequency, and in both methods, nausea and bradycardia were the most common complications. Vital signs also did not have significant differences compared in both groups, except for a higher RR in patients receiving propofol + midazolam prior to the surgery.

Our study faced some limitations. We used glucometer for measuring blood glucose level which is not as accurate as laboratory methods. Moreover, our subjects were not nil *per os* for a similar time, which could have affected their blood glucose level prior to the surgery.

CONCLUSION

Considering all the presented data above, light sedation methods of propofol + fentanyl and midazolam + fentanyl seemed not to have any differences in alteration of blood glucose level. Therefore, if there are no specific contraindications for using propofol or midazolam, it is suggested that both methods can be used in diabetic patients, and selection of each method is upon the anesthesiologist and with considering other factors.

ACKNOWLEDGMENTS

This study was financially supported by a grant (number 392124) from the vice-chancellor for research, Isfahan University of Medical Sciences, and was carried out in Feiz hospital, Isfahan University of Medical Sciences, Isfahan, Iran.

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Source of Support: A grant (number 392124) from the vice-chancellor for research, Isfahan University of Medical Sciences, and was carried out in Feiz Hospital, Isfahan University of Medical Sciences, Isfahan, Iran, **Conflict of Interest:** None declared.