Original Article

Investigation of the association between serum HbA1c level and hemodynamic variables in diabetic patients undergoing prostatectomy

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ABSTRACT

HbA1c is one of the most important predictors of complications in diabetic patients. present study aimed to investigate the association between the HbA1c level and hemodynamic variation during general anesthesia. 100 prostatectomy candidates patientes with type 2 diabetes were included in the study from 2018 to 2019 in two groups: (A) HbA1c < 6.5 and (B) HbA1c ≥ 6.5 . systolic and diastolic blood pressures, mean arterial pressure, and heart rate was measured before and 10 minutes and 60 minute after induction of anesthesia and compared between two groups. results were analyzed by Student‘s t-test and (ANOVA). The mean age of patients were the same in two groups (63.22 vs 63.78 years). No significant difference was found between the two groups in terms of mean BMI at a 95% confidence level. The mean BMI was 36.79 for Group A and 35.60 for Group B (P-V = 0.065). There was no significant difference between the two groups in terms of the duration of diabetes. The mean duration of diabetes for Groups A and B was 3.86 and 3.64 years, respectively (P = 0.522). The ANOVA results show that the mean variables of systolic pressure, diastolic pressure, MAP, heart rate, and blood glucose for patients of Group B, compared to Group A, changed significantly in the measured times (P-V>0.05). In patients with HbA1c below 6.5, hemodynamic variables are more stable during general anesthesia for prostatectomy.

Keywords: Hba1c, General anesthesia, Hemodynamic, Diabt

Introduction

An improvement in the level of anesthesia and consequently the safety of patients has been one of the most important reasons for the development of major surgeries during the last two decades. These surgeries have consequently reduced mortality and morbidity rates. Better control of the patient's conditions before, during, and after anesthesia by relying on pathophysiological knowledge, the discovery of safer drugs, and the use of advanced monitoring plays a major role in this regard [1]. Numerous drugs and anesthesia techniques can affect the cardiovascular, respiratory, metabolic, nervous, fluid, and electrolyte systems and increase the risk of hypotension in patients. Therefore, the use of drugs that provide the most hemodynamic stability during anesthesia should be taken into consideration [2]. Also, the dangerous consequences of major surgeries include metabolic disorders, insulin resistance, and hyperglycemia, especially in diabetic patients, resulting in increased mortality and morbidity [3]. Presently, more than half a billion people around the world suffer from diabetes. The disease is often associated with the involvement of various organs and is a major challenge for surgery and anesthesia [4].

It has been reported that careful control of blood glucose around the surgery time, reduces the risk of infection, cardiovascular events, disability, and mortality promote wound healing, and

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reduce the length of hospital stay [5]. It is also was significantly associated with medication adherence, satisfaction, and HbA1c level [6].

For better control of diabetes, it is essential to obtain accurate information about the type of diabetes, the status of blood glucose control, and the existence of chronic complications of diabetes before surgery and thus use the best method of hemodynamic and metabolic control and monitoring during surgery [7]. Blood glucose control after surgery in intensive care units (ICUs) reduces mortality and morbidity [8]. Diabetes in patients admitted to the ICU can also cause prolonged ileus and intolerance to gavage, resulting in some complications such as ventilator-related pneumonia [9]. In some studies, diabetes has been mentioned as an independent risk factor for eye problems in the ICU [10].

The incidence of resistant nosocomial infections is higher in diabetic patients hospitalized in ICU compared to non-diabetic patients and results in increased mortality in these patients [11]. Moreover, surgical stress and its responses can result in insulin failure and increased insulin resistance, and finally, reduced insulin secretion and increased blood glucose levels. Preoperative hyperglycemia can cause dehydration, fluid shift, electrolyte disturbances, infection, delayed wound healing, diabetic ketoacidosis, and postoperative hyperosmolar coma [12]. Some studies have investigated the impact of preoperative glucose concentration and others have investigated the impact of intraoperative glucose on postoperative consequences. Thus, measuring glucose during and after surgery is important in preventing the occurrence of postoperative problems. Moreover, knowing its association with preoperative care in patients undergoing surgery is of great importance [13].

BPH is the most common benign disease in men so 50% of men aged 51 to 60 years and 90% of men aged over 80 years are BPH-positive in histological tests. Moreover, 25% of 55-year-old men and 50% of 75 years-old-men suffer obstructive urinary symptoms [14]. Nearly, 14 million patients have been diagnosed with BPH in the United States [15]. and its prevalence is estimated at 300 million people around the world [16]. Many of these patients need surgery [17]. Since BPH is seen more in middle-aged and older people, most of them also suffer from underlying conditions such as diabetes. It has been observed that blood glucose control before and during surgery prevents nosocomial infections, accelerates wound healing, and decreases cardiovascular events [18]. Influencing the autonomic system, diabetes can cause an inappropriate response to stressful conditions such as surgery and anesthesia [19].

Hemoglobin HbA1c has long been used as an effective indicator of long-term control of blood glucose so HbA1c levels above 6.5 are considered an indicator of poor blood glucose control during the last three months [20]. Given the increase in the number of surgeries and the need to reduce the length of hospital stay, serious steps should be taken to reduce postoperative complications. Some of the strategies employed in this regard are the early diagnosis of diabetes and accurate and long-term control of blood glucose. Since HbA1c is an important indicator to control diabetes in people, the present study was conducted to evaluate the association between serum HbA1c level and the hemodynamic status during prostatectomy in patients referred to Bahonar Hospital of Kerman University of Medical Sciences in 2018-2019.

Materials and Methods

The statistical population of this descriptive-analytical study included all insulin-dependent diabetic Mellitus (IDDM) patients, who were candidates for open prostatectomy and referred to Shahid Bahonar Hospital in Kerman in 2018-2019. The sample size formula for repeated ANOVA tests is as follows:

$$n = \frac{2(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2\sigma^2}{d^2} \quad (1)$$

If $\alpha = 0.05$, $\beta = 20\%$, $\sigma = 25$, and $d = 10$ are the SBP variables, the sample size will be estimated at 100.

The required sample was selected using a convenience non-probabilistic sampling method and based on the inclusion criteria. Inclusion criteria were having an age of 40-65 years, no hypertension, no insulin use for at least one month, no use of steroids, no sepsis, no history of heart disease, no history of thyroid disease, and no history of taking drugs affecting CNS. The exclusion criterion, on the other hand, was the reluctance to continue to participate in the study. After obtaining the approval of the ethics committee of Kerman University of Medical Sciences, the objective of the study was explained to patients. Once the informed consent was the patients were informed one month before surgery, and they were referred to the laboratory for HbA1c testing. Based on the HbA1c level, the patients were divided into two groups A (HbA1c <6.5%) and B (HbA1c> 6.5%) [14]. Aspirin and statins were used until the surgery in both groups, regular morning insulin was removed and the patients received a half dose of morning NpH insulin. Along with receiving insulin on the day of hospitalization, they received a 5% dextrose infusion, and BS control was performed during the surgery according to the standard protocol. Systolic blood pressure, diastolic blood pressure, mean arterial pressure, arterial oxygen saturation, and blood glucose were measured before induction of anesthesia, immediately after induction of anesthesia, and 10, 20, 30, 40, 50, and 60 minutes after induction of anesthesia. All patients received 1-2 μg/kg of fentanyl and 0.5-1 mg of midazolam as a premedication. Anesthesia was induced with 2 mg/kg propofol and 0.5 mg/kg atracurium. The patients underwent maintenance with isoflurane. At the end of the surgery, patients were reversed with 0.02 mg/kg atropine and 0.04 mg/kg neostigmine. Finally, the data were analyzed through the statistical R software and independent t-test, and repeated ANOVA. The significance level of all tests was considered at 0.05.

Results and Discussion

A total of 100 people were included in the present study. Before comparing hemodynamic variables, to ensure that the initial conditions of the two groups were the same, the demographic variables of age, height, weight, BMI, and duration of diabetes were compared in two groups using the independent t-test. As shown in **Table 1**, the variables of age (p_value = 0.637), weight (p_value = 0.452), height (p_value = 0.365), BMI (p_value = 0.065), and duration of diabetes (p_value = 0.522) did not show a significant difference between the two groups.

Table 1. Comparison of the means of demographic variables

	Group A	Group B	statistic	p_value
Age	63.220	63.780	-0.473	0.637
Weight	79.980	81.540	-0.755	0.452
Height	172.020	172.900	-0.911	0.365
BMI	36.792	35.597	1.870	0.065
Duration of diabetes	3.860	3.640	0.642	0.522

In the next [3] stage, the means of hemodynamic variables in two groups A and B were compared at desired times by using a t-test. As shown in **Table 2**, the mean systolic blood pressure (SBP) in Group A at baseline was 134.48 mm Hg and it was 132.52, 129.82, and 128.38 mm Hg and at times of 10, 30, and 60 minutes after surgery, respectively. These values did not show a significant change compared to the baseline. However, in Group B, systolic pressure before induction (baseline) was similar to that of Group A (134.08) (pv = 0.816) while at times of 10, 30, and 60 minutes after the surgery, it was 132.26, 125.18, and 119.00 mm Hg, respectively, indicating a significant decrease compared to baseline (pv <0.05).

Table 2. Comparison of systolic blood pressures at different times in the two groups

Hemodynamic indexes	Time (mine)	Group A	Group B	P-Value
SBP/mm hg (Systolic blood pressure)	0	134.48	134.08	0.816
	10	132.52	132.26	0.900
	30	129.82	125.18	0.037
	60	128.38	119.00	0.000

Also, the mean diastolic blood pressure (DBP) at baseline in the two Groups A and B was 80.62 and 76.02 mm Hg, respectively, indicating no significant difference between the two groups (PV =). In comparison, at times of 10, 30, and 60 minutes after surgery, the mean diastolic pressure in Group A was 78.66, 76.34, and 75.92, respectively. However, in Group B, mean diastolic blood pressure at these times was 73.00, 68.82, and 62.44 mm Hg, respectively, which was significantly lower than that of Group A (P-V <0.05) **(Table 3)**.

Table 3. Comparison of diastolic blood pressures at different times in two groups

Hemodynamic indexes	Time (mine)	Group A	Group B	P-Value
DBP/mm hg (Diastolic blood pressure)	0	80.62	76.02	0.013
	10	78.66	4.751	0.001
	30	76.34	67.46	0.000
	60	75.92	62.44	0.000

By comparing the mean arterial blood pressures in the two groups, no significant difference was observed between the two groups at baseline (98.24 mm Hg in Group A and 95.06 mm Hg in Group B) (PV = 0.051). In comparison, at times of 30, 10, and 60 minutes after surgery in Group A (96.84, 94.66, and 92.66, respectively), the mean arterial blood pressure was significantly higher than that of Group B (92.42, 86.38, and 80.98, respectively) (PV <0.05), indicating better hemodynamic stability in Group A **(Table 4)**.

Table 4. Comparison of mean arterial blood pressures at different times in two groups

Hemodynamic indexes	Time(mine)	Group A	Group B	P-Value
MAP/mmHg (Mean arterial pressure)	0	98.24	95.06	0.051
	10	96.84	92.42	0.013
	30	94.66	86.38	0.000
	60	92.66	80.98	0.000

The mean heart rate at baseline in groups A and B was 77.6 and 78.24 pulse per minute, respectively, indicating no significant difference between the two groups (PV = 0.2). Also, at times 10 and 30 minutes after surgery, the mean heart rate in Group A was 77.22 and 74.30 pulse per minute, respectively. In Group B, the mean heart rate at times of 10 and 30 minutes after the surgery was 79.24 and 75.42, respectively, indicating no significant difference between the two groups (PV >0.05). At 60 minutes after the surgery, the mean heart rate in groups A and B was 74.10 and 68.34, respectively, which was significantly lower in Group B (PV <0.05) **(Table 5)**.

Table 5. Comparison of mean heart rates per minute in the two groups

Hemodynamic indexes	Time (mine)	Group A	Group B	P-Value
HR pulse/mine (Heart rate)	0	77.60	78.24	0.43
	10	77.22	79.24	0.222
	30	74.30	75.42	0.512
	60	74.10	68.34	0.000

The results of examining the blood glucose of patients before induction of anesthesia showed that the mean blood glucose was 111.80 mg/dL in Group A and 118.34 mg/dL in Group B, which was significantly lower in Group A than that in Group B (P-V = 0.01). At 30 minutes following the surgery, it was 111.12 mg/dL in Group A and 135.08 mg/dL in Group B (P-V = 0.00), and at 60 minutes after the surgery, it was 111.22 mg/dL in Group A and 153.84 mg/dL Group B (P-V = 0.00), In both times, the mean blood glucose in Group B was significantly higher than that of Group A (PV <0.05) **(Table 6)**.

Table 6. Comparison of mean blood glucose levels at different times

Time(Mine)	Blood sugare mg/dL		p.value
	GroupA	Group B	
0	111.80	118.34	0.01
30	111.12	135.08	0.00
60	111.22	153.84	0.00

The present study aimed to evaluate the relationship between serum HbA1c levels and hemodynamic status and blood glucose levels of patients during prostatectomy surgery under general anesthesia. The results revealed that although the mean systolic blood pressure, mean diastolic blood pressure, and mean arterial blood pressure of diabetic patients in the two groups before induction of anesthesia were the same, after induction of anesthesia, the mentioned hemodynamic variables in patients with HbA1c showed a significant reduction of more than 6.5 compared to the other group at different times. Also, serum blood glucose levels were significantly higher in the group with HbA1c> 6.5 with the induction of anesthesia than those of the second group. Diabetes has several complications in various organs, the most important of which are the involvement of the neurological, cardiovascular, autonomic, and renal systems. Several studies have indicated that a lack of blood glucose control can negatively affect patients' outcomes after surgery. For example, Jehan *et al*. showed that complications of diabetic patients with HbA1c above 6% after emergency surgery were four times higher than those with HbA1c < 6%. In the mentioned study, postoperative complications were investigated, while we investigated hemodynamic changes. The results of this study showed an increase in BS during surgery. Moreover, it was observed that in conditions of poor long-term blood glucose control characterized by HbA1c above 6.5%, the possibility of hemodynamic changes and an increase in blood glucose during surgery increases [21] Yong *et al*. indicated that the hbA1c level above 6.5% in patients aged over 54 years was an independent risk factor for postoperative complications. An increase in blood glucose and hemodynamic changes during surgery can also cause complications in diabetic patients after the surgery, which is in line with our results [22].

In a meta-analysis study conducted by Jinjing Wang, it was reported that high levels of HbA1c in diabetic patients can be associated with serious complications such as infection at the surgery site, renal failure, and cardiovascular events after cardiac surgery [23]. Moreover, in diabetic patients, it can result in increased mortality and renal failure. Our desired outcome was hemodynamic changes during the surgery. These complications were significantly higher in the HbA1c > 6.5% group. According to the results of the present study, it seems that type 2 diabetic patients who have not had accurate blood glucose control for a long time (HbA1c> 6.5%) are more prone to hemodynamic changes since anesthesia induction time until one hour later, compared to those accurately controlling their blood glucose.

Although the hemodynamic changes were not enough to cause disorder in this study, a more accurate focus on monitoring these patients seems to be necessary. Also, in type 2 diabetic patients with HbA1c> 6.5%, an increase in blood glucose during surgery was much higher than that of other groups. It can cause postoperative complications such as wound infection, delayed wound healing, and dehydration, highlighting the need for more careful control of blood glucose in these patients . Muhammad Abu Tailakh *et al*. indicated that diabetic patients with ME HbA1c > 7% after elective coronary artery bypass graft surgery had a more 5-year mortality rate than healthy individuals, indicating the importance of long-term blood glucose control to reduce stress-related complications such as heart surgery in diabetic patients [24].

In a study conducted on 409 patients who underwent heart surgery, Gandhi *et al*. showed that per 20 mg of increase in blood glucose above 100 mg during surgery, respiratory and renal complications increase by 30% [25]. One of the most important complications of diabetes is autonomic dysfunction, which is observed in 40% of patients with type I diabetes and 17% of patients with type 2. Symptoms of autonomic neuropathy include gastroparesis, bladder paresis, orthostatic hypotension, and diabetic diarrhea [26]. It has been indicated that accurate control of blood glucose can reduce the incidence of type 2 diabetic neuropathy. In a study conducted by Gaede P *et al*., the incidence of neuropathy was 30% in the control group and 54% in the non-control group. In our study, it was found that diabetic patients who had HbA1c levels below 6.5% were more likely to have more hemodynamic stability during surgery due to less involvement of the autonomic system [27]. Given the importance of the role of autonomic neuropathy, Gibbons *et al*. (2015) recommended that HbA1c should be reduced by 3 points within 3 months, leading to a decrease in autonomic neuropathy [28].

Cardiovascular diabetic neuropathy refers to the degradation of the autonomic cardiovascular system [29]. that can result in hemodynamic instability or myocardial infarction during surgery [30]. In a screening study by Andersen *et al*., it was found that 1.8% of well-controlled diabetic patients were affected by cardiovascular neuropathy [31]. In a study conducted by Pop-Busui R, the rate of mortality caused by cardiac events in patients with cardiovascular autonomic involvement was 3 times higher than that in the non-involved group, a part of which was due to hemodynamic changes during the surgery. Their result is in line with that of our study [32]. As our study results, several studies have revealed that the involvement of the autonomic cardiovascular system in diabetic patients causes hemodynamic instability during general anesthesia [32]. However, some studies have not reported differences between the two groups in terms of hemodynamic changes during general anesthesia, which may be due to differences in study design or anesthesia technique [33]. In two systematic review studies conducted in 2015, it was recommended that HbA1c measurement in diabetic patients before non-cardiac surgery was not valuable and did not play a role in reducing postoperative complications [34, 35], Laiteerapong showed that HbA1c above 7% in type 2 diabetic patients is associated with macro and microvascular complications and increased mortality [36]. Silva *et al*. reported that HbA1c could increase c-reactive protein, blood viscosity, and oxidative stress of mediators, which are involved in exacerbating cardiovascular problems. In comparison, in our study, HbA1c levels above 6.5% were associated with more hemodynamic changes during surgery [37].

Conclusion

Based on the results of the present study, more hemodynamic changes were observed in type 2 diabetic patients with HbA1c levels above 6.5% compared to those with HbA1c levels less than 6.5% during prostatectomy under general anesthesia. However, these changes were not at the level of hemodynamic instability in none of the groups. Hence, more accurate results might be obtained in future studies by identifying cases of autonomic cardiovascular system involvement in diabetic patients with HbA1c > 6.5% and comparing hemodynamic changes during anesthesia and surgery in this group of patients with those, in which the autonomic system is not involved. Moreover, an increase in blood glucose of patients with HbA1c above 6.5% during surgery was significantly higher than that of the other group, indicating the need to pay more attention to this group to control blood glucose during general anesthesia, since the severe increase in blood glucose can be associated with several complications. One of the limitations of the present study is the lack of mid-term and long-term follow-up of patients and the lack of investigating the changes in blood glucose on the mid-term and long-term survival of the patients.

Limitations

The small number of eligible patients and the impossibility of mid-term and long-term follow-up of patients.

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Conflict of interest: None

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Ethics statement: After the patients were given complete and understandable explanations about the study, they entered the study after obtaining written consent from the patients (IR.KMU.AH.REC.1397.163).

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