

The effects of two different doses of intravenous dexamethasone on blood glucose concentration intra-operatively and on postoperative pain and emesis in patients undergoing surgery under spinal anesthesia: A double-blind randomized clinical study



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ABSTRACT

Background: Spinal anesthetic techniques are relatively safe and associated with quick and uneventful recovery, but post-operative pain and postoperative nausea and vomiting (PONV) are major concerns after the effect weans off. Steroids by virtue of their anti-inflammatory effect are expected to reduce pain as well as PONV. **Aims and Objectives:** The study was conducted to evaluate the efficacy of two different doses of intravenous dexamethasone on blood glucose concentration intra-operatively and on post-operative analgesia and emesis for different surgeries under spinal anesthesia. **Materials and Methods:** This double-blind randomized clinical study was performed on 120 patients aged 20–60 year posted for surgery under spinal anesthesia who were randomly allocated into three groups to receive either normal saline (Group A: 40 pts), intravenous 4 mg dexamethasone (Group B: 40 pts), or iv 8 mg dexamethasone (Group C: 40 pts) immediately after spinal anesthesia. Hemodynamic parameters, respiratory rate, intraoperative blood glucose concentration, severity of post-operative pain, and incidence of PONV was compared among the groups. **Results:** Patients in Group C had significantly less severe post-operative pain and incidence of PONV ($P < 0.05$). Furthermore, less post-operative rescue analgesia was required in Group C ($P < 0.05$). There was a highly significant rise in intraoperative blood glucose level in Group C as compared to other groups, but it was well below the recommended guidelines (< 180 mg/dL). **Conclusion:** Our study concluded that i.v. dexamethasone 8 mg was more effective, although it caused raised blood glucose concentration intraoperatively, but it also provided prolonged post-operative analgesia, increased time of first rescue analgesic, less incident of post-operative nausea and vomiting, and better patient satisfaction.

Key words: Dexamethasone; Blood glucose concentration; Pain; Postoperative nausea vomiting; Spinal anesthesia

INTRODUCTION

Regional anesthesia techniques have been considered superior with many advantages as compared to general anesthesia. In 1989 August, Beir in Germany did the first

operation under spinal anesthesia.¹ Since then, it has been a modality of choice for anesthesia technique as it has an added advantage of decreased risk of failed intubation, aspiration of gastric contents, and fast recovery.² Postoperative pain and nausea vomiting (PONV) are the

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most common post-operative unpleasant experience after surgeries under spinal anesthesia. The overall incidence of PONV in adult population is around 20–30%,³ which is a common cause of delay in discharge and dissatisfaction among patients. Various adjuvants were added to intrathecal drugs such as opioids, alpha 2 receptor agonist, neostigmine, tramadol, magnesium, and dexamethasone to prolong post-operative analgesia with reduced incidence of PONV.⁴ Glucocorticoid being strong anti-inflammatory agent has been used to control post-operative pain in various surgeries. It also has antiemetic effect in addition to its anti-inflammatory and analgesic effect.²

By inhibiting the production of inflammatory mediators (PG and bradykinin), it prevents decrease in pain threshold as well as inhibits nausea and vomiting.² Antiemetic effect is through the blockage of corticosteroids receptor on the nucleus tractus solitarius of the central nervous system.⁵

Dexamethasone can be given intrathecally, epidurally, intravenously, perineurally, and orally, but various studies have suggested systemic dosage of dexamethasone 8 mg or 16 mg is more effective as compared to 2 mg or 5 mg.⁶ Adverse effects of using dexamethasone may include raised blood sugar, wound infections, delayed wound healing, and gastric ulcer.

Corticosteroids reduce peripheral and hepatic insulin sensitivity by affecting the post-receptor mechanisms and increase the blood glucose levels by promoting gluconeogenesis. Previous studies have shown that even low doses of corticosteroids can lead to hyperglycemia.⁷ Dexamethasone in higher dose is more likely to cause hyperglycemia.

In this study, we evaluated the effects of two different doses of intravenous dexamethasone on blood glucose concentration intra-operatively and its effect on post-operative pain and emesis for different surgeries under spinal anesthesia.

Aims and objectives

The aim of this study was to compare the effect of two different doses of intravenous dexamethasone on blood glucose concentration intra-operatively and on postoperative pain and emesis post-operatively.

Primary objective

The primary objective of this study was to compare the effect of two different doses of intravenous dexamethasone on post-operative pain and emesis post-operatively.

Secondary objective

The secondary objective of this study was to compare the effect of two different doses of intravenous

dexamethasone on blood glucose concentration intra-operatively.

MATERIALS AND METHODS

This prospective, randomized, double-blind study was conducted in anesthesiology department of G.R. Medical College Gwalior. The study included 120 patients of ASA Grade I and II, age 20–60 years, weight 40–60 kg, who underwent elective surgery under spinal anesthesia. Prior ethical permission was taken from the institutional ethical committee and review board.

- By considering study conducting by Parthasarathy et al.,² we considered comparison of visual analog scale (VAS) score in two groups at different time. The maximum sample size was achieved at 5 h. Considering mean VAS score in two groups 4.20 ± 0.41 and 4.0 ± 0 in saline group, sample size was calculated using formula.

$$n = 2S^2 (Z\alpha/2 + Z1-\beta)^2$$

Where S^2 is pooled variance = 0.28

Considering 5% α error

$$Z\alpha/2 = 1.96 \text{ and } 80\% \text{ power of test } Z1-\beta = 0.84$$

Δ = anticipated mean difference = 0.2

We obtained $n = 39$, approximate to 40. Hence, 40 patients were assigned in each group and total sample size was 120.

The patients were randomized on the day of surgery into 3 groups of 40 each by computer-generated random number Table. It was a double-blinded study as the drug was prepared by other person and characteristics in a pro forma were noted by someone else.

Group A: $n = 40$ (i. v. 2 mL normal saline [0.9%]).

Group B: $n = 40$ (i.v.4 mg dexamethasone).

Group C: $n = 40$ (8 mg dexamethasone).

Inclusion criteria

Patients giving consent, between age 20 - 60 years and belonging to ASA grade I and II, were included in the study.

Exclusion criteria

The following criteria were excluded from the study

1. Patients who had any deformity or local pathology in lumbar spine region
2. Patients with a history of convulsions, allergy to the drugs used, bleeding disorders, motion sickness, PONV, or addiction
3. Patients with severe neurological deficit, body mass index (BMI) $> 35 \text{ kg/m}^2$
4. Patients with significant cardiovascular, pulmonary, hepatic, renal, metabolic disease.

Pre-anesthetic checkup was done on the day before surgery and included a complete history, general and systemic

examination, and local examination of lumbar spine region. Pulse rate (PR), blood pressure, respiratory rate, and weight and height of the patients were noted. Relevant investigations were done in all the patients. Informed consent was obtained for performance of subarachnoid block after complete explanation about the study protocol and the procedure.

On arrival in the operating room, fasting status (at least for 6 h), and written consent was checked. Intravenous access with 18 G cannula was secured, and patients were preloaded with Ringer’s Lactate 10 mL/kg. All routine monitors were attached, and preoperative baseline readings of non-invasive blood pressure, heart rate (HR), and oxygen saturation were noted. All participants in 3 groups received study drug at the same period of time. Spinal anesthesia was performed at L3–L4 interspace with 0.5% hyperbaric bupivacaine using the midline approach. Total volume of intrathecal drugs in all three groups was 3 mL which was injected over 30 s with the patient in sitting position using a 25 G Quincke spinal needle. The patient was placed in supine position immediately after spinal injection. Intraoperative fluid management was done according to the blood loss and hemodynamic parameters. Following characteristics were recorded and entered into pro forma for statistical analysis.

1. Blood glucose level was checked by calibrated glucometer when the patient was taken to the operation room at 0 h (T0) and every hour thereafter as T1 (1 h), T2 (2 h), and T3 (3 h)
2. Severity of post-operative pain was based on VAS and was measured using 100 cm ruler according to subject assessment by the patient at 30 min and at 1, 2, 3, 6, 12, and 24 h
3. Blood pressure, HR, and respiratory rate were assessed at 30 min, then at 1, 2, 3, 6, 12, and 24 h
4. Time to first rescue analgesia, nausea, and vomiting was also assessed. Rescue analgesia consisted of an injection of diclofenac 75 mg intramuscular if the VAS is >50
5. Various complications (nausea, vomiting, shivering, tachycardia, hypertension, bradycardia, hypotension, and respiratory depression) were also observed and notified
6. Severity of post-operative vomiting was measured by Likert scale and if scale was >1, then injection metoclopramide 10 mg intravenously was used.

VAS at first pain medication

0	No pain
1–25	Mild pain
26–50	Moderate pain
51–75	Severe pain
76–100	Very severe pain

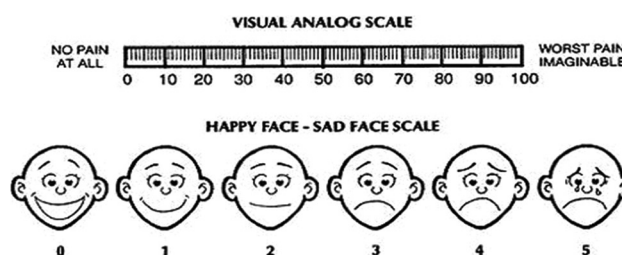
Likert scale for vomiting

0	None
1	1 Episode in 24 h
2	2–5 episodes in 24 h
3	6 episodes or more in 24 h or need for iv fluids
4	Hospitalization required

Grades to severity of vomiting

1	2	3	4
None	Mild	Moderate	Severe

Scale



Statistical analysis

Sample size was calculated at 95% confidence level, 80% study power, and α -error of 0.05 assuming S.D. of 2.132 as per the results of previous study. Data were analyzed and statistically evaluated using SPSS-PC-25 version.

Quantitative data were analyzed by the Student’s t-test (unpaired) or Mann–Whitney “U” test, while for more than two groups comparison, ANNOVA test or Kruskal–Wallis H test was used. Qualitative data were tested by Chi-square test or Fisher’s exact test. $P < 0.05$ was considered statistically significant.

RESULTS

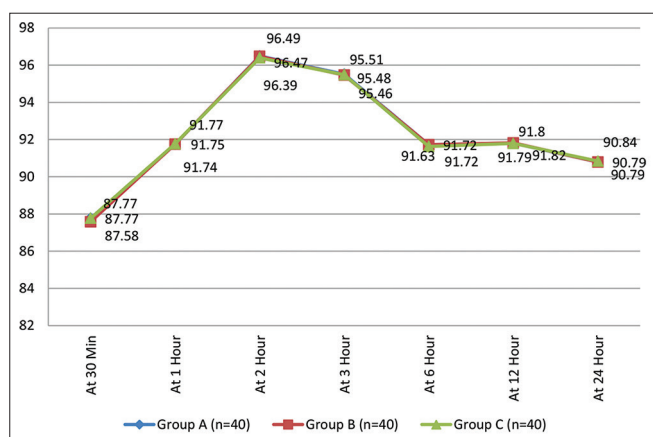
The mean age, body weight, height, BMI, SEX ratio, and duration of surgery were similar in both the groups with no statistical significant difference. ($P > 0.05$) as seen in Table 1.

Vital parameters such as HR, systolic BP, diastolic BP, mean BP, respiratory rate (RR), and SPO_2 were comparable in all three groups at all time intervals ($P > 0.05$) (Graph 1).

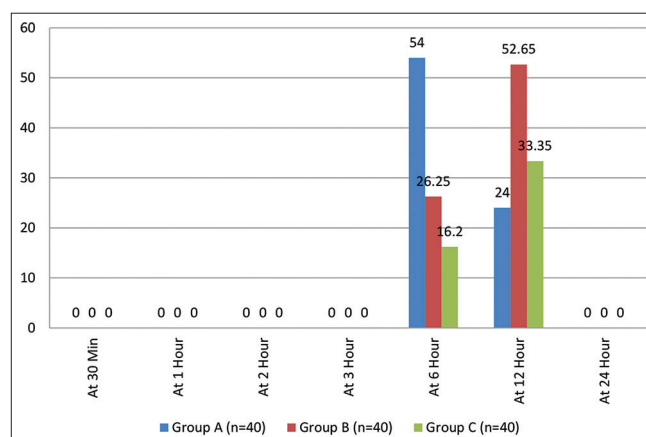
As per Graph 2, Group A has significantly lower blood sugar level in comparison to Group B and C in period T1, T2, and T3. Similarly, Group B is having less blood glucose level in comparison to Group C. Although there is highly significant rise in blood glucose level, it was well below the recommended guidelines (< 180 mg/dL) for the treatment of intraoperative hyperglycemia⁸⁻¹⁰ Hence, none of the patient required insulin treatment.

Demographic parameter	Group A (n=40)	Group B (n=40)	Group C (n=40)	P-value
Age (years)	42.98±11.70	40.35±11.64	44.98±10.74	0.19
Weight (in kg)	58.68±1.59	58.35±1.62	57.45±2.67	0.02
Height (in cm)	162.65±7.11	163.23±8.02	162.45±4.63	0.86
BMI (kg/m ²)	22.25±1.87	21.93±2.12	21.75±1.0	0.42
Duration of surgery (min)	130.75±17.92	122.0±22.94	128.13±28.34	0.23
Sex ratio (m/f)	19/21	21/19	19/21	0.87

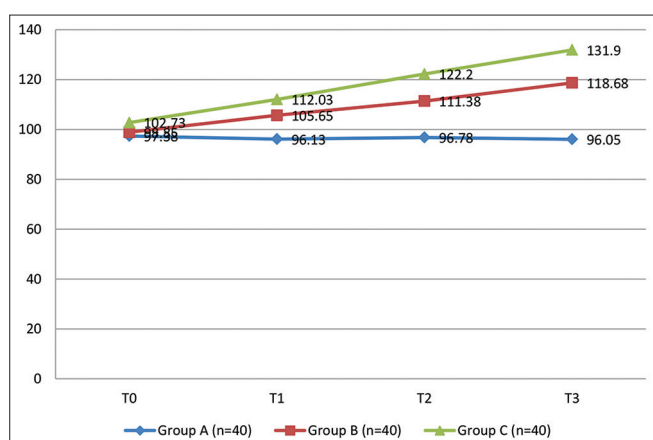
BMI: Body mass index



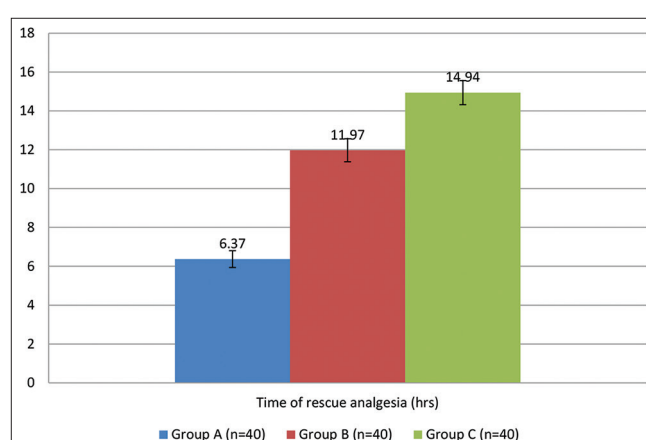
Graph 1: Trend of mean arterial blood pressure (mm of Hg) in study subjects



Graph 3: Changes in visual analog scale score in different groups at different interval



Graph 2: Perioperative blood glucose level in different groups at different interval



Graph 4: Time of rescue analgesia (h) of study participants

As seen in Graph 3, VAS scores were significantly lowest in group C at 6 h ($P < 0.01$) but at 12 h due to administration of rescue analgesic they were lowest in group A.

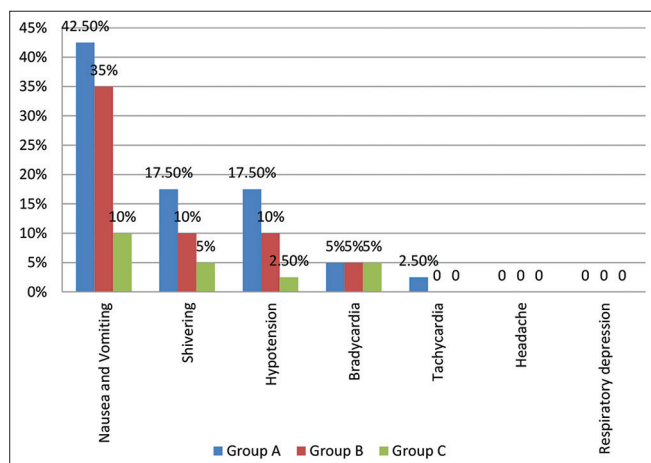
As per Graph 4, Time of rescue analgesia of the study participants showed a highly significant inclining trend between group A to Group C ($P < 0.01$).

As shown in Graphs 5 and 6, the incidence of nausea and vomiting was significantly lower in Group C with lowest Likert score ($P < 0.01$).

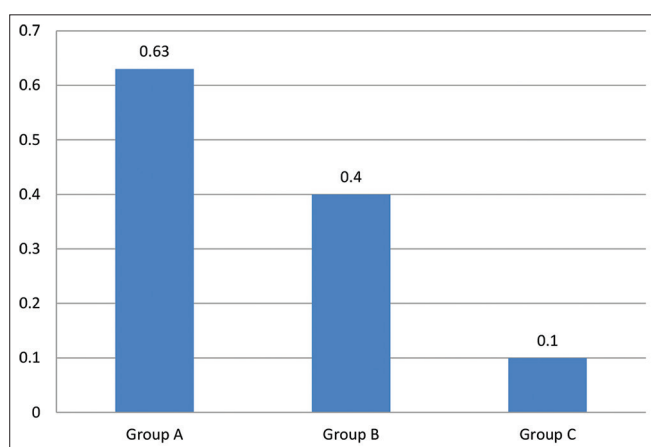
Shivering, bradycardia, and hypotension were statistically insignificant among 3 groups ($P > 0.05$).

DISCUSSION

Blood glucose level throughout the intraoperative period is a point of concern in major surgeries. Apart from blood glucose, inadequate post-operative pain relief has harmful physiological and psychological consequence which delays recovery, increases postoperative morbidity, and increases the duration of hospital stay.¹¹



Graph 5: Postoperative complications



Graph 6: Likert score

Various drugs are used to enhance the patient’s compliance during spinal anesthesia. Because of the diverse effects on various systems of the body, steroids are widely used group of drugs in the present day practice.¹²

In our study, demographic data were comparable in three groups ($P>0.05$) as seen in Table 1. PR, systolic blood pressure, diastolic blood pressure, mean arterial pressure, RR, and SPO_2 showed no statistically significant difference among the groups ($P>0.05$) (Graph 1).

The perioperative blood glucose levels were highest in Group C, with $P<0.01$ (Graph 2) which were statistically significant. The findings of our study coincided with the study conducted by Murphy *et al.*,¹³ Godshaw *et al.*,¹⁴ Gulmez *et al.*,⁷ and Purushothaman *et al.*¹⁵

Glucocorticoids have a ceiling effect on analgesics, thus not being sufficient as monotherapy after extensive surgery. It was found that, although dexamethasone provided postoperative analgesia, it was more in Group C (8 mg) than Group B (4 mg) ($P<0.01$). Similar findings were seen in a study done by Lakhan *et al.*¹⁶

VAS score was higher in Group A as compared to B and C (Graph 3). Time to first rescue analgesia was higher in Group C as compared to Group B and Group A ($P<0.01$) (Graph 4).

Dexamethasone has anti-emetic properties through the following mechanisms: anti-inflammatory effect, direct central action at the solitary tract nucleus, interaction with the neurotransmitter serotonin, and receptor proteins tachykinin NK1 and NK2, alpha-adrenaline, etc., regulation of the hypothalamic pituitary adrenal axis. Incidence of PONV was lowest in Group C as compared to other groups ($P<0.01$) (Graph 5). Our study findings were supported by a study done by Parthasarathy *et al.*,² All three groups were comparable in terms of side effects.

Limitations of our study

The major limitation of our study was that the investigator was unable to objectively quantify and evaluate postoperative pain, nausea, and vomiting, which being a subjective experience can be a major limiting factor in comparing and estimating the effectiveness of various modalities of treatment.

CONCLUSION

Administration of 8 mg i.v. dexamethasone after spinal anesthesia is more efficient than 4 mg dexamethasone in reducing postoperative pain, the requirement of rescue analgesia on the 1st postoperative day, and the incidence of PONV. Although its administration was associated with hyperglycemia in the perioperative period, it was not up to the extent of requiring any intervention.

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Author's Contribution

ST - Interpreted the results; reviewed the literature and manuscript preparation; **SuG** - Concept and design of the study, prepared first draft of manuscript; **AG** - Concept, coordination, statistical analysis, and interpretation; **ShG** - Preparation of manuscript and revision of the manuscript; **DK** - Coordination and manuscript revision.

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