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EFFECT OF ANTI-EMETIC DOSE OF DEXAMETHASONE ON POSTOPERATIVE BLOOD GLUCOSE LEVELS IN DIABETIC PATIENTS UNDERGOING LAPAROSCOPIC SURGERIES

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ABSTRACT

Background- Role of dexamethasone in preventing postoperative nausea and vomiting is well known. However, it may cause increased blood sugar level which may be concern perioperatively particularly in diabetics. Hence we studied effect on perioperative blood glucose levels in diabetic patients receiving PONV prophylaxis with dexamethasone. **Methods:**120 diabetic patients were enrolled into two groups of 60 patients each. Anaesthesia was induced using i.v. anaesthetic agents and maintained with isoflurane. Study group received 8mg dexamethasone and control group received ondansetron 4mg iv. Blood glucose concentrations were measured at induction and then every 60 min intraoperatively and every 120 minutes upto 24 hours postoperatively. Data were analysed using software IBM© SPSS©. **Results:** There was significant increase in blood sugar level in patients receiving dexamethasone which peaked around 2 hours and remain elevated compared to control group upto 24hours. The magnitude of rise from the baseline values, was significantly higher in the dexamethasone compared to control group. This difference was statistically significant when both groups were compared (<0.001). **Conclusion:** Results of our study demonstrated significant elevation of blood sugar level in diabetic patients receiving dexamethasone prophylactically for PONV. Hence strict monitoring of blood sugar level is recommended postoperatively in patient receiving dexamethasone.

INTRODUCTION

Dexamethasone, a potent corticosteroid, is commonly used agent in anaesthesia practice for its anti-inflammatory, analgesic and antiemetic effect. Preoperative dexamethasone not only prevents postoperative nausea and vomiting (PONV) but also likely to improve post discharge quality of recovery and fatigue[1]. The Society for Ambulatory Anaesthesia guidelines recommends 4-5 mg of dexamethasone prophylactically in patients who are at high risk of PONV.[2] Similarly Gan *et al.* also recommended 5HT3 antagonist and dexamethasone as first line of treatment for paediatric population[3]. Dexamethasone although found highly effective in prevention and treatment of PONV,[4, 5, 6] it can cause perioperative hyperglycaemia even with single dose. Detrimental effects of hyperglycaemia including fluid shift, dehydration, acidosis, wound infection and poor healing has shown some reluctance by clinicians to use it particularly in diabetics.[7,8,9,10,11] It has been found that even a single dose of dexamethasone can cause rise in blood sugars particularly in non-cardiac surgeries[12].

Multiple studies have been conducted to study effect of dexamethasone on blood sugar level perioperatively. However, very few studies investigating dexamethasone included a control group who did not receive dexamethasone, making it difficult to distinguish whether the postoperative hyperglycaemic effect is due to dexamethasone or the stress response to surgery.

Hence, we decided to do a prospective randomized controlled trial comparing the postoperative blood glucose levels in diabetic patients receiving PONV prophylaxis with dexamethasone with ondansetron as control.

METHODS

This prospective randomized double-blind controlled study was carried out in a tertiary care centre after obtaining approval from the institutional ethics and research committee. This study included 120 patients of American society of anesthesia physical status II and III aged between 18 to 70 years who are on oral hypoglycaemic and having blood sugar level <200mg/dl on morning of surgery, HbA1C level <7% and are posted for elective intra-abdominal laparoscopic surgeries under general anesthesia with endotracheal intubation lasting for at least 1hour and who were admitted to hospital for at least 24 hours postoperatively. Those with pregnancy, morbid obesity, having motion sickness with antiemetic therapy, on corticosteroid therapy, preoperative blood glucose levels greater than 200mg/dl on the morning of surgery, allergic to study drugs and refusing to participate in the study were excluded.

Patients were further divided into two groups of 60 each with the help of computer-generated table of random numbers and were investigated according to institutional protocol. Dexamethasone (study) group received dexamethasone 8 mg iv and the ondansetron (control) group received ondansetron 4 mg iv for PONV prophylaxis. The procedure to be done was explained to the patient and written informed consent was taken. Patients were instructed to omit the morning dose of oral hypoglycemic agents.

On the day of surgery NPO status of the patient was confirmed and finger prick capillary blood glucose was measured.

All the patients received oral pantoprazole 40 mg as premedication on the night before and on the day of the surgery. Perioperative monitoring included electrocardiogram, non-invasive blood pressure monitor, temperature probe and pulse oximetry. Peripheral iv line was taken with 20G IV cannula & normal saline solution was started. Patients were premedicated with injection midazolam 0.03mg/kg and fentanyl 2µg/kg. Patients were induced with inj propofol 2.5mg/kg and vecuronium 0.1 mg/kg was used as muscle relaxant. Intubation was done with suitable size endotracheal tube and placement was confirmed using capnograhy and chest auscultation. Immediately after intubation patients were given either dexamethasone (8mg) or ondansetron (4mg), total volume 2cc, as per the randomization chart. The study solution was prepared by the anesthesiologist not involved in the study.

Patients were maintained on oxygen (50%), air (50%), isoflurane (1 MAC) and intermittent boluses of vecuronium on closed circuit controlled ventilation to keep $ETCO_2$ between 28 to 32 mmHg. Intraoperative analgesia was maintained using iv fentanyl boluses of 1µg/kg hourly so as to keep hemodynamics within 20% of the baseline values. Intraoperative fluid replacement therapy consisted of normal saline at a rate of approximately 4 mL/kg/hour. Glucose containing fluids were avoided in the perioperative period.

Blood sugar levels were measured every 60 min intraoperatively by an anaesthesiologist by taking finger prick capillary blood sample. Neostigmine (0.06mg/kg) and glycopyrrolate (0.008mg/kg) were used to reverse neuromuscular blockade at the end of surgery and patient's trachea was extubated and postoperatively patient was shifted to post anaesthesia care unit.

Finger prick capillary blood samples were taken for measurement of blood glucose levels every 120 minutes postoperatively up to 24hrs in the postoperative recovery room by an anaesthesiologist.

Following insulin protocol (ICU Insulin Orders- IV Insulin Infusion Protocol- Revised 2/21/08) was used to maintain glycaemic control intraoperatively and postoperatively:

- 2 units/hr. regular insulin iv for blood sugar levels 210 to 239mg/dl.
- 3 units/hr. of regular insulin iv for blood sugar levels 240 to 269 mg/dl.
- 3 units/hr. of regular insulin iv for blood sugar levels 270 to 299 mg/dl.
- 4 units/hr. of regular insulin iv for blood sugar levels 300 to 329 mg/dl.

- 4 units/hr. of regular insulin iv for blood sugar levels 330 to 359 mg/dl.

Maximum blood glucose level from baseline to 24hrs post-operatively as well as total insulin requirement was noted in both the groups.

STATISTICAL ANALYSIS

Descriptive and inferential statistical analysis has been carried out in the study. Results on continuous measurements are presented as mean ± SD, and results on the categorical measurements are presented in number (%). Significance was assessed at 5% level of significance. Analysis of variance has been used to find the significance of study parameters between three or more groups of patients, and post hoc analysis between the groups was done by Fisher's least square difference test. Student's t-test (two-tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Intergroup analysis) on metric parameters. Chi-square/Fisher's exact test has been used to find the significance of study parameters on categorical scale between two or more groups. P≤ 0.05 has been considered as statistically significant. Statistical software Statistical software IBM© SPSS© (Statistical Package for the Social Sciences) version 18 (IBM © Corp., Armonk, NY, USA) was used for the analysis of the data; Microsoft Word and Excel have been used to generate graphs and tables.

RESULTS

We included a total of 120 patients in study. Demographic data is included in table 1. Both groups had comparable demographic data.

Table 1: Demographic parameters

Sr. no	Parameter	Dexamethasone group(Mean±SD) (n=60)	Ondansetron group (Mean±SD) (n=60)	P value
1	Age in years	47.63±8.525	45.90±6.055	0.202
2	Male: female (%)	18(30%):42(70%)	19(31.6%):41(68.33%)	0.747
3	Mean weight in kg	63.70±4.648	63.35±3.965	0.658
4	Duration of surgery(minutes)	124.35±2.35	124.98± 2.84	0.188

*P< 0.05 significant

Baseline blood sugars were comparable in both groups (table 2). However, blood sugar were elevated at the end of one hour and two hours in dexamethasone group compared to ondansetron group and difference was statistically significant. Similarly, blood sugar remained elevated postoperatively in dexamethasone group compared to ondansetron group as seen from table 3 and difference was statistically significant. There was rise in blood sugar levels post-operatively in both, dexamethasone as well as ondansetron group. The magnitude of rise from the baseline values, however, was significantly higher in the dexamethasone group (p<0.05). In the dexamethasone group, there was sustained rise in blood sugar levels compared to the baseline throughout 24 hours and highest rise was seen 4 hours postoperatively (53.6 mg/dl). However, this rise was not significant in ondansetron group (10.35 mg/dl)(Graph 1).

Table 2: Comparison of intraoperative blood sugar (mg/dl) at various time intervals

Sr. no	Time period	Dexamethasone group(Mean±SD) (n=60)	Ondansetron group(Mean±SD) (n=60)	P value
1	Baseline	128.62±8.866	129.13±7.738	0.734
2	At one hour	145.93±8.541	132.22±7.994	0.0001*
3	At two hours	160.05 ± 8.237	135.30 ±8.127	0.0001*

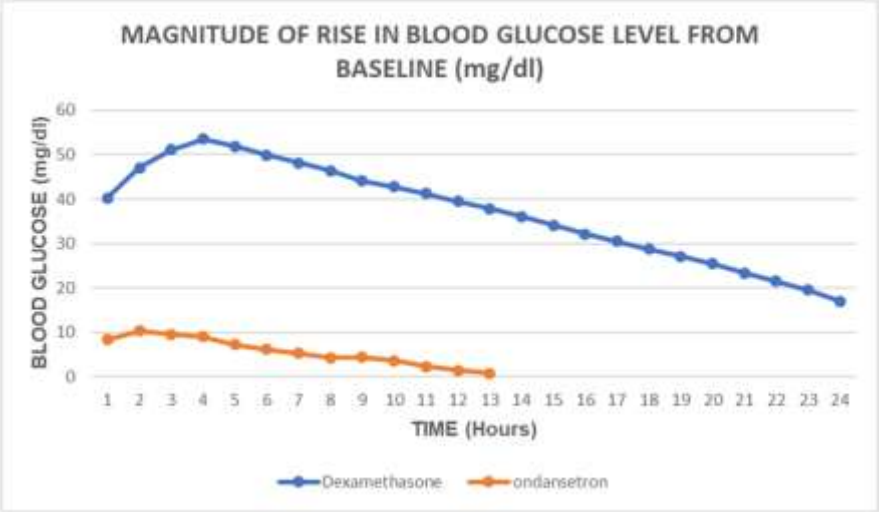
*P< 0.05 significant, P< 0.01 highly significant.

Table 3: Comparison of postoperative blood sugar (mg/dl) at various time intervals

Sr. no	Time interval	Dexamethasone group (Mean±SD) n=60	Ondansetron group(Mean±SD) n=60	P value
1	2 hour	175.75 ± 7.428	139.48 ± 8.752	0.0001*
2	4 hour	182.22±6.455	138.12± 9.298	0.0001*

3	6 hour	178.60± 6.076	135.33± 9.501	0.0001*
4	8 hour	175.08±5.832	133.42±9.403	0.0001*
5	10 hour	171.45±5.924	132.78±9.035	0.0001*
6	12 hour	168.13±6.429	130.57±8.973	0.0001*
7	14 hour	164.70±6.317	129.03±8.908	0.0001*
8	16 hour	160.80±6.167	127.95±8.650	0.0001*
9	18 hour	157.37±6.874	126.60±8.941	0.0001*
10	20 hour	154.13±7.087	126.02±8.723	0.0001*
11	22 hour	150.15± 7.327	124.05±8.018	0.0001*
12	24 hour	145.62±6.795	124.87±8.135	0.0001*

*P< 0.05 significant, P< 0.01 highly significant



Graph 1: Comparison of magnitude of rise in blood sugar levels from baseline between the two groups.

DISCUSSION

Dexamethasone is commonly used drug for PONV. In fact authors of large multicentric trial recommended dexamethasone as first line of drug for PONV[13,14,15]. However, despite this, clinicians are reluctant to use it because of concern regarding adverse effects of corticosteroids in perioperative period. Of many side effects of corticosteroids, hyperglycaemia can be of particular concern induced by hepatic gluconeogenesis and insulin resistance and can result in poor outcome in postsurgical patients[16,17].

Dexamethasone has its peak effect at 2-12 hours and lasts for 72 hours however its effect on blood sugar level may persists for 24 hours[18]. Few studies have also demonstrated its effect on blood sugar level is same in diabetic and non diabetic patients[19,20].

In our study, we found that diabetic patients receiving dexamethasone had greater rise in sugar compared to those diabetics receiving ondansetron and this rise was seen as early as one hour following dexamethasone injection. All patients receiving dexamethasone showed rise in blood sugar level compared to those receiving ondansetron lasting up to 24 hours of surgery.

Although dexamethasone is well established drug in prophylaxis of PONV[21,22], its use been debated due to potential side effects including hyperglycaemia in perioperative period[23]. Few studies have demonstrated rise in blood glucose level following prophylactic dose of dexamethasone for PONV warranting its use for prophylaxis of PONV particularly in diabetic patients [15,24,25,26].

Hans *et al.* conducted a study on type 2 diabetes patients and nondiabetic patients receiving dexamethasone 10mg as prophylaxis for PONV demonstrated parallel increase in blood sugar levels in both group which peaked around 2 hours following injection and this rise was comparatively higher in diabetic group[27]. However lack of control group ie patients not receiving dexamethasone could not conclude that rise in sugar level was because of stress response of surgery or dexamethasone.

Pasternak *et al.* and Lukins *et al.* demonstrated in their studies that larger increase in blood sugar levels occur in nondiabetics particularly in those receiving dexamethasone in intraoperative and postoperative period than in patients not receiving dexamethasone or those who are already on dexamethasone therapy in preoperative period in elective patients undergoing craniotomy[25,28]. Highest increase in blood sugar level was noted in patients receiving intraoperative dexamethasone.

Study conducted by Abdelmalak *et al.* in patients undergoing non-cardiac surgeries having included both type I and Type II diabetics as well as non-diabetics found that greater increase in blood glucose level in non-diabetics receiving dexamethasone compared to diabetics . However, this could be attributed to randomly inclusion of both type I and type II diabetics as well as timing and frequency of blood sugar measurements which was more during intraoperative period[29]. Above studies did not find any exaggerated rise in blood glucose level in diabetics receiving dexamethasone as compared to nondiabetic population. This rise in blood sugar level could be a dose dependent of dexamethasone as found by Low *et al.*[30]. They found higher increase in blood sugar level in diabetics following 8-10 mg of dexamethasone administration compared to 4mg and hence concluded that smaller dose may be preferred in diabetics.

Significant finding of our study was rise in blood sugar level in diabetic patients receiving dexamethasone which peaked at the end of 1-2 hours and remain consistently elevated for 24 hours postoperatively compared to group receiving ondansetron. Percentage of rise in blood sugar level was also higher in group receiving dexamethasone compared to ondansetron. This rise in blood sugar level maybe related to increased neoglucogenesis and increase in insulin resistance. Tien *et al.* also demonstrated similar rise in blood sugar level in patients given dexamethasone for PONV prophylaxis[11].

We had few limitations in our study. First, we had very small group of patients in our study and large group of patients needs to study to confirm findings. We have included patients undergoing different kind of surgeries performed laparoscopically. So there may be variation in stress response postoperatively in patients. We compared single dose of dexamethasone and further studies are needed comparing different doses.

CONCLUSION

Dexamethasone causes significant rise in blood sugar level in diabetic patients particularly 2-4 hours postoperatively and it remains elevated significantly in early postoperative period upto 24 hours. Clinical judgement is needed before administration of dexamethasone in diabetic patients for PONV prophylaxis.

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