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EVALUATION OF HYPERGLYCAEMIC RESPONSE TO ANTI-EMETIC DOSE OF DEXAMETHASONE IN DIABETIC PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANESTHESIA

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Abstract

Background: To evaluate hyperglycaemic response to anti-emetic dose of dexamethasone in diabetic patients undergoing laparoscopic cholecystectomy.

Materials & methods: A prospective study was conducted on 120 ASA I and II, aged 16-60 years patients posted for laparoscopic cholecystectomy under general anaesthesia. A detailed pre-anesthetic evaluation was carried out to rule out the presence of any significant co-morbidity. Demographic data collected was age, weight, height and BMI. Patient's HbA_1c was also done and recorded. Hyperglycaemia is defined as blood glucose greater than 125 mg/dl while fasting and greater than 180 mg/dl 2 hours postprandial. All the patients were divided into two groups: Group A: 60 diabetic patients and Group B: 60 non-diabetic patients. On the day of surgery a baseline RBS of all the patients was taken and recorded. A standardized general anesthesia technique was used for the two groups.Injection dexamethasone 8mg was given to all the patients in both the groups. Blood glucose levels were estimated for all the patients preoperatively and then at 1,2,3 and 4 hours after giving injection dexamethasone. After surgery, patients were extubated in the operating room. In post-operative care unit patients were evaluated for nausea and vomiting. Post operative pain was assessed by numeric rating scale for pain (0 = no pain, 10= worst possible pain). Data was analysed using Statistical Package for Social Sciences, version 23 (SPSS Inc., Chicago, IL). Student t- test was used for group comparison. A 'p' value of less than 0.05 was considered statistically significant.

Results: It was observed that the association of age and weight was significant in both the groups ($p<0.05$). Age and weight was more in group A patients. The preoperative RBS was also statistically significant in Group A while statistically insignificant in group B. HbA_1C and mean RBS also showed statistically significant corelation. The corelation between BMI and mean RBS was found to be statistically significant ($p<0.05$). There was also no postoperative nausea and vomiting in majority of the patients after Dexamethasone injection.

Conclusion: Antiemetic dose of dexamethasone causes significant rise in blood sugar in diabetic patients but the hyperglycaemic response is not exaggerated beyond expected physiology.Therefore no pharmacological intervention is required.

Introduction

Dexamethasone is a synthetic glucocorticoid with potent anti-inflammatory and metabolic effects". It is a long acting,synthetic derivative of cortisol(hydrocortisone). It is an agonist of glucocorticoid receptor. It is widely used as a premedication in patients undergoing surgeries under general anaesthesia. It is frequently administered in the perioperative period, most commonly for the prophylaxis and treatment of postoperative nausea and vomiting(PONV).[1]

International guidelines recommend a prophylactic intravenous (IV) dose of 4 to 5 mg for adults but 8 mg is recommended as having additional analgesic benefits.[2] Dexamethasone is a glucocorticoid steroid associated with potential risks including impaired wound healing, increased blood glucose levels and an increased risk of infection,[3] making its use in diabetics controversial. Perioperative hyperglycemia is reported in 20-40% of patients undergoing general surgery and approximately 80% of patients after cardiac surgery.[2,4] A recent report examining point-of-care glucose testing in 3 million patients, across 575 American hospitals, reported a prevalence of hyperglycemia (blood glucose>180 mg/dl, 10 mmol/l) as 32% in both intensive care (ICU) patients and non-ICU patients. Most patients with hyperglycemia have a known diagnosis of diabetes. However, 12-30% of patients who experience intra and/or post-operative hyperglycemia do not have a history of diabetes before surgery,a state often described as stress hyperglycemia. [5,6] Stress hyperglycemia typically resolves as the acute illness or surgical stress abates. However, cross-sectional and longitudinal studies show that between 30-60% of these patients have impaired carbohydrate intolerance when assessed by oral glucose tolerance testing after hospital discharge.[7] Furthermore, 60% of patients admitted with new hyperglycemia had confirmed diabetes after one year.[7] Measurement of HbA1c in patients with hyperglycemia during hospitalization provides the opportunity to differentiate patients with stress hyperglycemia from those with diabetes who were previously undiagnosed.[8] The Endocrine Society guidelines indicate that patients with hyperglycemia and HbA1C of 6.5% or higher can be identified as having diabetes. [9]

There is relatively little published information regarding the effects of dexamethasone on perioperative glycaemic control in patients with Type-2 diabetes mellitus."Two studies reported that the administration of dexamethasone led to an increase in postoperative blood glucose levels that was comparable between diabetic and non-diabetic patients,"whereas another study found that non-diabetic patients experienced a greater intra operative increase mean glucose blood levels compared with diabetics.[5] Thus it remains unclear whether the hyperglycemic response to dexamethasone administration is greater in diabetic,compared with non-diabetic patients. Hence, this study was done for the evaluation of perioperative hyperglycaemic response to anti emetic dose of dexamethasone in diabetic patients undergoing cholecystectomy.

Materials & methods

A prospective study was conducted, over 120 ASA I and II, aged 16-60 years patients posted for laparoscopic cholecystectomy under general anaesthesia. A detailed pre-anesthetic evaluation was carried out to rule out the presence of any significant co-morbidity. Demographic data collected was age, weight, height and BMI. Patient's HbA_1c was also done and recorded. Hyperglycaemia is defined as blood glucose greater than 125 mg/dl while fasting and greater than 180 mg/dl 2 hours postprandial.

All the patients were divided into two groups; Group A: 60 diabetic patients and Group B: 60 non-diabetic patients. On the day of surgery a baseline RBS of all the patients was taken and recorded. A standardized anesthetic technique was used for both the groups. Patients were pre-medicated with 1mg midazolam, injection glycopyrrolate 0.01 mg/kg and injection fentanyl 2 mcg/kg.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 sevoflurane (0.5-1.0 MAC) in oxygen (FiO2-0.5). The ventilation was controlled and adjusted to keep end tidal carbondioxide between 30-35 mmHg. Injection dexamethasone 8mg was given to all the patients in both the groups. Blood glucose levels were estimated for all the patients preoperatively and then at 1,2,3 and 4 hours after giving injection dexamethasone. 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 Accu-check Sensor glycemia monitor (Roche,Mannheim Germany) calibrated daily. After surgery, patients were extubated in the operating room.In post-operative care unit patients were evaluated for nausea and vomiting.Post operative pain was assessed by numeric rating scale for pain (0 = no pain, 10= worst possible pain). Data was analysed using Statistical Package for Social Sciences, version 23 (SPSS Inc., Chicago, IL). Student t- test was used for group comparison. A 'p' value of <0.05 was considered statistically significant.

Results

It was observed that the mean age of Group A and Group B of patients was 52.26±6.79 years and 40.0±11.72 years respectively. The mean height(cms) of Group A and Group B of patients was 156.40±3.63 and 157.62±3.25 respectively. The mean weight (kg) of Group A and Group B of patients was 63.68±5.12 and 61.08±4.65 respectively. The mean BMI (kg/m^2) of Group A and Group B of patients was 26.05±1.65 and 25.67±1.41 respectively. The association of age and weight in both groups was found to be statistically significant ($p<0.05$).

Table 1: Distribution of studied patients based on comparison of demographic details of patients of both the groups

	Group-A (n=60)	Group-B (n=60	p-value
Age in years (Mean±SI	52.26±6.79	40.0±11.72	**<0.001**
Height (cms)	156.40±3.63	157.62±3.25	0.056
Weight (kg)	63.68±5.12	61.08±4.65	0.045
BMI (kg/m^2)	26.05±1.65	25.67±1.41	0.180

It was observed that the mean value of baseline RBS (Preoperative) in Group A and Group B was 135.7±7.94 and 109.9±15.02 respectively. The mean value at 1 hour in Group A and Group B was 139.4±8.72 and 112.5±16.03 respectively. The mean value at 2 hours in Group A and Group B was 143.4±9.0 and 113.8±12.78 respectively. The mean value at 3 hours in Group A and Group B was 142.3±9.15 and 112.5±10.06 respectively. The mean value at 4 hours in Group A and Group B was 139.2±9.58 and 111.1±11.58 respectively. The association of RBS in group A was found to be statistically significant ($p<0.05$).The association of RBS in group B was found to be statistically non-significant($p>0.05$).

Table 2: Distribution of studied patients based on comparison of RBS in both groups

RBS	Group-A (n=60)	p-value	Group-B (n=60)	p-value
	Mean±SD		Mean±SD	
Baseline (Preoperative)	135.7±7.94	**<0.001**	109.9±15.02	0.143
At 1 hours	139.4±8.72	**<0.001**	112.5±16.03	0.156
At 2 hours	143.4±9.0	**<0.001**	113.8±12.78	0.133
At 3 hours	142.3±9.15	**<0.001**	112.5±10.06	0.164
At 4 hours	139.2±9.58	**<0.001**	111.1±11.58	0.125

When the corelation between HbA_1C and mean RBS was studied, it was observed that in the patients with $HbA_1C \leq 7.50$ the preoperative (baseline) mean RBS was 135.02 while in patients with $HbA_1C \geq 7.51$ mean RBS was 137.29. Subsequently at one hour, two hours,three hours and four hours of dexamethasone injection , mean RBS in patients with $HbA_1C \leq 7.50$ was 138.30,142.27,141.88 and 138.00 respectively. Similarly in patients with $HbA_1C \geq 7.51$ mean RBS at same intervals was 142.17,146.17,143.47 and 142.23 respectively. The corelation between HbA_1C and mean RBS was found to be statistically significant ($p<0.05$).

Table 3: Distribution of studied patients based on correlation between HbA1c and blood sugar

Time duration	HbA1c levels (%)	N	RBS Mean	Std. Deviation	P value
Preoperative RBS	**≤7.50**	43	135.02	8.44	**<0.001**
	7.51+	17	137.29	6.43	
	Total	60	135.66	7.94	
RBS_at_01hrs after Inj dexamethasone	**≤7.50**	43	138.30	8.90	**<0.001**
	7.51+	17	142.17	7.79	
	Total	60	139.40	8.72	
RBS_at_02hrs after Inj dexamethasone	**≤7.50**	43	142.27	9.45	**<0.001**
	7.51+	17	146.17	7.24	
	Total	60	143.38	9.00	
RBS_at_03hrs after Inj dexamethasone	**≤7.50**	43	141.88	9.84	**<0.001**
	7.51+	17	143.47	7.28	
	Total	60	142.33	9.15	
RBS_at_04hrs after Inj dexamethasone	**≤7.50**	43	138.00	8.85	**<0.001**
	7.51+	17	142.23	10.93	
	Total	60	139.20	9.58	

When the corelation between BMI and RBS was studied, it was observed that the patients with BMI ≤ 25.0 the preoperative (baseline) mean RBS was 120.72 while in patients with BMI ≥25.0 the mean RBS was 124.16. Subsequently at one hour, two hours, three hours and four hours of dexamethasone injection , mean RBS in patients with BMI ≤ 25.0 was 123.75,125.97,124.77 and 123.22 respectively. Similarly in patients with BMI≥25.0 mean RBS at same intervals was 142.17,146.17,143.47 and 142.23 respectively. The corelation between BMI and RBS was found to be statistically significant ($p<0.05$).

Table 4: Distribution of studied patients based on correlation between BMI and mean RBS

Time duration	BMI	N	Mean	Std. Deviation	P value
RBS Preoperative	**≤25.0**	48	120.72	20.41	**<0.001**
	>25.0	72	124.16	17.94	
	Total	120	122.79	18.96	
RBS at 01 hrs of Inj. Dexamethasone	**≤25.0**	48	123.75	21.34	**<0.001**
	>25.0	72	127.37	18.26	
	Total	120	125.92	19.54	
RBS at 02 hrs of Inj. Dexamethasone	**≤25.0**	48	125.97	22.07	**<0.001**
	>25.0	72	130.36	19.20	
	Total	120	128.60	20.42	
RBS at 03 hrs of Inj. Dexamethasone	**≤25.0**	48	124.77	21.62	**<0.001**
	>25.0	72	129.15	19.26	
	Total	120	127.40	20.26	
	≤25.0	48	123.22	22.02	**<0.001**

RBS at 04 hrs of Inj. Dexamethasone	**>25.0**	72	126.41	18.50	
	Total	120	125.14	19.95	

It was observed that majority 91(75.83%) patients had mild pain and 29(24.17%) patients had no pain.

Table 5: Distribution of studied patients based on numeric rating scale for pain

No pain (%)	Mild Pain (%)	Moderate Pain (%)	Severe Pain (%)
29(24.17%)	91(75.83%)	0(0%)	0(0%)

The distribution of studied patients based on postoperative nausea and vomiting and it was observed that majority 116 (96.67%) patients belonged to no nausea/no vomiting group and 4 (3.33%) patients belonged to nausea and vomiting group respectively.

Table 6: Distribution of studied patients based on postoperative nausea and vomiting

No nausea/No vomiting (%)	Nausea and Vomiting (%)
116 (96.67%)	4 (3.33%)

Discussion

Dexamethasone is commonly used for postoperative nausea and vomiting (PONV) prophylaxis. It has similar efficacy to ondansetron, does not have any sedative side-effects, improves the quality of patient recovery and may have some postoperative analgesic effect. "However, because of the known adverse effects of corticosteroid use, there is some concern regarding the possible side-effects of dexamethasone administration in the peri-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[74]. Several studies have reported postoperative hyperglycaemia in patients receiving dexamethasone perioperatively. [11,12]

Administration of glucocorticoids during the perioperative period can reduce the inflammatory, hormonal, and immunological effects of surgical stress, and prevent complications such as postoperative nausea, vomiting and laryngeal edema. Additionally, these corticosteroids can also reduce peripheral and hepatic insulin sensitivity by affecting the post-receptor mechanisms and increase the blood glucose levels by promoting gluconeogenesis or in other words, the production of glucose from amino acids and fats. "This effect may impair blood glucose regulation in both patients with and without diabetes and previous studies have shown that even low doses of corticosteroids can lead to hyperglycemia.[13]

In the present study, 60 (50.0%) patients were diabetic (Group A) and 60 (50.0%) patients were non-diabetic (Group B). The majority of the cases were females in both the studied groups 83.3% and 70.0%in group A and group B respectively. It was observed that the mean age of Group A and Group B of patients were 52.26±6.79 years and 40.0±11.72 years respectively and the difference was found statistically significant for age ($p<0.05$). The incidence of gallstones is more in females than males. At age 50 to 65 years, approximately 20% of women and 5% of men have gallstones.[14] Our findings were consistent with those of Hans P et al[15] who studied the blood glucose concentration profile after 10 mg dexamethasone in non-diabetic and type 2 diabetic patients undergoing surgery reported comparable findings as in the present study with female predominance and insignificant difference between the diabetic and non-diabetic group regarding demographic and anthropometric variables ($p>0.05$).On the contrary, Mohammad AH et al[16] and Gülmez DD et al[17] in their study found no statistically significant differences in demographic data between two groups with regard to patient's age, sex, height, body weight and duration of surgery.

Contrary to our study, Nazar et al[18] (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. Purushothaman AM et al[19] studied that dexamethasone 8 mg causes a greater hyperglycaemic response in non-diabetics compared to diabetics at 8 hours post administration.

In the present study, when rise in random blood sugar was compared on the basis of preoperative HbA1c in diabetic patients, it was found statistically significant. It was observed that diabetic patients having more HbA1c preoperatively are found to have more increase in blood sugar perioperatively. "In any individual, HbA1c is known to reflect blood glucose values over the two previous months. Hence, it reflects the efficacy of treatment in diabetic patients". Our study is consistent with a study by "Hans P et al in which a significant linear correlation was observed between HbA1c and maximum blood glucose concentrations, the higher the HbA1c, the higher the blood glucose concentration.

In our study, it is also observed that diabetics as well as non- diabetics having BMI >25 kg/m^2 have significant rise in blood glucose perioperatively after giving antiemetic dose of prophylactic dexamethasone for PONV. Our study is consistent with a study by P.Hans et al who studied the correlation between BMI and RBS in diabetic and non- diabetic patients and concluded that high BMI values leads to more hyperglycemia perioperatively after giving anti emetic dose of 10 mg dexamethasone in both diabetics and non-diabetics undergoing abdominal surgery".

In our study, mild pain was experienced by 75.83% cases whereas 24.17% experienced no pain and only 3.33% experienced nausea and vomiting of total 120 cases studied. Our study is consistent with a study done by Gupta R et al[20] in which fixed dose Midazolam which is usually used as a premedicant, 0.04 mg/kg was used with variable doses of Dexamethasone. Minimum dose for prevention of nausea was 4 mg of dexamethasone and for vomiting it was 2 mg. There was significant reduction in nausea and pain severity as well as in incidence of use of rescue antiemetic and analgesics in 4 mg and 8 mg group of D compared with placebo. The results were similar to those of Yeo J et al[21] and El-Deeb A et al[22] , that combination of studied drugs is more effective for PONV prevention.Out of 120 patients, mild pain was experienced by 75.83% cases in which we have to give rescue analgesic drug whereas 24.17% experienced no pain at all.

Conclusion

In our study, it was observed that dexamethasone caused significant rise in blood sugar in diabetic patients but the hyperglycaemic response was not exaggerated beyond expected physiology, so no pharmacological intervention was required. There is insignificant rise in blood sugar in non-diabetic patients and there was no incidence of hyperglycaemia. A peak in blood glucose was observed at 120 minutes after injecting dexamethasone in both the groups. "HbA_1c is significantly correlated with preoperative blood glucose, suggesting that higher preoperative blood glucose reflected poor baseline glucose control, which is a risk factor for exaggerated hyperglycaemic response to dexamethasone. As dexamethasone is proved to be good anti-emetic and analgesic, it is recommended that in diabetic patients, a close monitoring of RBS can be done after giving prophylactic antiemetic dose, 8 mg of dexamethasone or a low dose 4-5 mg for PONV prophylaxis would be preferred. A good control of blood sugar and weight is suggested for diabetic patients for any type of surgery. Our secondary objective was to assess post operative nausea and vomiting and post operative pain by numeric rating scale. In our study there is very less or no need to use rescue antiemetics and rescue analgesic drugs in post operative period.

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