

**The effect of dexamethasone on postoperative blood glucose levels in diabetic and non-diabetic Patients who are undergoing laparoscopic cholecystectomy**

Ayman H. Mohammed<sup>a</sup>, Mahmoud M. A. Ismail<sup>a</sup>, Hatem S. Mohammed<sup>a</sup>

<sup>a</sup>Department of Anesthesiology and Intensive Care and pain management, Faculty of Medicine, South Valley University, Qena, Egypt.

**Abstract:**

**Background:** Dexamethasone is a potent corticosteroid when administered alone or in combination. Alone has proven efficacious in preventing nausea and vomiting (PONV) perioperative.

However, the administration of even a single dose has been associated with hyperglycemia.

**Objectives:** This is a study that evaluates the effect of 8 mg dexamethasone on blood glucose concentrations among diabetics and non-diabetics in patients who are undergoing laparoscopic cholecystectomy.

**Patients and Methods:** After obtaining ethical clearance 60 American Society of Anesthesiologists I and II patients undergoing laparoscopic cholecystectomy aged 18 to 65 years of either gender with body mass index <30 kg/m<sup>2</sup> scheduled for elective laparoscopic cholecystectomy under general anesthesia will be included in the study. Patients will be divided into two groups: Group A, 30 diabetic patients receiving 8 mg dexamethasone and group B, 30 non-diabetic patients receiving 8 mg dexamethasone. Blood glucose level will be estimated at 0, 6h, 12h, and 24h.

**Results:** The baseline blood glucose values were higher in diabetics compared to non-diabetics (125.77±22.55 vs. 95.47±15.45 mg/dL). Throughout the study period, blood glucose was significantly higher in diabetic than in non-diabetic patients. All patients in the study who received dexamethasone had significantly higher blood glucose levels subsequently. The rise of blood glucose from baseline was compared between the diabetic and non-diabetic groups at T6 and T12. The rise of blood glucose was similar in both diabetics and non-diabetics at T6. However, at T12, the non-diabetic patients had statistically significant rise in blood glucose levels in comparison with diabetics.

**Conclusion:** The maximum rise in blood glucose was in the range of 40–45 mg/dl in the patients. The clinician should use his clinical judgment before administering dexamethasone for PONV prophylaxis/treatment.

**Key words:** Dexamethasone; diabetes mellitus; hyperglycemia; postoperative nausea and vomiting.

**Introduction**

Postoperative nausea and vomiting (PONV) are a common distressing symptoms in patients undergoing laparoscopic surgery and can contribute to anxiety, dehydration, metabolic abnormality, wound disruption, delayed recovery and other issues. The incidence of PONV varies from 20 to 80%

treatment of nausea and vomiting should be aimed at specific receptors/mediators that appear to be largely contributing to an individual patient's experience. A greater appreciation of which particular mechanisms are playing a major role for an individual patient may lead to eliminate nausea and vomiting, minimize treatment-induced

adverse effects, and optimize patient outcomes (Rojas et al., 2010). Dexamethasone, a corticosteroid, was first reported as an effective anti-emetic agent in patients undergoing cancer chemotherapy. In 1981, Wang et al. confirmed that dexamethasone is most effective when it is administered at the induction rather than at the termination of anesthesia. However, the mechanism underlying the anti-emetic effects of dexamethasone is still unknown. It may be involved in central inhibition of prostaglandin synthesis, or it may cause a decrease in serotonin turnover in the central nervous system (Wang et al., 2000). However, because of the known adverse effects of corticosteroid use, there are some concerns regarding the possible side effects of dexamethasone administration in the post-operative setting. For example, corticosteroids are known to increase blood glucose levels by inducing hepatic gluconeogenesis and increasing insulin resistance and this may be associated with poor outcomes in critically ill and postsurgical patients. We therefore decided to perform a prospective randomized controlled trial to compare postoperative blood glucose levels in non-diabetic and diabetic patients receiving PONV prophylaxis with dexamethasone.

#### **Patients and methods:**

The study was performed in Qena university Hospitals-general surgery Unit between October 2017 and April 2019. After obtaining the approval of the Ethics Committee of the School of medicine and written informed consent of the patients, non-diabetic patients and diabetics underwent elective laparoscopic cholecystectomy. Patients aged 18 to 65 years of either gender with American Society of Anesthesiologists physical status

ASA I or ASA II and body mass index <30 kg/m<sup>2</sup> scheduled for elective laparoscopic cholecystectomy under general anesthesia were included in the study. Patients who were receiving corticosteroids, insulin, vasoactive drugs and those who had received glucose or oral hypoglycemic agents on the day of surgery were excluded. All patients had a preoperative fast of at least 8 hours and there was no administration of intravenous fluids (iv) prior to anesthetic induction.

**Exclusion criteria:** 1-patient refusal. 2-pregnancy. 3-patients with pre-operative blood glucose levels greater than 11.1 mmol/l (200 mg/dl). 4-patients currently or recently receiving steroid treatment. A total of 60 patients scheduled for laparoscopic cholecystectomy under general anesthesia were divided into two groups: Group A, 30 diabetic patients received 8 mg dexamethasone. Group B, 30 non-diabetic patients received 8 mg dexamethasone. All of the patients were admitted a day before surgery. Blood glucose level was estimated. Patients were kept on fasting 8 hours before surgery and an informed written consent from all patients was obtained. 1 hour pre-operative blood glucose level was estimated. Upon arrival in the operating room, patients were monitored with standard anesthetic monitors. A standardized anesthetic technique was used in the two groups. Patients were pre-medicated with 0.1 mg/kg midazolam one hour before induction of anesthesia in order to decrease pre-operative stress and its associated metabolic changes. Thereafter anesthesia was induced by propofol (2-2.2 mg/kg), atracurium (0.6 mg/kg) as muscle relaxant to facilitate endo-

tracheal intubation. Anesthesia was maintained with isoflurane or sevoflurane (0.5-1.0 MAC) in oxygen (FiO<sub>2</sub> 0.5) and fentanyl titrated to maintain hemodynamic stability (mean arterial pressure and heart rate  $\pm$  20% of the baseline). The ventilation was trolled and adjusted to keep ETCO<sub>2</sub> between 30-35 mmHg. Intraoperative fluids included Ringer's lactate solution and there was no administration of solutions containing glucose. The surgical technique was standardized and performed by the same surgical team. Prior to the anesthetic induction, diabetic and non-diabetic patients were randomly distributed by numbers generated computationally in two groups: Group A, 30 diabetic patients received 8 mg dexamethasone. Group B, 30 non-diabetic patients received 8 mg dexamethasone.

After surgery; patients were extubated in the operating room. Blood glucose level was estimated for all patients at 0 -6 h-12 h-24 h. Blood glucose levels were measured by the "hemoglucotest" technique of a capillary blood sample obtained from a patient's pulp with a lancet and using the Accucheck Sensor glycemia monitor (Roche, Mannheim, Germany) calibrated daily. A baseline measurement was obtained before the anesthetic induction and then every 6 hours from T<sub>0</sub> until completing 24 hours. All measurements were made by researchers who did not know the group to which the patients belonged. All patients received 60 mg of iv ketorolac after induction of anesthesia. Postoperative pain management was performed with an i.v. infusion of ketorolac 90 mg in 24 hours plus 3 mg of iv morphine.

The postoperative emetic events were treated with 1 mg of iv droperidol followed by a second dose of 4 mg of iv ondansetron if necessary. The use of non-anesthetic drugs was recorded in the study period. There were no interventions to manage the glycemia during the entire study.

#### **Statistical Analysis:**

All patients had been analyzed using Statistical package for Social Sciences (SPSS).

#### **Results:**

We recruited a total of 60 patients in the study. The patient demographic data are presented in Table 1. There were no statistical significant differences in demographic data between the two groups as regards patients' age, sex, height, body weight and duration of surgery. All patients were ASA physical status I and II (Table 1). Throughout the study period; blood glucose was significantly higher in diabetic than in non-diabetic patients (table 2). The rise of blood glucose from baseline was compared between the diabetic and non-diabetic groups at T<sub>6</sub> and T<sub>12</sub> (table 3). The rise of blood glucose was similar in both diabetics and non-diabetics at T<sub>6</sub>. However, at T<sub>12</sub>, the non-diabetic patients had statistically significant rise in blood glucose levels in comparison with diabetics.

**Table 1: Demographic data**

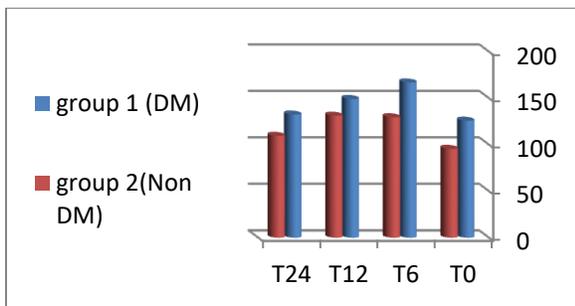
	Group A	Group B	P-Value
Age (y)	39.33 ± 9.192	40.64 ± 6.622	0.717
Sex (male / female)	13/17	14/16	0.750
Weight (kg)	73.26 ± 12.472	76.41 ± 11.283	0.452
Height (m)	1.65 ± 0.09	1.69 ± 0.11	0.264
Duration of surgery (min)	86.64 ± 10.29	83.85 ± 12.47	0.513

Data are expressed as mean ± SD.  
P value > 0.05 and it is insignificant.

**Table2: Blood glucose concentrations during the study in D.M and non D.M.**

time	Group A DM (30)	Group B non DM (30)	P value
T0	125.77±22.55	95.47±15.45	<.0001*
T6	166.80±25.91	129.40±25.26	<.0001*
T12	149.10±17.02	131.10±28.08	.003*
T24	132.37±20.18	109.47±19.50	<.0001*

Data are expressed as mean ± SD.  
P value < 0.05 and it is significant.



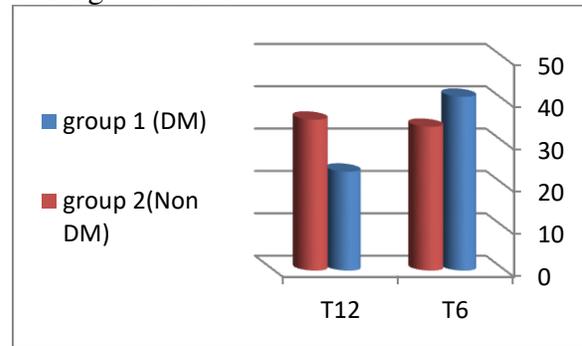
**Figure 1: Blood glucose concentrations during the study period (mg/dl). T0**

(baseline), T6 (after 6 hours), T12 (after 12 hours) and T24 (after 24 hours).

**Table3: the mean rise of blood glucose level from baseline at T6 and T12 post dexamethasone.**

T6	Non dm	33.93±22	P value =.1
	DM	41.03±14.64	
T12	Non dm	35.63±23.21	P value=.04*
	DM	23.33±22.39	

Data are expressed as mean ± SD.  
P value > 0.05 and it is insignificant at T6 and significant at T12



**Figure 2: The mean rise of blood glucose from baseline (mg/dl). T0 (baseline), at T6 and T12 after test drug administration.**

**Discussion:**

Dexamethasone has been used widely in clinical specialties including anesthesia. It is regarded as one of the ideal peri-operative agents being readily available, cheap, anti-inflammatory agent, prevents and treats post-operative nausea and vomiting (PONV),promotes appetite, suppress inflammation, a good analgesic agent both as intravenously or as an adjuvant to peripheral nerve blocks, it provides a sense of well-being and is considered to have a good quality of recovery and early discharge in patients from anesthesia. One of the most common side effects of dexamethasone is hyperglycemia. So in our study we compare the glycemic effect of anti-emetic dose of

dexamethasone in diabetics and non-diabetics who are undergoing laparoscopic cholecystectomy. In our study, dexamethasone administration for PONV prophylaxis resulted in significant elevation of blood glucose in both diabetic and non-diabetic patients. Also the rise of blood glucose was similar in both diabetics and non-diabetics at T6. However, at T12, the non-diabetic patients had statistically significant rise in blood glucose levels in comparison with diabetics. **Hans et al., (2006)** in their study analyzed blood glucose levels in the first 6 h postoperatively in non-Diabetics, and patients with type 2 diabetes receiving IV dexamethasone 10 mg for PONV prophylaxis, they found that blood glucose concentration profile although parallel, was significantly higher in type 2 diabetic than in non-diabetic patients and peaked 120 min after injection. In our study patients received dexamethasone had significant rise in blood glucose in the range of 40–43 mg/dl which peaked between 6 and 12 h post dexamethasone administration.

These findings are similar to that of **Nazar et al., (2009)** where thirty obese patients who received 8 mg dexamethasone had higher maximum blood glucose concentrations (187 mg/dl) compared with controls (158 mg/dl). However, a drawback of that study is that they have infused glucose-containing IV fluids during the study. Similar to our findings, **Nazar et al., (2011)** in another study demonstrated that diabetic patients did not show higher susceptibility than non-diabetics to develop postoperative hyperglycemia after the use of prophylactic dexamethasone 8 mg for PONV. Contrary to our study where both groups had a hyperglycemic response, the findings of another study found that there was no dexamethasone-induced hyperglycemic effect for diabetic patients and non-diabetic patients showed a greater increase in blood glucose level. **Low et**

**al.,(2015).** In a retrospective database study found that dexamethasone 8–10 mg was associated with a significantly greater perioperative increase in blood glucose compared with a 4 mg dose. **Tien et al., (2016)** showed that PONV prophylaxis with IV dexamethasone (8 mg) significantly increases postoperative blood glucose values compared with ondansetron (4mg). This effect was comparable between non-diabetic and diabetic patients, regardless of baseline blood glucose levels. In our study, 8 mg of dexamethasone caused a greater magnitude of hyperglycemic response in non-diabetics when compared with diabetics. The reason for this cannot be explained.

Our study has a few limitations:

- There was no control group in our study.
- Small sample size
- There is single dose of dexamethasone experienced in our study, in future studies we need to compare between different doses.

#### **Conclusion:**

Dexamethasone 8mg causes a greater hyperglycemic response in non-diabetics compared to diabetic patients at 12 h post administration. Diabetics have an exaggerated hyperglycemic response post dexamethasone administration. However, the maximum rise in blood glucose was in the range of 40–43 mg/dl in patients who received dexamethasone 8 mg, and the clinician should use his clinical judgment before administering dexamethasone for PONV prophylaxis/treatment.

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#### **Conflicts of interest**

There are no conflicts of interest.

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