Analgesic Effect of Intravenous Dexamethasone Prior to Spinal Anesthesia Among Parturient Undergo Cesarean Section at Gandhi Memorial Hospital, Addis Ababa, Ethiopia, Prospective Cohort Study, 2019

Eyayalem Melese*, Adamu Tesfaye, Lemelem Getachew and Tinbet Daniel
Department of Anesthesia, Health Science College, Addis Ababa University, Ethiopia

Corresponding author: Mr. Eyayalem Melese, Department of Anesthesia, Health Science College, Addis Ababa University, Ethiopia, Tel: 251913002201; E-mail: eyayalem@yahoo.com

Keywords: Analgesic effect; IV dexamethasone; Spinal anesthesia; Cesarean section

Introduction

Cesarean section (CS) can be life-saving to both the mother and the fetus by preventing poor obstetric outcomes. However, there is a growing concern on the increasing percentage of the procedure of live births globally. The risks and costs associated with caesarean deliveries are significant, especially where there was no medical indication. 6.9% of CS performed in Addis Ababa had no medical indication [1].

According to the latest data from 150 countries, currently 18.6% of all births occur by CS, ranging from 6% to 27.2% in the least and most developed regions, respectively. Latin America and the Caribbean region have the highest CS rates (40.5%), followed by Northern America (32.3%), Oceania (31.1%), Europe (25%), Asia (19.2%) and Africa (7.3%). The use of CS worldwide has increased to unprecedented levels although the gap between higher- and lower-resource settings remains [2]. At national level, The Ethiopian national CS rate is low at 1.5%, while in Addis Ababa, the capital city, the CS rate is 21.8%. An increase in the rate of referral by health care workers and a decrease in hospital instrument deliveries can partially explain the increase in CS rate [3].

Spinal anesthesia has evolved as the preferred anesthetic technique for most cases of CS [4-6]. Spinal anesthesia is induced by injecting small amounts of local anesthetic into the CSF. Spinal anesthesia is easy to perform, reliable and avoids the depressant effects of anesthetic drugs and has the potential to provide excellent operating conditions for CS (Figure 1) [7]. The International goal for protection of future mothers is 80-90% of all Cesarean section to be carried out under spinal anesthesia [5].

By prolonging the duration of sensory-motor block and limiting the cumulative dose requirement of local anesthetics, co-administration of adjuvant has the potential to improve efficacy of regional blocks and decrease local anesthetic toxicity. They contribute in their own special manner to potentiate the analgesic effect of the local anesthetics [8]. Dexamethasone is a potent anti-inflammatory agent which has been investigated in the last decade for its role as an adjuvant to local anesthetics in neuroaxial as well as peripheral nerve blocks. Systemic anti-inflammatory and immunosuppressive properties may be responsible for the prolongation of analgesia when administered intravenously [9].

Abstract

Background: By prolonging the duration of spinal anesthesia sensory block co-administration of adjuvant has the potential to improve efficacy of regional blocks. However this technique has its own complications. Hence, drugs having minimal side effects and prolonged analgesia is always looked for. This is because postoperative pain in obstetric patients is left untreated and it’s the main cause of chronic pain among women. The aim of the study is to determine the effect of preoperative dexamethasone on prolongation of the analgesic effect of spinal anesthesia after elective cesarean section.

Methods: Sixty four pregnant women undergoing elective cesarean section were randomly assigned to two groups, and spinal anesthesia was administered with different approaches; Bupivacaine alone or bupivacaine with prior administration of IV dexamethasone. Thirty two parturient per group were randomly selected for quantitative determination of severity of postoperative pain and duration of postoperative pain management.

Results: The effect of preoperative dexamethasone on prolongation of the analgesic effect of spinal anesthesia after elective cesarean section were assessed. Groups’ comparison indicated significant difference in terms of severity of postoperative pain, in which the dexamethasone group were lower with p=0.018. Similarly, time to the requirement of first rescue analgesia was prolonged in dexamethasone group with median (interquartile range) score of 6.5 (2.4) as compared to non-dexamethasone group 4.1 (1.8).

Conclusion: Preoperative IV administration of dexamethasone 0.1 mg/kg before administrating spinal anesthesia for cesarean section is efficient in reducing postoperative.
Spinal anesthesia is the most commonly used anesthetic technique for lower abdominal surgeries and lower limb surgery. But it has the drawback of short duration of action and lack of postoperative analgesia. Larger dose of analgesic is required to provide pain relief and there may be a paradoxical effect where the administration of opioids to reduce pain can be the catalyst that sensitis patients to painful stimuli.

**Objective**

**General objective**
- To determine the effect of preoperative intravenous dexamethasone on prolonging the analgesic effect of spinal anesthesia after elective cesarean section in Ghandi Memorial Hospital.

**Specific objectives**
- To compare severity of early post-operative pain between two groups in first 24 hours using NRS score.
- To compare the time to requirement of the first rescue analgesia between the two groups.
- To compare total 24 hour analgesic consumption between two groups.

**Materials and Methods**

It is an institutional based Prospective observational cohort study design was conducted from January 2019 to May 2019. The study was conducted at Gandhi Memorial Hospital located in Addis Ababa the capital city of Ethiopia. The Hospital provides Gynecologic, Obstetric and many other reproductive health services. The hospital has 110 beds and an average of 25 new born delivered each day. The hospital has four operation theatres and average number of elective caesarian deliveries done at the hospital is four per day. All pregnant mothers who underwent elective caesarian section under spinal anesthesia at Gandhi Memorial Hospital, Addis Ababa, Ethiopia were a source population. Elective cesarean section patients falling in classification of American Society of Anesthesiologists (ASA) as Class II and Induction of spinal anesthesia using 2.5 ml of 0.5% Isobaric Bupivacaine was included in the study.

The Exclusion criteria were Mothers used combined spinal epidural anesthesia, Spinal anesthesia changed into General anesthesia or sedation intraoperative, Uses of other adjuvant like opioids, catecholamine’s, clonidine, tramadol, neostigmine and other adjuvant, Patient who take sedative or analgesics premedication within 24 hrs.
preoperatively and intraoperatively, Chronic steroid therapy and use of corticosteroids, using local anesthetics other than 12.5 mg of 0.5%

isobaric bupivacaine. Patients who have chronic pain and mothers with social problem, stress and Malingers, peripheral neuropathy or nerve injuries, Bleeding abnormality and Patients who took nerve block.

Sample size calculation

Sample size was determined by considering a power of 80%, confidence interval 95% and ratio of two groups to 1:1 which the mean results estimated from pilot study done prior to actual study. The pilot study sample size was determined by taking 10% of previous literatures sample size [26]. From pilot study mean score of time to requirement of first rescue analgesic in hrs was 7.6 ± 0.47 in dexamethasone group and 7.3 ± 0.3 in non-dexamethasone group (mean, SD). This sample size was determined using G-power version 3.1.9.2 and rechecked by manual calculation.

Where n=sample size per group

\[ Z_1 = 1.96 \text{ for a error of } 5\% (95\% \text{ confidence level}) \]

\[ Z_2 = 0.84 \text{ for } 80\% \text{ power} \]

\[ S_1 = \text{standard deviation in dexamethasone} \]

\[ S_2 = \text{standard deviation in non-dexamethasone} \]

Planning to get 80% chance of significant result and Adding 10% of non-response rate a total of 64 patients was involved in the study sample size was \[ n_1 = 32 \text{ and } n_2 = 32 \]  (Figure 2).

![Figure 2: Sampling procedure for elective cesarean section scheduled at Gandhi Memorial Hospital.](image)

Sampling procedure

Stratified Systematic random sampling technique used till to get the required sample size during the study period. The daily operation schedule list was used as a sampling frame. The situational analysis show that 16 patient who fulfill our inclusion criteria was operated in Gandhi Memorial Hospital log book per week; according to this data we had 128 patients in our study period from whom we collected data from only 64 patients. Therefore, \( K = N/n = 128/64 = 2 \) (skip interval) and the first participant (random start) was selected using lottery method. Then, every next patient included in this study from the daily operation schedule list.

Data collection

Data was collected from selected study participants using pretested questionnaire. Data was collected from January 01, 2019 to March 20, 2019. Anesthesia management for elective CS in the study hospital is carried out by trained Anesthetists. The data collection was done by Anesthetists and nurses after being familiar with the questionnaires and appropriate training. The principal investigator checked completeness of data every day. All patients who were scheduled for elective caesarean delivery who fulfill inclusion criteria and volunteer to take part in the study were instructed on how to self-report pain using the eleven point of Numerical pain rating scale (NRS) score 0 to 10 in the morning of operation day at ward with trained nurses or anesthetists. Patients were followed for 24 hrs. The primary outcome measure is NRS score, with being no pain to 10 the worst imaginable pain. Time to requirement of first rescue analgesia and total postoperative analgesic consumption was used to assess efficacy of analgesia as secondary outcome measures. Additionally time to maximum sensory block onset was assessed.

Anesthesia management for caesarean delivery clients in the study hospital is usually carried out by Anesthetist. Pre anesthetic evaluation is done before surgery. Patients usually pre medicated with metoclopramide 10 mg IV. Vital sign, Organ function test together with history and physical examinations are among the parameters used to decide for anesthesia plan and weather to cancel or proceed. Monitoring equipment applied and prophylactic IV dexamethasone might administer 1 minute before spinal injection depending on anesthetist preference. During this time data collectors identify patients who were given 0.1 mg/Kg IV dexamethasone and who were not and assign the study participant to the appropriate group. During preparation of the skin and during spinal anesthesia induction, lactated Ringer’s or normal saline solutions were administered for co-loading. Sub arachnoids block is done with 0.5% of 2.5 ml bupivacaine for all parturient. Level of block was checked with needle pin prick. The level of sensory block was evaluated with cold sensation.

On arrival to the recovery Postoperative pain was assessed in all groups using a NRS for pain assessment. The scale consists of horizontal lines ranging from 0 (no pain) to 10 (worst imaginable pain). Asked to report their pain based on 11 point Numerical rating scale (NRS) score recorded at recovery (0 hrs) and then every three hours for the first six hours and every six hours for the remaining postoperative period until 24 hr. The pain score was assessed during a quiet breathing period or at rest (static NRS) and after voluntary cough (dynamic NRS). The time to requirement of first rescue to analgesia was recorded from patient chart after admission to recovery and total analgesic consumption of each patient was recorded. The principal investigator checked completeness of data every day (Figure 3).

![Figure 3: NRS score Adopted from the National Initiative on Pain Control™ (NIPC™).](image)
Data processing and analysis

Data was checked manually for completeness and then it was coded and entered, cleaned and analyzed with SPSS version 20 computer program. Descriptive statistics was used to summarize data, tables and figures. Chi square test used for discrete variables and student’s t-test used for comparing numerical variables of normally distributed data or Mann-Whitney U test used for skewed data of two groups. Data expressed in terms of mean ± SD for normally distributed data and median ± inter quartile range for skewed data. P-value less than 0.05 considered as statistically significant. The results were presented by using text, tables, and graphs. To assure the quality of data, training on the objectives and relevance of the study and brief Orientations on the Wilk test, p value>0.05. An independent-samples t-test was conducted to compare the demographic characteristics scores between two groups with the value as shown in (Table 1).

There was no statistically significant difference in scores between two groups (Table 2).

A chi-square test indicates there was no significant difference between the dexamethasone and non-dexamethasone groups regarding clinical characteristics’ including parity and history of previous CS. Results between groups were comparable. An independent-samples t-test was conducted to compare the surgery time score between two groups. There was no significant difference in scores between two groups (Table 2).

### Results

Thirty two patients were studied in each group. All patients were included in the study as they were complete and showed consistency of response. All the demographic data were normally distributed (Shapiro Wilk test, p value>0.05). An independent-samples t-test was conducted to compare the demographic characteristics scores for dexamethasone and non-dexamethasone groups. There was no significant difference in scores between two groups with the value as shown in (Table 1).

### Table 1: Demographic characteristics of the study participants, who underwent Elective cesarean section at Gandhi memorial hospital, Addis Ababa, Ethiopia.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Dexamethasone group (n=34)</th>
<th>Non-dexamethasone group (n=34)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>26.2 ± 3.48</td>
<td>26.59 ± 3.41</td>
<td>0.66</td>
</tr>
<tr>
<td>Height in cm</td>
<td>164 ± 3.93</td>
<td>162.8 ± 3.48</td>
<td>0.206</td>
</tr>
<tr>
<td>Weight in kg</td>
<td>63.7 ± 4.71</td>
<td>62.8 ± 5.4</td>
<td>0.496</td>
</tr>
<tr>
<td>BMI</td>
<td>23.8 ± 1.8</td>
<td>23.6 ± 1.98</td>
<td>0.85</td>
</tr>
</tbody>
</table>

Values are presented as: Mean ± SD, independent student t-test and p<0.05 were taken statistically significant.

### Table 2: Clinical characteristics of patients who underwent Elective cesarean section at Gandhi memorial hospital, Addis Ababa, Ethiopia, 2018/19.

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Dexamethasone exposed</th>
<th>Non-dexamethasone exposed</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parity</td>
<td>Nulli parous</td>
<td>14 (43.8)</td>
<td>15 (46.9)</td>
</tr>
<tr>
<td>History of previous C.S.</td>
<td>Yes</td>
<td>13 (20.3)</td>
<td>15 (23.4)</td>
</tr>
<tr>
<td>BMI</td>
<td>40.7 ± 7.93</td>
<td>39.9 ± 8.02</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Values are presented as frequency (%), chi square test and mean ± standard deviation, independent t-test.

### Table 3: Comparison of postoperative pain using 11 point NRS score (0-10) at rest and voluntary coughing.

<table>
<thead>
<tr>
<th>Time interval</th>
<th>0 hr</th>
<th>3 hr</th>
<th>6 hr</th>
<th>12 hr</th>
<th>18 hr</th>
<th>24 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Non-dexamethasone</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>P value</td>
<td>0.01*</td>
<td>0.001</td>
<td>0.001</td>
<td>0.004*</td>
<td>0.0001*</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed using median (IQR); Mann-Whitney U test *=statistically significant.
An independent-samples t-test was conducted to compare the minute to achieve maximum sensory level for dexamethasone and non-dexamethasone groups. There was no significant difference in scores between two groups (Table 5).

Table 5: The minute to reach maximum sensory level.

<table>
<thead>
<tr>
<th></th>
<th>Dexamethasone group</th>
<th>Non-dexamethasone group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minute of to achieve maximum sensory level</td>
<td>4.06 ± 1.73</td>
<td>4.64 ± 1.42</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation, independent samples t-test, p value<0.05 statistically significant.

Discussion

In this study, confounding factors such as demographic characteristics, duration of surgery and History of previous CS were all comparable between the groups thus; the difference in pain severity, time requirement of first rescue analgesia and total 24 hr analgesic consumption between groups was likely due to exposure of dexamethasone between the groups.

The study was seen exposure of dexamethasone decrease postoperative pain, reduced total Tramadol consumption, and prolonged the median time to requirement of first rescue analgesia in postoperative period after elective cesarean section compared to patients who didn’t take dexamethasone. Strong anti-inflammatory properties of dexamethasone have caused to introduction of "dexamethasone induced postoperative pain reduction" theory; some previous studies demonstrate that administration of intravenous dexamethasone have benefit on postoperative analgesia management in different surgeries undergoing under spinal anesthesia [24,27-32]. Although analgesic mechanism of dexamethasone is still unclear, it is believed that Inhibition of cyclooxygenase (COX) enzyme, which takes part in the biosynthesis of prostaglandins (PGs) and thromboxane (TX), is the mechanism of action. PGs and TXs are important mediators of fever, pain, and inflammation [33-35].

Dose of IV dexamethasone differs in different types of surgeries ranging from 4 mg to 16 mg, however; the optimal dose is still not defined. In a study conducted by oliveria et al., comparison into 3 groups, low dose (0.1 mg/kg), 0.2 mg/kg and >0.2 mg/kg. They concluded that a dose of dexamethasone at 0.1 mg/kg is an effective adjuvant in multimodal strategies to reduce postoperative pain and analgesic consumption. This is similar to the dose which used in our study [36].

Comparing the NRS score between dexamethasone and non-dexamethasone groups was the main interest of our study. We observed that NRS median score of 1 (1-2.75) at 3rd hr,3 (2-3) at 6th hr, 3.5 (2-4) at 12th hr and 3 (2-4) at 24th hr at rest for dexamethasone groups and 3.5 (1.25-4) at 3rd, 4.5 (3-6) at 6th, 4.5 (3-6) at 12th hr and 4 (3-6) at 24th hr for non-dexamethasone group. This was significantly lower for dexamethasone group with p value 0.01, 0.0001, 0.016, 0.004 and 0.0001 respectively. This observation was in line with randomized control study done in Egypt by Ahmed M Maged, et al. in 2017 in patients undergoing cesarean section under spinal anesthesia. Which showed that mean VAS Score at 6, 12 and 24 in Dexamethasone group were 4.12 ± 1.22, 5.58 ± 1.5 and 7.7 ± 1.6 in order given, which were significantly lower compared to placebo group with mean VAS score.

The data for the time to the requirement of first rescue analgesia was not normally distributed. Mann Whitney U test’ used for analysis and median score used to present the values. A Mann-Whitney U Test revealed significant difference in the time to the requirement of first rescue analgesia of dexamethasone group (Median=6.58 hrs, n=32) and non-dexamethasone group (Median=4.1 hrs, n=32), in which the result in dexamethasone group is significantly higher than non-dexamethasone group.

A Mann-Whitney U Test revealed significant difference in total Tramadol consumption of dexamethasone and non-dexamethasone groups. Otherwise there is no statistically significant difference in total diclofenac consumption between the two groups (Table 4).

Table 4: Total analgesic consumption between two groups.

<table>
<thead>
<tr>
<th>Observation</th>
<th>Dexamethasone group</th>
<th>Non-dexamethasone group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Tramadol consumption</td>
<td>0.0 (0.0-37.5)</td>
<td>50 (0-50)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total Diclofenac consumption</td>
<td>75 (0)</td>
<td>75 (0)</td>
<td>0.204</td>
</tr>
</tbody>
</table>

Value are presented as median (inter quartile range), Mann-Whitney U test, p value<0.05 statistically significant.
6.95 ± 2.29, 7.7 ± 1.7 and 8.45 ± 1.5 respectively with p value<0.0001 [33]. The similarity with our study may be due to the resembling of the method and the sentiment that dexamethasone having Strong anti-inflammatory properties which decrease the pain score.

This study is also in line with the study done in India by Priyanka Sunil, et al. on the efficacy of IV* dexamethasone in prolonging the duration of spinal anesthesia in elective cesarean section in which they found significantly lower mean VAS scores for dexamethasone group at 6th, 12th, 18th and 24th hrs. The mean VAS score for dexamethasone group was 3 at 6th hr, 3 at 12th hr, 4 at 18th hr and 5 at 24th hr and for non-dexamethasone group 5 at 6th hr, 5 at 12th hr, 5.5 at 18th hr and 6 at 24th hr [26]. The 3hr VAS score is also comparable to a study done by Prabha Parthasarath, et al. in Patients Undergoing Surgery under Spinal Anesthesia with mean score of 1.93 ± 0.58 in dexamethasone group and 3.65 ± 0.70 in control group with p value<0.001 [37].

A randomized controlled trial done by U Ituk, et al. in 2018 on the effect of a single intraoperative dose of intravenous dexamethasone 8mg on post-cesarean delivery analgesia observed that median (interquartile range) NRS Score at rest during 6th hr, 12th hr and 24th hr in Dexamethasone group were 1 (0-2), 1 (0-1) and 1 (0-2) in order given, which were not significantly different compared to placebo group with median NRS score 1 (1-3), 2 (1-3) and 1 (1-3) respectively with p value>0.05. Which was in contrary to our finding showing that NRS median score of 3 (2-3), 3.5 (2-4) and 3 (2-4) in dexamethasone group and 3 (1.25-4), 4.5 (3-6) and 4 (3-6) in non-dexamethasone groups and statistically significant difference between two groups [27]. The disparity with our study may be due to a difference in study design, dose of dexamethasone used and the time of dexamethasone administration. They administer the dexamethasone after delivery and clamping of the umbilical cord, which contrast the idea that preoperative administration may allow enough time for intracellular diffusion and be relevant to reducing postoperative pain.

Observing the time to the requirement of first rescue analgesia in hrs was another interest of our study. A study done in India by Prabha Parthasarath, et al. in Patients Undergoing Surgery under Spinal Anesthesia found that Mean time of request for first analgesic dose (hr) is 3 for dexamethasone group and 6.6 for control group with p value<0.001 which was in line with our finding showing median score (Interquartile range) of 4.1 (1.8) non-dexamethasone and 6.5 (3.68) in dexamethasone group [37].

In contrary to this study, a study done by Priyanka, et al., in 2017 on cesarean section patients, they observed that Mean time for first rescue analgesia in hr is 8.6 and 4.4 in dexamethasone and placebo group respectively with p value<0.001. According to their finding there is high score of time to the requirement of the first analgesia for dexamethasone group compared to our study. The disparity with our study may be due to the different doses of intravenous dexamethasone used by two studies [26].

This study also observed that The median score for total consumption of Tramadol in 24 hr post operatively has been 0mg in exposed group as compared to 50 mg in non-exposed group with p value<0.0001 our result is in line with the study done by Ahmed M. Maged, et al. on cesarean section patients which shows administering intravenous dexamethasone reduce total opioid consumption in the first 24 hrs postoperatively. Otherwise we found that there was no statistically significant difference in median score of total diclofenac consumption between the two groups with median score of 75 mg (0 mg) in both groups. In contrast to our finding Study done by Sourabh Roy, et al. found that the Total dose of diclofenac (mg) mean (range) were 7.5 (0-75) and 31.5 (0-225) in dexamethasone and control group respectively [27]. And another study done by prabha et al. found that There was difference in terms of total diclofenac use between treatment (average of 160 mg) and control (average of 217 mg) groups (P<0.001) [37]. The difference with our finding might be explained by disparate management of postoperative pain between the hospitals. They only used diclofenac IM injection for postoperative pain management.

The study conducted by Prabha, et al. found that there is no statistically significant difference between control (3.23 ± 0.62) and treatment (3.1 ± 0.66) group in mean Time to achieve maximum sensory level (min) with p value 0.43 [37]. Their result is corresponding to our result with mean time in dexamethasone group (4.06 ± 1.73) and non-dexamethasone group (4.64 ± 1.42) with p value 0.14. A study done by Siddesh N Kadur, et al. also concluded that there is no statistically significant difference between the two groups in time to achieve maximum sensory block [24,38].

Conclusion

We concluded that preoperative administration of dexamethasone 0.1 mg/kg intravenously for patients underwent cesarean section with spinal anesthesia was efficient in reducing postoperative pain, total Tramadol consumption on the first postoperative day and prolonging the time to the requirement of first rescue analgesia.

Ethical Approval

The study conducted after approval by Addis Ababa University, Health science college Ethical review board to conduct the study. A legal letter submitted to Ghandi memorial hospital, where the study took place.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

References


