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A Prospective Observational Study On The Impact Of Low-Dose Dexamethasone On Perioperative Blood Glucose Concentrations In Type 2 Diabetics And Non-Diabetics In Infra-Umbilical Surgeries Under Sub-Arachnoid Block

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Abstract

Introduction: Dexamethasone is proven effective for the prophylaxis and treatment of post operative nausea and vomiting, clinicians have some reluctance to use it due to the fear of hyperglycemia. This study was designed to compare the effect of administration of single low dose dexamethasone on blood sugar levels in non-diabetic and diabetic patients undergoing infraumbilical surgeries under spinal anaesthesia.

Materials & Methods: 126 patients between the age of 20 to 70 years, of either gender, ASA physical status I & II scheduled to undergo elective infraumbilical surgeries under spinal anaesthesia were included in the study. The patients were divided into two groups of 63 each.Group DM-4: consisted of 63 patients who had well controlled type 2 diabetes mellitus.Group ND-4: consisted of 63 patients who were non-diabetic.Both groups received low dose dexamethasone (4 mg) diluted in 5 ml of normal saline over 30 seconds prior to administration of spinal anaesthesia. The groups were compared for demographic parameters including age, gender distribution and weight, blood sugar levels up to 24 hours after administration of dexamethasone, hemodynamic parameters (systolic, diastolic and mean blood pressure) up to 60 minutes after spinal anaesthesia, vasopressor requirements and postoperative nausea and vomiting (PONV).

Results: Dexamethasone administration in a dose of 4mg resulted in increase in blood sugar levels in both diabetic and non-diabetic patients (p-value<0.05). , the percentage increase from baseline was similar in both diabetic and non-diabetic patients (p-value>0.05). The requirement for vasopressors was not significantly different between diabetic and non-diabetic patients (p-value>0.05).Incidence of postoperative nausea and vomiting was similar in both diabetic and non-diabetic patients (p-value>0.05).

Conclusion: A single preoperative dose of 4 mg dexamethasone did not result in greater increase in blood sugar level in well controlled diabetic patients as compared to non-diabetic patients undergoing infra-umbilical surgeries under spinal anaesthesia.

Keywords: Hyperglycemia, dexamethasone, nausea & vomiting

Introduction

Dexamethasone is commonly used for postoperative nausea and vomiting (PONV) prophylaxis. Its efficacy is similar to ondansetron [1], does not have any sedative side-effects, and improves the quality of patient recovery [2]. Ready availability and cost-effectiveness make it one of the ideal peri-operative

agent. It has anti-inflammatory action, promotes appetite, and suppresses inflammation. It is a good analgesic agent both intravenously or as an adjuvant to peripheral nerve blocks. It provides a sense of well-being and is considered to promote a good quality of recovery and early discharge in patients after anaesthesia. However, use of dexamethasone is also associated with many side effects. Several studies [3–7] and a recent meta-analysis[8] reported increased postoperative blood glucose in patients receiving PONV prophylaxis with dexamethasone. This effect was seen in both diabetic and non-diabetic patients, leading some authors to caution against the use of dexamethasone in patients with diabetes mellitus[9]. Hence, although dexamethasone is proven effective for the prophylaxis and treatment of PONV, clinicians have some reluctance to use it due to the fear of hyperglycemia. The literature with respect to the use of dexamethasone in diabetic patients is limited[3,8,9,10,] .

In view of the paucity of literature regarding the effect of dexamethasone on blood sugar levels in diabetic patients, this study was designed to compare the effect of administration of single low dose dexamethasone on blood sugar levels in non-diabetic and diabetic patients undergoing infraumbilical surgeries under spinal anaesthesia.

Aims And Objectives: Primary Aim: To evaluate effect of administration of low dose intravenous dexamethasone on intraoperative & postoperative capillary blood glucose level in both Type 2 diabetic and non-diabetic patients.

Secondary Aim: To evaluate effect of administration of low dose intravenous dexamethasone on postoperative nausea and vomiting, intraoperative hemodynamics and need for vasopressor agents (Ephedrine/Phenylephrine).

Materials And Methods: This study entitled "A prospective observational study on the impact of low-dose dexamethasone on perioperative blood glucose concentrations in type 2 diabetics and non-diabetics in infra-umbilical surgeries under sub-arachnoid block" was conducted in the Department of Anesthesiology and Critical Care, Sher-i-Kashmir Institute of Medical Sciences, Srinagar over a period of two years from 2020 to 2022. After obtaining approval from the Institutional Ethical Committee, a written informed consent was taken from all the patients. A total of 126 patients in the age group of 20-70 years of either sex of the American Society of Anesthesiologists (ASA) physical status Class I and II, scheduled to undergo elective lower extremity and infraumbilical surgeries under spinal anesthesia were included in the study.

A detailed history and thorough general physical examination of the patient was carried out a day before surgery and recorded. All the patients were investigated preoperatively for baseline investigations: Hemogram, Kidney function test (KFT), Liver function tests (LFT), pre-operative blood glucose, Chest X ray (CXR), Electrocardiogram (ECG) and any specific investigation if required. All the patients were kept nil by mouth for 8 hours before surgery.

Inclusion Criteria

1. Adult patients 20-70 years of age
2. Any gender
3. ASA I & II.
4. Surgical procedures of <3hour duration

Exclusion Criteria

1. Contraindication to regional anesthesia
2. Patient refusal
3. Uncontrolled blood sugar level
4. Patients <20 and >70 years old
5. Patients chronically on steroids
6. Long surgeries >3hours
7. Surgeries needing conversion to G/A
8. ASA III and IV.

Technique:

After obtaining a written informed consent, patients were divided in two groups. Sixty-three diabetic patients with type 2 diabetes were allocated to the diabetic group (Group DM-4) and sixty-three non-diabetic patients to the non-diabetic group (Group ND-4). Patients in both groups DM- 4 and ND- 4 received 4 mg intravenous dexamethasone prior to spinal anesthesia.

On arrival to the operating room, standard perioperative monitoring including electrocardiogram (ECG), noninvasive blood pressure (NIBP) monitor, and pulse oximetry(SPO2) were attached to the patients. An 18 gauge intravenous (i.v.) cannula was inserted, and normal saline infusion was instituted. The test drug was diluted with normal saline to

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achieve a volume of 5 ml and was administered over 30 seconds intravenously immediately before performing spinal anesthesia. An independent investigator prepared and administered the study drug. Patients and investigators collecting intraoperative and postoperative data were blinded to patient group allocation. A standardized anesthetic technique was followed. Spinal anesthesia was administered in the sitting position. Using an aseptic technique, a 27 gauge Quincke needle was inserted through a midline approach into the L3–L4 or L4-L5 interspace. Anesthesia was established with a single bolus of 3.5 ml of 0.5% hyperbaric bupivacaine with 25 mcg of fentanyl as an adjuvant. The level of sensory blockade was assessed regularly by the level of cold touch sensation before surgical incision. Sensory level of T6–T8 was considered adequate. Supplemental oxygen 5 L/min through a face mask was administered during the surgery. Estimated fluid requirement and maintenance fluid was replaced with 0.9% normal saline. A standard postoperative analgesic regimen of paracetamol 1 g intravenous (i.v.) infusion as required was prescribed for postoperative pain relief. Finger prick capillary blood glucose was measured immediately before dexamethasone administration (T0) and at 1 hour (T1), 2 hour (T2), 3 hour (T3), 4 hour (T4), 8 hour (T5) and 24 hours (T6) thereafter using a glucometer. Postoperatively, patients were administered dextrose free IV fluids at 2 ml/kg/h till the study ended 24 hours after dexamethasone administration. No dextrose containing solution was administrated during the study. Post-spinal hypotension was treated by bolus of injection ephedrine or by injection phenylephrine.

Diabetic patients requiring intervention in the form of insulin therapy or glucose for any hyperglycemic or hypoglycemic episodes during study period were excluded in the follow up from the study.

The data thus collected was analyzed statistically.

Results And Observations:

There was a statistically significant difference between the groups with respect to age with higher age in the diabetic group (p- value<0.001) Diabetic patients were older and had higher mean weight as compared to non-diabetic patients (p-value<0.05). [Table 1].

The groups were comparable with respect to gender distribution [Table 1].Diabetic patients had higher mean preoperative blood sugar levels as compared to non-diabetic patients (p-value<0.05). Dexamethasone administration in a dose of 4mg resulted in increase in blood sugar levels in both diabetic and non-diabetic patients (p-value<0.05). Although diabetic patients had higher mean blood sugar levels than non-diabetic patients at all study stages, the percentage increase from baseline was similar in both diabetic and non-diabetic patients (p-value>0.05)[Table 3]. Intraoperative systolic diastolic and mean arterial blood pressure was comparable between diabetic and non-diabetic patients (p-value>0.05).The requirement for vasopressors was not significantly different between diabetic and non-diabetic patients (p-value>0.05).[Table 4] Incidence of postoperative nausea and vomiting was similar in both diabetic and non-diabetic patients (p-value>0.05).[Table 5].

Table 1: Comparison of baseline characteristics between the two groups

Parameters	Group DM-4 (n=63) Mean±SD	Group ND-4 (n=63) Mean±SD	p-value
Age (years)	58.7 ± 6.72	46.7 ± 5.95	<0.001*
Gender distribution	37/26	39/24	0.716

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(Male/Female)			
Weight(Kg)	68.2± 8.02	64.3 ±6.54	0.005*
SBP (mm Hg)	132.8±8.91	133.9±7.83	0.488
DBP (mm Hg)	84.1±7.10	85.0±9.12	0.556
MAP (mm Hg)	100.3±7.00	101.3±7.89	0.491

Table 2: Comparison of Mean Blood sugar levels (mg/dl) between the two groups at various intervals of time

Time Interval	**Group DM-4 (n=63) Mean ± SD**	**Group ND-4 (n=63) Mean ± SD**	**P-value**
At Induction	125.63±12.56	91.13±7.46	<0.001*
1 Hour	132.82±12.52	95.23±7.29	<0.001*
2 Hour	145.02±13.62	103.23±7.25	<0.001*
3 Hour	156.25±12.67	112.60±8.58	<0.001*
4 Hour	165.20±12.76	120.73±8.67	<0.001*
8 Hour	154.67±13.54	110.78±7.42	<0.001*
24 Hour	132.70±12.72	97.05±7.72	<0.001*

Table 3: Comparison of intra-operative hemodynamic parameters between the two groups

Parameter		At induction	5 min	10 min	15 min	20 min	25 min	30 min	45 min	60 min
Systolic Blood Pressure	**Group DM-4 Mean ±SD**	136.25± 8.78	131.08 ±7.15	128.87±6.83	126.17±5.78	125.63 ±7.49	123.63±7.11	126.32±6.18	128.47 ±7.12	132.30 ±7.55
	Group ND-4 Mean ± SD	137.42± 7.64	132.97 ±7.07	130.32±8.55	127.42±8.97	126.23 ±7.21	124.02±6.80	128.17±6.90	130.12 ±6.43	133.65 ±7.51
	P value	0.439	0.149	0.307	0.366	0.656	0.763	0.125	0.185	0.328
	Group DM-4 Mean ±	86.20±6 .85	82.63± 7.80	78.50 ±5.64	76.67 ±4.11	73.45± 4.68	70.60 ±4.21	73.25 ±6.47	75.88± 7.25	79.47± 6.85

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Diastolic Blood Pressure	**SD**									
	Group ND-4 Mean ± SD	87.17±9.04	84.27±6.08	80.75±5.20	77.15±5.69	74.93±6.94	72.50±6.53	75.65±6.04	78.12±5.95	80.63±6.02
	P value	0.510	0.203	0.025	0.595	0.172	0.126	0.138	0.168	0.324
Mean Arterial Blood Pressure	**Group DM-4 Mean ± SD**	102.88±6.81	98.78±6.39	95.29±4.59	93.17±3.32	90.84±3.98	88.28±3.94	90.94±5.14	93.41±5.95	97.05±6.02
	Group ND-4 Mean ± SD	103.92±7.80	100.50±6.06	97.27±5.18	93.91±5.96	92.03±5.37	89.67±4.70	93.16±5.40	95.45±5.37	98.30±4.75
	P value	0.441	0.134	0.128	0.403	0.171	0.281	0.113	0.251	0.309

Table 4: Comparison of use of vasopressor agents (ephedrine/phenylephrine) between the two groups

Vasopressor Agent	**Group DM-4**		**Group ND-4**		**P-value**
	No. of patients(n)	**percentage**	**No. of patients(n)**	**percentage**	
Required	8	12.7	7	11.1	0.783
Not required	55	87.3	56	88.9	
Total	63	100	63	100	

Table 5: Comparison of incidence of postoperative nausea and vomiting (PONV) between the two groups

Postoperative nausea & vomiting	**Group DM-4**		**Group ND-4**		**P-value**
	No. of patients(n)	**percentage**	**No. of patients(n)**	**percentage**	
Yes	5	7.9	4	6.3	0.729
No	58	92.1	59	93.7	
Total	63	100	63	100	

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Discussion: It is well established that dexamethasone is an effective drug for PONV prophylaxis[4]. However, routine use of dexamethasone for PONV is debated due to potential side-effects[13,14]. Several studies have documented an increase in blood glucose levels in the postoperative period following anti-emetic doses of dexamethasone[6,15-17], leading some to caution against its use for PONV prophylaxis in diabetic patients. However, there is limited evidence regarding the effects of antiemetic doses of dexamethasone on blood glucose levels in patients with type-2 diabetes.

Dexamethasone administration significantly increased blood sugar in both diabetic and non-diabetic patients. When the magnitude of change of blood sugar from baseline (mean percentage change) was calculated, the magnitude of rise of blood sugar was similar in both diabetic and non-diabetic patients at all the study stages This finding in our study is in concordance with study by **Hans P** et al.[7] (2006) who studied the effect of administration of 10 mg dexamethasone in patients undergoing abdominal surgery. They observed that blood glucose concentrations remained significantly higher in type 2 diabetic than in non-diabetic patients undergoing routine abdominal surgery. **Tien M** et al.(2016)[12] also observed similar results in their study. They observed that dexamethasone (8 mg) significantly increases postoperative blood glucose values compared with ondansetron (4 mg). However, this effect was comparable between non-diabetic and diabetic patients, regardless of baseline blood glucose levels. A single preoperative dose of dexamethasone intravenous 8 mg attenuated the post-spinal hypotension in geriatric patients undergoing orthopaedic surgeries in a double-blind study by **Ashoor TM** et al.[18] Their study had several differences from our study. The patient population in their study was older than in our study. The dose of dexamethasone received was much higher than in our study. Also, in our study there was no control group who didn't receive any dexamethasone. In patients undergoing caesarean section under spinal anaesthesia, ondansetron 8 mg was proven to be more efficacious in preventing spinal anaesthesia induced hypotension than dexamethasone 8 mg[19].

The incidence of postoperative nausea and vomiting was similar in both groups with only 5 patients (7.9%) in diabetic group and 4 patients (6.3%) in non-diabetic group having PONV In agreement with our results **Prabha Parthasarathy** et al.[20], in 2018 aimed to explore the role of intravenous dexamethasone on postoperative nausea and vomiting. They concluded that in dexamethasone receiving group (n = 30) only6.6%of patients had episodes of PONV, compared to placebo receiving group (n = 30) in which33.33% of patients had PONV[20].

The efficacy of dexamethasone as antiemetic is well established. However, the mechanism of antiemetic effect is not fully understood. Glucocorticoids may act via the following mechanisms: (1) anti-inflammatory effect; (2) direct central action at the solitary tract nucleus, (3) interaction with the neurotransmitter serotonin, and receptor proteins tachykinin NK1 and NK2, alpha-adrenaline, etc.; (4) maintaining the normal physiological functions of organs and systems; (5) regulation of the hypothalamic-pituitary-adrenal axis; and (6) reducing pain and the concomitant use of opioids, which in turn reduces opioid-related nausea and vomiting[21].

Limitation: There was no control group in our study, where no dexamethasone administration was given. This could help differentiate the hyperglycaemia of stress response to surgery and hyperglycaemia due to dexamethasone. Also, duration of study was limited to 24 hours postoperatively. So, the effect of dexamethasone on blood sugar levels was beyond that period cannot be commented upon.

Conclusion: The results of our study demonstrate a single preoperative dose of 4 mg dexamethasone did not result in greater increase in blood sugar level in well controlled diabetic patients as compared to non-diabetic patients undergoing infra-umbilical surgeries under spinal anaesthesia. The effect of dexamethasone on hemodynamic parameters was also similar in both diabetic and non-diabetic patients. Dexamethasone 4 mg was equally efficacious as an antiemetic agent in both type-2 diabetic and non-diabetic patients.

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