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Efficacy of intravenous dexamethasone for post-operative pain relief in elective cesarean section

Swetha Purohit[1], Chandrashekarappa Kavi[2], Shobha MM[3]

[1]Associate Professor, [2]Professor, [3]Assistant Professor, Department of Anesthesiology, Subbaiah Institute of Medical Sciences, Shivamogga, Karnataka, India

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ABSTRACT

Background: Various additives have been evaluated for the purpose of enhancing quality of analgesia and prolonging duration of spinal anesthesia. **Aims and Objectives:** This randomized study was conducted to evaluate the efficacy of intravenous dexamethasone in spinal anesthesia. **Materials and Methods:** A total of 100 patients scheduled for lower segment cesarean section under spinal anesthesia were randomly allocated into two groups, Group-1 and Group-2, including 50 patients each. All the patients received injection bupivacaine 0.5% heavy 10 mg for spinal anesthesia. Group-1 received injection dexamethasone 8 mg intravenously, and Group-2 received injection normal saline 2 cc immediately after spinal anesthesia. Duration of sensory and motor block, post-operative analgesia, visual analog pain scale (VAS) score, time of rescue analgesia, total analgesic requirement in the first 24 h, intra- and post-operative hemodynamics, and side effects if any were recorded. **Results:** The mean duration of sensory block (min) in Group-1 and Group-2 was 162.50 and 106.17, respectively. Time to the requirement of first rescue analgesia was 8.67 h in Group-1 and 4.40 h in Group-2. Significant changes seen in VAS score in post-operative period after 1 h of surgery in Group-1 and Group-2. Group-1 had more duration of sensory block, prolonged requirement of first rescue analgesia. Duration of motor block and intra- and post-operative hemodynamic parameters was comparable in both the groups. No side effects were recorded in both the groups. **Conclusion:** We conclude that administration of dexamethasone 8 mg intravenously prolongs the duration of post-operative analgesia and sensory block in patients undergoing lower segment cesarean section under spinal anesthesia.

Key words: Dexamethasone; Post-operative analgesia; Spinal anesthesia

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INTRODUCTION

Spinal anesthesia technique is widely used for perioperative anesthesia and analgesia in cesarean section patient. There is a distinct advantage of this severing as ambulatory anesthesia and reducing immediate post-operative pain.[1] Lack of control of post-operative pain following cesarean section causes high chance of morbidity and increases the risk of chronic persistent pain in the future.[2,3] Furthermore, due to inadequately controlled post-operative pain patients will have difficulty with walking and to carry out minimal routine activities, which can lead to complications of recumbency such as atelectasis, pneumonia, and venous thromboembolism.[4] Unwanted effects of anesthetic drugs which are used during general anesthesia, maternofetal transfer, stress of laryngoscopy, and tracheal intubation can be avoided with the use of regional anesthesia.[5]

Chemical mediators responsible for pain includes proinflammatory cytokines, serotonin, bradykinin, as well prostaglandins. Control of post-operative pain is an important part of the management of any surgery. It becomes more important in cases of LSCS because post-operative pain, if severe, may affect the ability of woman to lactate the new born which can cause catastrophic consequences such as hypoglycemic seizures in new-born.

Address for Correspondence:
Dr. Swetha Purohit, Associate Professor, Department of Anesthesiology, Subbaiah Institute of Medical Sciences, Shivamogga, Karnataka, India. **Mobile:** +91-8151065298. **E-mail:** swethabadami84@gmail.com

Moreover, studies have also suggested that inadequate control of pain in post LSCS patients is associated with a higher incidence of post-traumatic stress disorder. Therefore, adequate post-operative pain relief is the cornerstone of the management of these patients.[6]

The duration of analgesia and sensory block is relatively short with single shot subarachnoid block. Due to which, adjuvants such as fentanyl, morphine, clonidine, ephedrine, pethidine, and dexmedetomidine are used along with local anesthetic.[7] However, these do have a few adverse effects such as sedation, nausea, vomiting, pruritus, respiratory depression, hypotension, and psychotomimetic effects.[8] Hence drugs with minimal adverse effects and prolonged analgesia are preferred.

Glucocorticoids are strong anti-inflammatory agents, whose properties can be used to control post-operative pain following various surgeries. Dexamethasone has also an antiemetic effect, in addition to its anti-inflammatory and analgesic effects.[9] The suggested theories for mechanism of action of glucocorticoids include: Inhibition of production of inflammatory mediators (prostaglandin, bradykinin), preventing reduction of "pain threshold," which occurs in surgeries, and reducing tissue swelling due to anti-inflammatory effects and, therefore, inhibit nerve compression by inflammatory tissue.[9]

Dexamethasone is potent, selective glucocorticoid having minimal mineralocorticoid action.[10,11] Systemic anti-inflammatory and immunosuppressive properties may be responsible for the prolongation of analgesia when administered intravenously. They also have a proven efficacy in prolonging the effects of regional nerve blocks.[12] We decided to conduct the present study to look for the effects of intravenous (IV) dexamethasone on subarachnoid block in patients posted for lower segment cesarean section.

The aim of our study was to evaluate the efficacy of IV dexamethasone in prolonging the duration of post-operative analgesia and to study the effect on spinal anesthesia (sensory and motor block). Secondary outcomes include effects on hemodynamics and incidence of complications.

Aims and objectives

The aim was to evaluate the efficacy of IV dexamethasone in prolonging the duration of post-operative analgesia following spinal anaesthesia.

MATERIALS AND METHODS

This study was a prospective randomized controlled study. It was conducted on 100 pregnant women from June 2018 to June 2019. The Institutional Ethical Clearance and informed consent were taken. Patients between the age 25 and 30 years posted for elective cesarean section belonging to the American Society of Anesthesiologists (ASA) health status classes I and II were included in the study. Patients with bleeding diathesis, severe hypovolemia, infection at the site of injection, fetal distress, severe preeclampsia, eclampsia, cord prolapse, and patients on chronic steroid therapy, were excluded from the study.

Patients were randomly divided into two groups, Group-1 and Group-2, including 50 patients each. Randomization was done using random numbers in sealed envelopes and this was assigned to the patients by an anesthesiologist blinded to the procedure. Spinal anesthesia with 0.5% heavy bupivacaine 2 cc was given in both the groups. All routine investigations for elective surgery and a pre-anesthetic examination were done. An informed written consent was taken after explaining the procedure to the patients. Before administering spinal anesthesia, in the operation theater, baseline vital values of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and oxygen saturation were recorded. IV access was secured, and injection ondansetron 4 mg given through IV route. 10 mg/kg Ringer lactate solution was used IV in all patients as preload before subarachnoid block. Spinal anesthesia was administered with a 26-gauge Quincke needle, under aseptic precautions, intrathecally at L3–L4 or L4–L5 inter-vertebral space with the patient in sitting position. Injection bupivacaine 0.5% heavy 10 mg, used as the anesthetic agent, was injected after a successful dural puncture. Patients were placed supine after administration of drug. Pinprick method with a small gauge needle was used to check for the sensory level and the assessment of motor block was done using Bromage score. The level of D6 block was achieved in all patients. Visual analog scale (VAS) scores, which were explained to all patients preoperatively, were recorded for 24 h postoperatively.

All the patients were allocated randomly to either case group who received 8 mg IV Dexamethasone (Group-1) or control group who received 2 mL normal saline (Group-2) based on simple randomization process using generated random digit numbers by the Statistical Package for the Social Sciences (SPSS). Neither the participants, nor the investigators responsible for following the participants, collecting data and assessing the outcomes were aware of the intervention assignments.

After subarachnoid block, systolic and DBPs were recorded every 5 min till the end of surgery. The time from intrathecal drug administration to the time of the first complaint of pain or VAS score more than 4 was recorded as duration of analgesia. Additional analgesia was administered only

when the VAS score was more than 4 or when the patient complained of pain, whichever occurred earlier. This was termed as the rescue analgesia. The time of rescue analgesia and total analgesic dose in the first 24 h was recorded. Data were compiled systematically and Mann–Whitney U-test was used to analyze the data. P<0.05 was considered statistically significant and P<0.001 as highly significant.

Statistical analysis

SPSS version 19.0 was used for statistical analysis. Assuming alpha error of 0.05 and power of 90% the effective sample size on the basis of VAS score over 24 h was found to be around 37. To control the confounding variables, the sample size was increased and rounded off to 50. Hence, we used 50 patients per group in this study. t-test was used to analyze the parametric variables such as age, weight, HR, SpO_2, SBP, and DBP, whereas Mann–Whitney test was used for non-parametric data like VAS. *P*<0.05 was considered statistically significant.

RESULTS

This study included 100 pregnant women who were divided into two equal groups. Patient's demographic profiles were matched with regard to age, weight, and ASA status in both the groups (Table 1). In the present study, mean duration of sensory block in Group-1 was 162.50 min, whereas, in Group-2, it was 106.17 (Figure 1). The difference was statistically significant with P<0.001, whereas the difference was statistically insignificant with respect to the mean duration of motor block. The duration of motor block in Group-1 and Group-2 was 169.5 and 163.17, respectively, (P>0.05) (Figure 1).

In addition, there was also a high statistically significant difference with respect to the mean time to requirement of the first rescue analgesia, which was 8.67 h in Group-1 and 4.40 h in Group-2, (P<0.001) (Figure 2). Both Groups 1 and 2 had significant changes with respect to the VAS score in the post-operative period after 1 h of surgery (Figure 3). As compared to pre-operative value, there was no significant difference seen in HR, SBP, DBP, and oxygen saturation in both the groups throughout the study (Table 2).

Table 1: Demographics

S. No.	Group-1	Group-2
Age (years)	28.4	28.9
Weight (Kgs)	66.8	68.2
ASA	Gr-1: 27 Gr-2: 23	Gr-1: 24 Gr-2: 26
BMI	26.5	27.2

ASA: American society of Anesthesiologists, BMI: Body mass index

DISCUSSION

The study comprised 100 patients who underwent lower segment cesarean section under spinal anesthesia. The main aim was to analyze effectiveness of a single dose IV dexamethasone on post-operative pain. Since inflamation

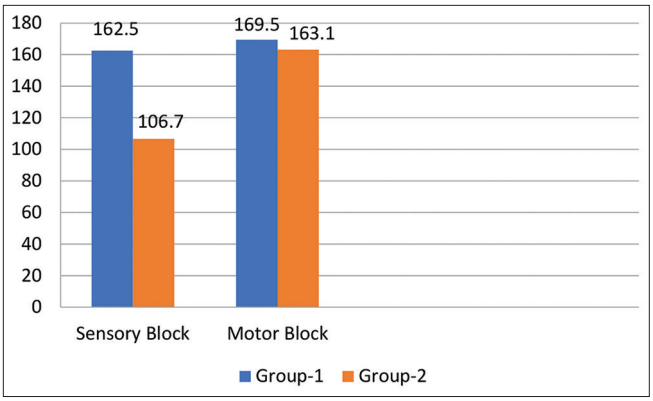

Figure 1: Duration of sensory and motor block in both the groups

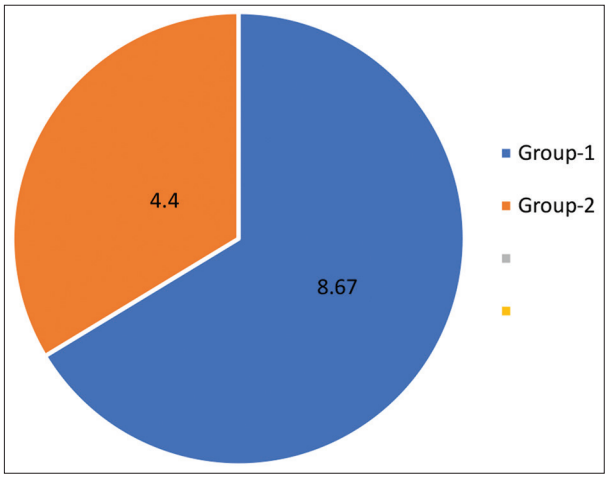

Figure 2: Mean time to requirement of the first rescue analgesia (in hours)

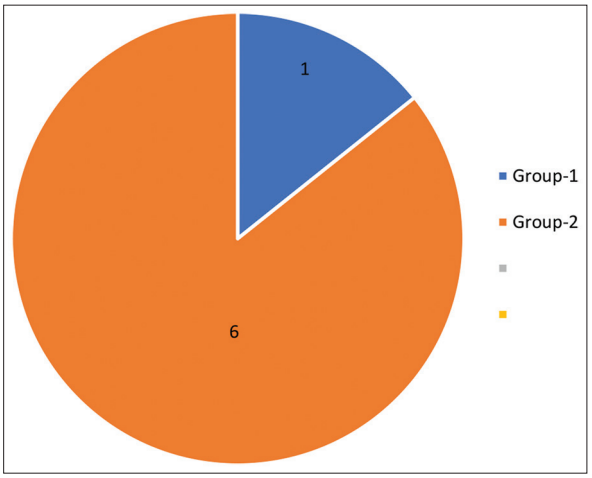

Figure 3: Mean VAS score at 1 h after surgery

Table 2: Differences in parameters in both groups

Parameters (Mean)	Pre-operative Group-1	Post-operative Group-1	Pre-operative Group-2	Post-operative Group-2
Heart rate	80 beats/min	81 beats/min	78 beats/min	82 beats/min
Systolic blood pressure	122 mm Hg	122 mm Hg	118 mm Hg	122 mm Hg
Diastolic blood pressure	80 mm Hg	82 mm Hg	76 mm Hg	80 mm Hg
Oxygen saturation	98%	97%	97%	97%

caused by release of proinflammatory cytokines is one of the key factors in causation of pain and vomiting, steroids by their anti-inflammatory effect are expected to reduce the pain as well as nausea and vomiting.

The results of the present study show a positive response for prolonging the duration of sensory block and post-operative analgesia by administering of dexamethasone (8 mg) intravenously in patients undergoing lower segment cesarean section under spinal anesthesia without any complications. Multimodal analgesia is the most appropriate and feasible modality to render patient pain free.[13,14] Strong anti-inflammatory properties of dexamethasone have caused to introduction of "dexamethasone induced post-operative pain reduction" theory. Although analgesic mechanism of dexamethasone is still unclear, it seems that a decrease in cyclooxygenase and lipoxygenase production, through inhibition of peripheral phospholipase, plays a main role.[15]

Intrathecal adjuvants such as alpha 2 agonists and opioids have been used for the prolongation of regional blockade. This also holds good for additives through IV route which gives us the multimodal analgesia that is the most feasible modality for post-operative pain control.[13,14] Dexamethasone, a highly potent glucocorticoid, has been used successfully for prolonging the action of local anesthetic drugs.[10,11] This action of Dexamethasone is due to when used perineurally causes vasoconstriction and slower the absorption local anesthetic drug and prolongs its action.[9] There are various studies reporting perineural use of dexamethasone in regional nerve blocks for the prolongation of both sensory and motor block.[14,16-18]

Several authors in their studies have inferred that perineural and IV dexamethasone have equal efficacy. Abdelmonem and Rizk, in their study, concluded that post-operative analgesia can be extended by dexamethasone, whether IV or local is added to bupivacaine in perianal block.[19] Desmet et al.,[20] and Maged et al., had similar findings in their study, where they found that both IV and local subcutaneous infiltration of dexamethasone to the wound markedly reduced the sensation of pain and the need for post-operative analgesics up to 24 h after the surgery.[21]

The optimal dose of dexamethasone is still not defined. Dexamethasone dosage ranges from 4 mg to 16 mg and differs in different types of surgeries. Oliveira et al., in his study, divided the patients into three groups based on the dose of dexamethasone used, low dose (0.1 mg/kg), intermediate dose (0.1–0.2 mg/kg), and high dose (more than 0.2 mg/kg). It was found that dexamethasone at 0.1 mg/kg is most effective in terms of adjuvant in multimodal strategies to reduce post-operative pain and opioid consumption.[11] The difference in dose of dexamethasone may be dependent on the extent of surgery and intensity of tissue damage and hence the requirement.[16] In our study, we found that 8 mg dexamethasone to be sufficient as an adjuvant for reducing post-operative pain and opioid consumption.

Shahraki et al., in his study, found that within-group comparisons including severity of pain, MAP, RR, and HR had significant differences ($P<0.001$ for all variables) during the study period. Between group comparisons indicated significant differences in terms of pain severity ($P<0.001$), MAP ($P=0.048$), and HR ($P=0.078$; marginally significant), which, in case group, were lower than the control group. On the basis of these findings, the authors concluded that IV dexamethasone efficiently reduces post-operative pain severity and the need for analgesic consumption after cesarean section.[22] Similar beneficial effects of dexamethasone were also reported by authors such as Coloma et al.,[23] and Romundstad et al.,[24] after various ambulatory surgeries.

The time of onset of action of glucocorticoid is generally from 1 to 2 h. Hence, it has to be administered couple of hours before the incision and drug administered immediately before the incision does not suppress mediators of inflammation. This is because glucocorticoids exert their effect through a gene transcription by altering protein synthesis. Several studies have been conducted with variations in the time of administration of drug. As the analgesic effect is seen when the peak level of the drug is achieved, studies in which dexamethasone was administered early showed better post-operative pain relief and reduced analgesia requirement.[16,25] Bisgaard et al., have shown decrease in post-operative pain in patients undergoing laparoscopic surgery where they had administered dexamethasone 90 min before skin incision.[25] IV dexamethasone was administered immediately after spinal anesthesia in our present study.

Nonetheless, in the literature, it is studied that 8 mg is the most effective dose. It was found that single dose does not inhibit hypothalamic pituitary adrenal axis. In addition, there is no adverse effect seen as impaired wound healing, increase blood sugar level, and gastrointestinal discomfort.[4] Hence, it is unlikely that the patients in our study exhibited any delayed untoward effects.

Single dose of IV dexamethasone in otherwise healthy individuals is less likely to alter hemodynamic stability of the patients and virtually does no harm to the patients. Many authors reported that while single dose of dexamethasone is effective in reducing post-operative pain as well as incidence of nausea and vomiting it does not have any harmful effect on hemodynamic stability of the patients. Aldivia-Sánchez and Prieto-Duarte concluded that dexamethasone better controlled postsurgical pain and had adequate hemodynamic stability.[26] Similar hemodynamic stability was also reported by the authors such as Buland et al.,[27] and Ituk and Thenuwara.[28]

In our study, VAS was significantly lower with dexamethasone group as compared to control group. We observed increase in the duration of post-operative analgesia and the first analgesic requirement was also prolonged. Prolongation of sensory blockade is also seen without delaying in motor blockade. These findings are in consistent with other studies where IV dexamethasone is proved better for post-operative pain relief.[11,29,30]

Mehdiratta et al.; in their study, observed that dexamethasone 8 mg administered IV before skin incision for cesarean delivery under spinal anesthesia and in combination with a multimodal post-operative analgesic regimen did not reduce maternal opioid consumption or pain scores. However, they also concluded that these findings need to be interpreted cautiously in light of the methodological limitations of their study.[31]

There are certain limitations to our study. We conducted this study only on ASA 1 and ASA 2 group of pregnant patients posted for lower segment cesarean section under spinal anesthesia. Second, we followed up the patients only till 24 h. The minimum therapeutic dose of IV dexamethasone capable of prolonging the duration of analgesia has not been evaluated. Hence, it is possible that dose used may have been more than the required.

Limitations of the study

Firstly, this study was conducted only on ASA 1 and ASA 2 group of pregnant patients. Secondly, the patients were followed up only till 24 hours.

CONCLUSION

The duration of post-operative analgesia and sensory block can be significantly prolonged with the administration of injection dexamethasone 8 mg IV ly in patients undergoing lower segment cesarean section under spinal anesthesia.

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Authors' Contributions:
SP- Concept, coordination, statistical analysis and interpretation, preparation of manuscript and revision of the manuscript; **CK-** Concept and design of the study, prepared first draft of manuscript; **SMM-** Interpreted the results; reviewed the literature and manuscript preparation.

Work attributed to:
Department of Anesthesiology, Subbaiah Insitute of Medical Sciences, Shivamogga - 577 222, Karnataka, India.

Orcid ID:
Dr. Swetha Purohit- https://orcid.org/0000-0002-0866-654X
Dr. Chandrashekarappa Kavi- https://orcid.org/0000-0002-1015-3233
Dr. Shobha MM- https://orcid.org/0000-0002-0970-8430

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