



Anaesthesiology

TO EVALUATE THE EFFECT OF TWO DIFFERENT ANTIEMETIC DOSES OF DEXAMETHASONE ON POST OPERATIVE BLOOD GLUCOSE LEVELS IN PATIENTS UNDERGOING LAPAROSCOPIC SURGERIES- A RANDOMISED CONTROL DOUBLE BLINDED STUDY

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ABSTRACT

Background and Aims: This study was done to evaluate the effect of two different antiemetic doses of dexamethasone 8 mg and 4 mg IV respectively on postoperative blood glucose levels and duration of antiemetic effect for 24 hours in patients undergoing laparoscopic surgeries. **Methods:** After obtaining ethical committee clearance and approval from institution, patients fulfilling inclusion criteria who give informed consent will be included in the study. Total of 80 patients will be selected and randomized into 2 groups of 40 each Group D8- Dexamethasone 8 mg IV and Group D4- Dexamethasone 4 mg IV respectively. Baseline GRBS will be checked in pre-op room. Group D8 and Group D4 will receive Inj. Dexamethasone 8 mg IV and Inj. Dexamethasone 4 mg IV respectively after induction of anesthesia. Finger prick capillary blood glucose levels will be measured before dexamethasone administration (T0) and at 60 minutes (T1), 120 minutes (T2), 180 minutes (T3), 240 minutes (T4), 300 minutes (T5) and 360 minutes (T6). Postoperatively, patients were administered dextrose free IV fluids -NS till study ended eight hours after dexamethasone administration. Postoperative nausea vomiting will be observed every hour till 24 hours. Rescue antiemetic will be Inj. Ondansetron 4 mg IV. **Results:** The demographics of the patients between the two groups are comparable. There was no significant difference between Mean BMI between two groups (p value=0.695). Baseline mean blood glucose levels (T0) between the Group D8 and Group D4 were similar (P value> 0.05). There was statistically significant rise in the blood glucose levels with respect to the dose of Dexamethasone at T1, T2, T3, T4, T5 and T6 intervals (P value< 0.05). The duration of antiemetic effect in dexamethasone 8 mg and dexamethasone 4 mg are 13.9hrs and 13.6hrs respectively. There was no statistically significant difference in Postoperative nausea and Postoperative vomiting between the Group D8 and Group D4 (P value> 0.05). **Conclusion:** Dexamethasone causes significant increase in the blood glucose levels in nondiabetic patients. The maximum rise in blood glucose levels is in the range of 20-25 mg/dl. Antiemetic dose of dexamethasone 4 mg is comparable with dexamethasone 8 mg with better glycemic control.

KEYWORDS : Dexamethasone, laparoscopic surgeries, blood glucose levels.

INTRODUCTION

- Postoperative nausea and vomiting (PONV) after general anaesthesia occurs with average risk of 20-30%. The risk of PONV may vary by surgical site and type of operation, appearing higher after breast augmentation, strabismus repair, ENT operations, gynaecological surgery, orthopaedic surgery and laparoscopic procedures. (1) Stretching and irritation of the peritoneum from insufflation of gas during laparoscopy may be a specific emetogenic stimulus and laparoscopy associated with a relatively high absolute risk of PONV in several reports. (1)
- Prophylactic administration of dexamethasone 4 mg, ondansetron 4 mg or droperidol 1.25 mg decreases postoperative nausea and vomiting. (2)
- Dexamethasone is fluorinated derivative of Prednisolone and isomer of Betamethasone. Dexamethasone prevents postoperative nausea and vomiting only when given prior to beginning of surgery, probably by reducing surgery induced inflammation due to inhibition of prostaglandin synthesis. In addition, dexamethasone may exert antiemetic effects by increasing release of endorphins resulting in mood elevation and appetite stimulation. (2)
- Dexamethasone, a very potent and highly selective glucocorticoid also inhibits the use of glucose in peripheral tissue and promotes hepatic gluconeogenesis (2). Its administration may be associated with increased blood glucose levels by inducing hepatic gluconeogenesis and increasing insulin resistance. Hyperglycemia in the perioperative period can cause dehydration, fluid shifts, electrolyte abnormalities, infections, impaired wound healing, ketoacidosis and hyperosmolar states. (3)

AIM AND OBJECTIVES

- To evaluate the effect of two different antiemetic doses of dexamethasone 8 mg and 4 mg IV respectively on postoperative blood glucose levels in patients undergoing laparoscopic surgeries.

- To evaluate duration of antiemetic effect for 24 hours.

METHODOLOGY**Source of data:**

Patients undergoing elective surgery under general anaesthesia in all hospitals attached to Bangalore Medical College and Research Institute.

Study design: Double blinded, randomized control study.

Study period: November 2019 to May 2021.

Place of study:

Patients undergoing elective laparoscopic surgery under general anaesthesia in all hospitals attached to Bangalore medical college and research institute.

Inclusion criteria:

- Patients who have given written informed consent.
- Patients aged 18-60 years, either sex.
- Patients with ASA grade I & II.
- Patients with blood glucose levels 90-180 mg/dl on the day of surgery.
- Patients with BMI 19-28 kg/m².
- Patients scheduled for elective surgery lasting for 60-90 minutes under general anaesthesia.
- Patients who received dextrose free fluids till 8 hours after dexamethasone administration.

Exclusion criteria:

- Patients not willing to give written informed consent.
- Patients who are known case of diabetes mellitus.
- Patients on chronic corticosteroid therapy.
- Patients who had recent parenteral or oral steroid therapy or those who had received a dose of steroid within last 48 hours.

- Patients who received dextrose containing fluids within 8 hours after dexamethasone administration and correction of intraoperative blood glucose levels.
- Patients who have allergy to Dexamethasone.
- Patients with electrolyte abnormalities, Hepatic or Renal insufficiency.
- Pregnant women/Breastfeeding mothers.

MATERIALS AND METHODS

- After approval from institutional ethics committee, written informed consent from patients who fulfill eligibility criteria and routine pre anesthetic evaluation done, patients will be randomly allocated to one of the two groups using numbers generated from www.random.org. 80 patients of either sex will be randomly allocated to either of two study groups of 40 each as described below.
- Group D8 -Patients are given Inj. Dexamethasone 8 mg IV after induction of anaesthesia. Group D4 -Patients are given Inj. Dexamethasone 4 mg IV after induction of anaesthesia. The study drug will be prepared by anesthesiologist not involved in the study.
- A proforma will be used to collect the data which includes patient's particulars, indication for surgery, the anesthetic details, intraoperative monitoring etc.
- All patients to be kept fasting overnight, patients will be given Tablet Alprazolam 0.5 mg and Tablet Ranitidine 150 mg on the previous night of surgery.
- Monitoring includes electrocardiography (ECG), plethysmography(SpO₂ & HR), noninvasive blood pressure(NIBP), end tidal carbon dioxide (EtCO₂). Intravenous access will be established and IV fluids- NS will be started.
- All the patients will be pre medicated with Inj. Glycopyrrolate 0.005 mg/kg IV, Inj. Midazolam 0.03 mg/kg IV and Inj. fentanyl 2 mcg/kg IV. After preoxygenation for 3 minutes with 100% oxygen, patients in each group will be induced by Inj. propofol 2 mg/kg IV followed by Inj. Vecuronium 0.1 mg/kg IV. Laryngoscopy and intubation will be done with appropriate sized cuffed endotracheal tube for male (8.0 or 8.5mm cuffed) and female (7.0 or 7.5mm cuffed).
- After induction of anaesthesia, patients in group D8 and group D4 will receive Inj. Dexamethasone 8 mg IV and Inj. Dexamethasone 4 mg IV respectively. Anaesthesia will be maintained with Oxygen /air/Isoflurane mixture with Mac of 1. Inj. Vecuronium 0.02mg/kg IV will be given for maintenance of muscle paralysis. Isoflurane will be switched off at the last suture. At the end of surgery patient will be reversed with glycopyrrolate 0.001mg/kg IV and neostigmine 0.05mg/kg IV and will be extubated.
- Finger prick capillary blood glucose levels will be measured before dexamethasone administration(T₀) and at 60 minutes(T₁), 120 minutes(T₂), 180 minutes(T₃), 240 minutes(T₄), 300 minutes(T₅) and 360 minutes(T₆) using Accu-Check Active® glucometer that was calibrated daily. Postoperatively, patients were administered dextrose free IV fluids -NS till study ended eight hours after dexamethasone administration. No dextrose containing solution was administered during study.
- Postoperative nausea vomiting will be observed every hour till 24 hours. Rescue antiemetic will be Inj. Ondansetron 4 mg IV.

Sample Size Estimation:

Based on previous study, Purushothaman AM (2018) the baseline blood glucose values were higher in diabetics compared to non-diabetics (128.57±22.26 vs 94.99±12.82).

Sample size is calculated using the formula,

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

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \cdot 2 \cdot \sigma^2}{d^2}$$

n= sample size; α complement of level of confidence = 0.05

$$Z_{\alpha} = 1.96 \quad (Z_{\alpha/2})^2 = 3.84 \approx 4$$

$$Z_{\beta} = 0.84$$

$$\sigma \text{ Standard deviation} = 22.26 + 12.82 = 17.54$$

$$d = \text{difference in mean of 2 groups} = 11$$

$$n = \frac{2 \times 7.84 \times 307.6512}{11^2} = 39.867 \text{ in each group}$$

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$$n \approx 40$$

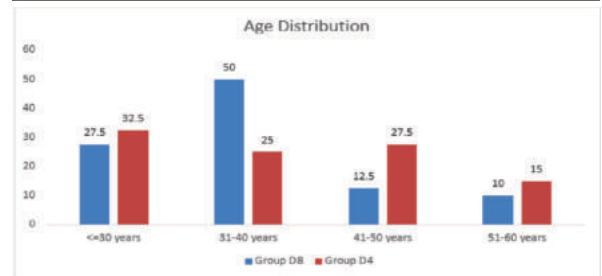
After considering clinical errors and dropouts, a minimum of 40 patients would be required in each group, keeping confidence interval (α) at 95% and power of study (β) at 80%.

RESULTS

Age Distribution

Table 1: Age distribution

		Group D8		Group D4	
		Count	%	Count	%
AGE	<=30 years	11	27.5	13	32.5
	31-40 years	20	50	10	25
	41-50 years	5	12.5	11	27.5
	51-60 years	4	10	6	15
Chi Square Value: 6.15 P value: 0.104					
P value more than 0.05 hence both the groups are comparable					



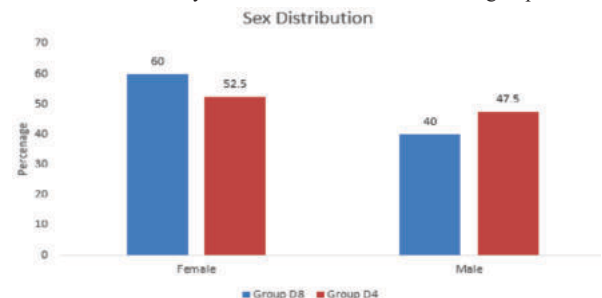
Graph 1: Age distribution

Sex distribution between two groups

		Groups		Group D4	
		Group D8		Count	%
Sex	Female	24	60	21	52.5
	Male	16	40	19	47.5

Table 2: Sex distribution

There is no statistically difference between sex in the two groups.



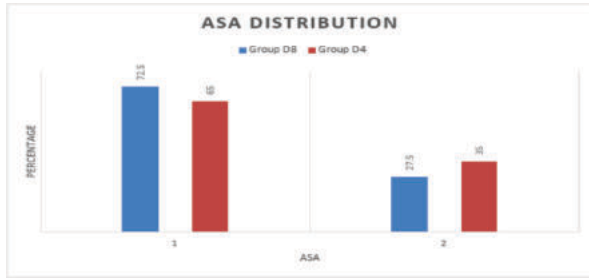
Graph 2: Sex distribution

ASA distribution between two groups

Table 3: ASA distribution

		Groups		Group D4	
		Group D8		Count	%
ASA	1	29	72.5	26	65
	2	11	27.5	14	35
Chi Square Value: 0.524 P value: 0.469					
P value more than 0.05 hence both the groups are comparable					

In Group D8, 72.5% had ASA 1 and 27.5% had ASA 2.
In Group D4, 65% had ASA 1 and 35% had ASA 2.



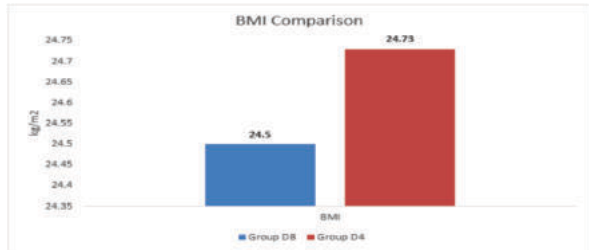
Graph 3: Asa Distribution
Mean BMI between two groups.

Table 4: mean BMI

	Groups				
	Group D8		Group D4		P Value
	Mean	SD	Mean	SD	
BMI (kg/m2)	24.5	2.67	24.73	2.42	0.695

Mean BMI in Group D8 was 24.5 ± 2.67 kg/m² and Mean BMI in Group D4 was 24.73 ± 2.42 kg/m².

There is no significant difference between Mean BMI between two groups (p value=0.695).

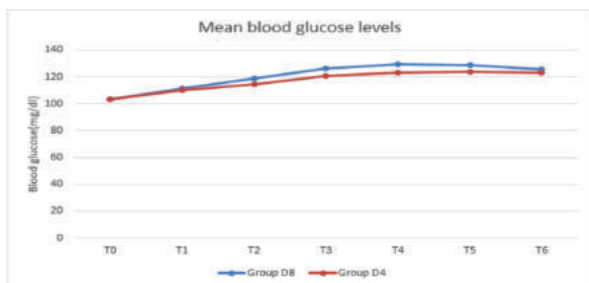


Graph 4: BMI comparison

Mean blood sugar levels between two groups.

BLOOD GLUCOSE LEVELS	Group	Mean	Std. Deviation	Std. Error Mean	P value
T0	D4	103.53	6.373	1.008	1.000
	D8	103.53	8.747	1.383	
T1	D4	109.85	5.480	.866	0.442
	D8	111.15	9.116	1.441	
T2	D4	114.63	5.550	.878	0.036
	D8	118.58	10.293	1.627	
T3	D4	120.58	8.038	1.271	0.049
	D8	126.40	16.568	2.620	
T4	D4	123.08	6.837	1.081	0.005
	D8	129.28	11.549	1.826	
T5	D4	123.95	7.111	1.124	0.042
	D8	128.65	12.518	1.979	
T6	D4	123.45	10.000	1.581	0.307
	D8	125.85	10.852	1.716	

There is statistically significant difference between the two groups in T2, T3, T4 and T5 (p value < 0.05). Mean blood glucose levels is more in the D8 Group than in the D4 Group.



Graph 5: Mean blood glucose levels

Table 5: Mean blood sugar levels between two groups.

Mean rise in blood glucose level from baseline in dexamethasone 4 mg group

DEXAMETHASONE 4 MG GROUP						
		Paired Differences		t	df	P Value
		Mean	Std. Deviation			
Pair 1	BLOOD GLUCOSE LEVELS T0 - T1	6.26	3.18	-12.268	38	.000
Pair 2	BLOOD GLUCOSE LEVELS T0 - T2	11.03	3.79	-18.149	38	.000
Pair 3	BLOOD GLUCOSE LEVELS T0 - T3	17.00	9.04	-11.743	38	.000
Pair 4	BLOOD GLUCOSE LEVELS T0 - T4	19.44	7.77	-15.616	38	.000
Pair 5	BLOOD GLUCOSE LEVELS T0 - T5	20.15	9.60	-13.105	38	.000
Pair 6	BLOOD GLUCOSE LEVELS T0 - T6	19.49	13.71	-8.873	38	.000

Table 6: Mean rise in blood glucose level from baseline in dexamethasone 4 mg group

The maximum rise in the blood glucose levels in dexamethasone 4 mg group is 20.15 mg/dl seen after 5 hours following induction of anesthesia.

Mean rise in blood glucose levels from baseline in dexamethasone 8 mg group

DEXAMETHSADONE 8 MG GROUP						
		Paired Differences		t	df	P Value
		Mean	Std. Deviation			
Pair 1	BLOOD GLUCOSE LEVELS T0 - T1	7.63	3.91	-12.343	39	.000
Pair 2	BLOOD GLUCOSE LEVELS T0 - T2	15.05	5.31	-17.923	39	.000
Pair 3	BLOOD GLUCOSE LEVELS T0 - T3	22.88	17.95	-8.060	39	.000
Pair 4	BLOOD GLUCOSE LEVELS T0 - T4	25.75	12.63	-12.896	39	.000
Pair 5	BLOOD GLUCOSE LEVELS T0 - T5	25.13	15.35	-10.353	39	.000
Pair 6	BLOOD GLUCOSE LEVELS T0 - T6	22.33	14.53	-9.720	39	.000

Table 7: Mean rise in blood glucose levels from baseline in dexamethasone 8 mg group

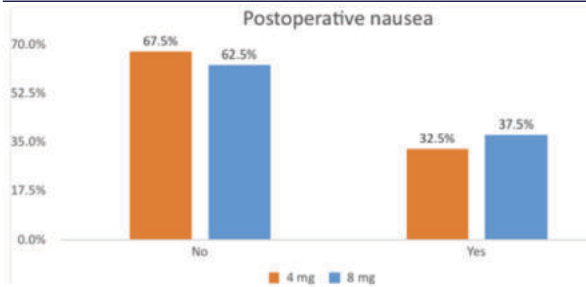
The maximum rise in the blood glucose levels in dexamethasone 8 mg group is 25 mg/dl seen after 4 hours following induction of anesthesia.

Postoperative nausea

Table 8: Postoperative nausea

		DOSE OF DEXAMETHASONE				Pearson Chi-Square Value	df	P Value
		4 mg		8 mg				
		Count	%	Count	%			
POSTOPE RATIVE NAUSEA	No	27	67.5%	25	62.5%	0.22	1	0.639
	Yes	13	32.5%	15	37.5%			
Total		40	100.0%	40	100.0%			

There is no statistically significant difference between two groups (p value=0.639).



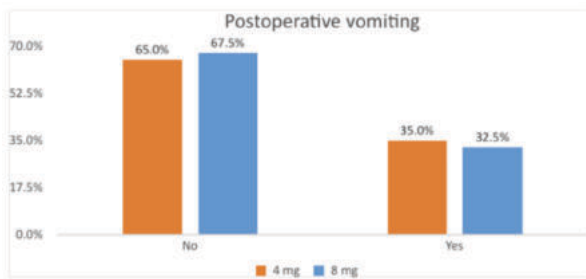
Graph 6: Postoperative nausea

Postoperative vomiting.

Table 9: Postoperative vomiting.

		DOSE OF DEXAMETHASONE				Pearson Chi-Square Value	df	P Value
		4 mg		8 mg				
		Count	%	Count	%			
POSTOPERATIVE VOMITING	No	26	65.0%	27	67.5%	0.056	1	0.813
	Yes	14	35.0%	13	32.5%			
Total		40	100.0%	40	100.0%			

There is no statistically significant difference between the two groups (p value=0.813).



Graph 7: Postoperative vomiting

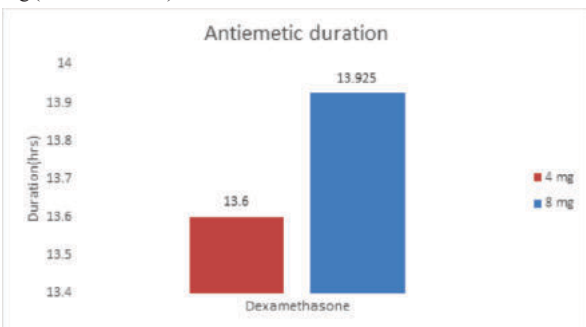
Duration of Antiemetic Effect

Table 10: Duration of Antiemetic Effect

	Dose of dexamethasone								
	4 mg			8 mg					
	N	Mean	Std. Deviation	N	Mean	Std. Deviation	t	df	P Value
Antiemetic duration	40	13.600	10.5704	40	13.925	10.7689	-.136	78	0.892

The duration of antiemetic effect in dexamethasone 8 mg and dexamethasone 4 mg are 13.9hrs and 13.6hrs respectively.

There is no statistically significant difference in the duration of the antiemetic effect between dexamethasone 8 mg and dexamethasone 4 mg (P value=0.892).



Graph 8: Antiemetic duration

DISCUSSION

Laparoscopic surgeries are associated with relatively high absolute risk of postoperative nausea and vomiting because of the stretching and irritation of the peritoneum from insufflation of gas during laparoscopy. Dexamethasone is known to cause hyperglycemia, but it has added advantages like antiemetic, anti inflammatory and anti edema features. In view of this the present study was undertaken to study two different antiemetic doses of dexamethasone to decide antiemetic dose with better glycemic control.

Huang JC et al (2001) did the randomized double blinded, placebo controlled study to evaluate the prophylactic effect of low dose dexamethasone (5 mg) on PONV in women undergoing ambulatory laparoscopic tubal ligation and found that prophylactic dexamethasone IV 5 mg significantly reduced incidence of PONV in women undergoing laparoscopic tubal ligation and more effective than metaclopramide 10 mg or placebo(4). In our study, we found similar results that low dose Dexamethasone (4 mg) is equally effective in the reduction of PONV compared to dexamethasone 8 mg in laparoscopic surgeries.

Habib et al (2006) studied the effect of antiemetic dose of dexamethasone 8 mg IV on blood glucose levels in the perioperative period in the nondiabetic patients undergoing elective surgery under general anesthesia. Patients received either dexamethasone 8 mg after induction of anesthesia or ondansetron 4 mg IV at the end of the surgery. They found that there was no difference between the two groups in baseline blood sugar, or change in blood glucose from baseline at 2hrs, 4hrs, and 24hrs following induction of anaesthesia. PONV prophylaxis with dexamethasone 8 mg did not result in a significant increase in blood sugar, compared with patients not receiving dexamethasone.(5). In our study we found a contrary results, that there was a significant difference in blood glucose levels from baseline at 1hrs, 2hrs, 3hrs, 4hrs, 5hrs and 6hrs following induction of anaesthesia more in the group that received dexamethasone 8 mg IV than group that received dexamethasone 4 mg IV.

Hans P. et al (2006) compared the blood glucose concentration profile after dexamethasone 10 mg in non-diabetic and type 2 diabetic patients undergoing abdominal surgeries and looked for any association with preoperative glycosylated hemoglobin. Blood glucose concentrations increased significantly and peaked at 120 min after 10 mg dexamethasone in each groups. Poorly controlled diabetes and severe obesity can influence in the development of the hyperglycemia(6). In our study we found similar results that blood glucose concentrations increased significantly and peaked at 4hrs and 5 h following induction of anesthesia receiving dexamethasone 8 mg and dexamethasone 4 mg respectively.

Nazar et al (2008) did a double blind, randomized study on obese patients with impaired glucose tolerance who received dexamethasone 8 mg IV for PONV prophylaxis and isotonic saline as control who underwent laparoscopic Roux-en-Y gastric bypass surgery They found that blood glucose concentrations measured after beginning of surgery were higher than baseline values. Dexamethasone group showed higher glucose concentrations than the isotonic saline group from 6th to the 12th hour of study. Dexamethasone 8 mg IV at beginning of laparoscopic bariatric surgery significantly increased postoperative blood glucose concentrations. In our study, we evaluated in nondiabetes patients whose BMI 19- 28kg/m2 and compared dexamethasone 8 mg and dexamethasone 4 mg in laparoscopic surgeries. There is no control group in our study(7). We found similar results that dexamethasone showed the raising trend of the blood glucose values from baseline. Dexamethasone 8 mg raised the blood glucose levels than dexamethasone 4 mg from the baseline and statistically significant values were seen at 1hrs, 2hrs, 3hrs, 4hrs, 5hrs and 6hrs following induction of anesthesia.

Tien M. , Gan T. J, et al (2016) performed a prospective randomised controlled study to compare postoperative blood glucose levels in non-diabetic and diabetic patients receiving Postoperative nausea and vomiting(PONV) prophylaxis with dexamethasone 8 mg IV or ondansetron 4 mg IV. Blood glucose levels were measured at baseline and then 2hrs, 4hrs and 24hrs following induction of anesthesia. Increase in blood glucose levels are greater in patients receiving IV dexamethasone compared with those ondansetron. Diabetic patients required more insulin for the maintenance of blood glucose levels(8). In our study we included nondiabetes patients undergoing

laparoscopic surgeries. We measured blood glucose levels at 1hr, 2hrs, 3hrs, 4hrs, 5hrs and 6hrs following induction of anesthesia and found a similar results that dexamethasone 8 mg and dexamethasone 4 mg increases the blood glucose levels from baseline significantly and there is no need for the insulin in our patients.

Purushothaman et al (2018) conducted prospective randomized study on the impact of dexamethasone 8 mg and 4 mg on perioperative blood glucose concentrations in diabetes and nondiabetics in patients undergoing elective infra umbilical surgeries under spinal anaesthesia. They found that baseline blood glucose values were higher in diabetics compared to non-diabetics (128.57 ± 22.26 vs 94.99 ± 12.82). The maximum rise in blood glucose levels was in range of 40-45 mg/dl in patients who received dexamethasone IV. The PONV prophylaxis with IV dexamethasone 4 or 8 mg causes significant increase in blood glucose levels compared to placebo. Diabetes have an exaggerated hyperglycemic response at 4hrs post dexamethasone 4 mg administration(3). In our study, we conducted on nondiabetic patients undergoing laparoscopic surgeries. We found similar results that dexamethasone 8 mg and dexamethasone 4 mg increases the blood glucose levels which peak at 4hrs and 5hrs respectively following induction of anesthesia. The maximum rise in blood glucose levels after receiving dexamethasone 8 mg and dexamethasone 4 mg are 25.75 mg/dl and 20.15 mg/dl respectively.

CONCLUSION

We conclude that in laparoscopic surgeries antiemetic doses of dexamethasone causes increase in the blood glucose levels in nondiabetics patients. The maximum rise in blood glucose levels after receiving dexamethasone 8 mg and dexamethasone 4 mg are 25.75 mg/dl and 20.15 mg/dl respectively. However antiemetic dose of dexamethasone 4 mg is comparable with dexamethasone 8 mg with better glycemic control.

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