



# INTRATHECAL BETAMETHASONE; THE ROLE OF ADMINISTRATION OF EFFECTIVE POST OPERATIVE ANALGESIC IN GYNECOLOGIC PROCEDURES, AT A TERTIARY CARE CENTRE IN KARACHI, PAKISTAN.

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**Article received on:**

01/12/2016

**Accepted for publication:**

15/03/2017

**Received after proof reading:**

06/05/2017

**Conflict of interest:** There is no conflict of interest.

**ABSTRACT... Objectives:** The aim of our study to determine the use of intrathecal betamethasone administration as effective post-operative analgesic in gynecologic procedures. **Study Design:** Randomized control trial. **Period:** 6 months duration from April 2015 to end of September 2015. **Setting:** Tertiary Care Centre in Karachi, Pakistan. **Method:** The study population consisted of n= 120 (divided into three groups using a random number generator) patients, who presented to our setup either via emergency or through the outpatient. The patients belonged to ASA class I and II, and underwent cesarean section. The group A was the control group, patients who received 0.5ml normal saline IV with bupivacaine 0.5% in 3ml, with 0.5ml of normal saline intrathecally. Group B consisted of patients who received 0.5ml IV normal saline, with 0.5% in 3ml bupivacaine along with 0.5ml betamethasone as 4mg per ml. The last group, group C consists of patients who received 0.5ml betamethasone IV (4ml/ml) along with 0.5% 3ml bupivacaine with 0.5ml of normal saline intrathecally. For the subjective measurement of pain level a visual analog scale was used. Various time intervals as time of initial first analgesic effect, time between intrathecal injection and first administration of diclofenac as rescue analgesic and the total number of analgesics used in the first twenty four hour period were also recorded in the proforma. Various side effects such as nausea, vomiting and headache were noted. Data was analyzed using SPSS version 23. **Results:** The study population consisted of n= 120 patients, divided into three groups using a random number generator, the demographic data like age, whether the procedure performed was elective or emergency etc did not show any difference p value of >0.05. The Visual analog scales scores at the 4 hour and 6 hour mark showed statistically significant difference, the values being lower in the medication groups versus the control group. But no difference was found between the control and medication groups in the VAS score measured at 12 hour and 24 hours respectively. The requirement for use of Diclofenac as rescue analgesia was also lower in the intrathecal and intravenous (group B and C) as compared to the control group at the 24 hour mark post operatively, and the dose required was even lower in the intrathecal group as compared to the intravenous group having a p value of 0.014. N= 27 patients suffered nausea and vomiting during the procedure, N= 40 patients reported headache following the 24 hour period post operatively. **Conclusion:** According to the results of our study intrathecal betamethasone administration is an effective method of post-operative pain reduction in cesarean section surgeries and it also decreases the need for rescue analgesia required.

**Key words:** Intrathecal Drugs, Betamethasone, Cesarean Section, Postoperative Analgesia.

**Article Citation:** Raza H, Ahmed B, Kamlaish. Intrathecal betamethasone; the role of administration of effective post-operative analgesic in gynecologic procedures, at a Tertiary Care Centre in Karachi, Pakistan. Professional Med J 2017;24(5):733-738. DOI: 10.17957/TPMJ/17.3749

## INTRODUCTION

One of the most focused areas of concentration in the field of modern surgical sciences is post-operative care and pain relief. In the field of gynecology and obstetrics it's an even more important consideration, for the health benefits of both the mother and child. Inadequacies in

post-operative care and appropriate pain relief wreck havoc by increasing the health care costs, delaying psychological bonding between the mother and the child and reduce the patient satisfaction overall, in addition it causes increase in hospital stay, delay recovery and healing. In light of these after affects of inadequate pain

relief post-operative it is imperative that early treatment with analgesics be started.<sup>1,2</sup> Recently several methods and techniques were used to achieve this effect, multimodal approach with multiple different drug combinations and different routes of administration of these medications have yielded results with minimal side effects and good analgesia.<sup>3</sup> The effect of steroids have been studied as for use as analgesic in light of the fact that steroids inhibit the release of arachidonic acid from the damaged tissues during surgery, also its effect on the GABA receptors in spinal sites is known to make steroids an effective analgesic.<sup>4</sup> The various methods for administration of steroid medication are as adjuvant in nerve blocks, central neuraxial block, intrathecal, parenteral and local infiltration at the site of operation, and these methods show varying efficacies and effects.<sup>3,5,6,7</sup> In the treatment of chronic pain various studies propose intrathecal administration of steroids.<sup>8,9,10,11</sup>

But studies regarding the use of intrathecal administration (which also produces higher local concentration in addition to less side effects<sup>4</sup>) route as post-operative pain relief are lacking, to which objective our study is directed, as it is the aim of our study to determine the use of intrathecal betamethasone administration as effective post-operative analgesic in gynecologic procedures.

## MATERIALS AND METHODS

The type of study is a randomized control trial, conducted for a period of 6 months duration from April 2015 to end of September 2015, at a tertiary care centre in Karachi, Pakistan. The study population consisted of n= 120 (divided into three groups using a random number generator) patients, who presented to our setup either via emergency or through the outpatient clinics and agreed to participate in the study after giving a full informed consent.

The patients belonged to ASA class I and II, and underwent cesarean section for delivery between the age of 20 and 40 years. The group A consisted of the control group, of patients who received 0.5ml normal saline IV with bupivacaine 0.5% 3ml with 0.5ml of normal saline intrathecally.

Group B consisted of patients who received 0.5ml IV normal saline, with 0.5% in 3ml bupivacaine along with 0.5ml betamethasone as 4mg per ml. The last group, group C consists of patients who received 0.5ml betamethasone IV (4ml/ml) along with 0.5% 3ml bupivacaine with 0.5ml of normal saline intrathecally.

The exclusion criteria was all those patients who refused to participate in the study, were already receiving analgesics or other steroid medications, had any other significant co morbid condition, or there was any contraindication to the use of regional anesthesia.

For the subjective measurement of pain level a visual analog scale was used and was divided into ten incremental points starting with 0 as no perception of pain to 10 being the most extreme pain ever experienced. The surgical procedure was performed according to set standardized protocol, monitoring in the operating room was done for various variables such as electrocardiogram, pulse oximetry and blood pressure etc.

An intravenous preload of 5ml per kg ringers lactate solution was given prior to the dural procedure via a 16 gauge intravenous canula. The spinal needle was inserted between the L3 and L4 intervertebral space with a 25 gauge needle inserted via a midline approach, the drugs were administered over a period of 0.5 min, respectively. Various variables were noted for the patients in a predesigned proforma, characteristics such as pre and post spinal anesthesia administration mean arterial pressure and heart rate, noted at intervals of time 0min, 10min, 20min and 30min respectively. In case the VAS score was more than 4 a suppository of 100mg of diclofenac was administered. Various time intervals as time of initial first analgesic, time between intrathecal injection and first administration of diclofenac as rescue analgesic and the total number of analgesic used in the first twenty four hour period were also recorded in the proforma. Various side effects such as nausea, vomiting and headache were also noted. The VAS score were recorded at fixed time intervals of 4, 6, 12, and 24 hours post

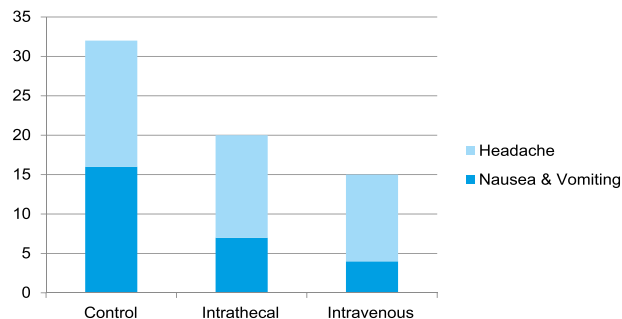
intrathecal injection of drugs.

Data was analyzed using SPSS version 23. Various values were expressed as means and standard deviations and or frequency and percentages respectively. Chi square test was used for categorical variables, also various tests such as ANOVA were used. A p value of less than 0.05 was considered to be statistically significant.

**RESULTS**

The study population consisted of n= 120 patients, divided into three groups using a random number generator, the demographic data like age, whether the procedure performed was elective or emergency etc did not show any difference p value of >0.05. Similarly characteristics such as heart rate and mean arterial blood pressure did not show any significant difference, regardless of preoperative and intra operative measurements. However the Visual analog scales scores at the 4 hour and 6 hour mark showed statistically significant difference (Refer to Table-I) the values being lower in the medication groups versus the control group. But no difference was found between the control and medication groups in the VAS score measured at 12 hour and 24 hours respectively. The requirement for use of Diclofenac as rescue analgesia was also lower in the intrathecal and intravenous (group B and C) as compared to the control group at the 24 hour mark post operatively, and the dose required was

even lower in the intrathecal group as compared to the intravenous group having a p value of 0.014. Time duration for administration of rescue analgesia also showed improvement in the medication groups as compared to the control group, refer to Table-I. In terms of the observed side effects, both during the procedure and post operatively, no significant difference was found in all the three groups. However 27 patients suffered nausea and vomiting during the procedure, the frequency and percentages were as follows, n= 7 (25.92%) in group B, n= 4 (14.81%) in group C and n= 16 (59.25%) in the control group, group A, which is statistically significant. N= 40 patients reported headache following the 24 hour period post operatively, and the distribution was as follows n= 13 (32.5%) in group B, n= 11 (27.5%) in group C and n= 16 (40%) in the control group, no statistically significant difference was found. Refer to Figure-1.



**Figure-1. Side effect profile of patients belonging to the three groups.**

Variable	Group A, Control group	Group B, Intrathecal group	Group C, Intravenous group	P value
Age in years	26.4 +/- 6	25.3 +/- 5	25 +/- 4	
<b>Type of surgical procedure</b>				
Elective	14 (35%)	16 (40%)	19 (47.5%)	
Emergency	26 (65%)	24 (60%)	21 (52.5%)	
<b>Visual Analog Scale</b>				
VAS at 4 hours	6.1 +/- 2	3.16 +/- 1.4	4 +/- 1.3	<0.0001
VAS at 6 hours	7.8 +/- 1.7	2.5 +/- 1.1	4 +/- 1.7	<0.0001
VAS at 12 hours	2.4 +/- 2.2	2 +/- 1.7	2.5 +/- 1.6	0.5
VAS at 24 hours	2.2 +/- 2.2	1.5 +/- 1.6	1.6 +/- 1.5	0.2
Rescue analgesia as diclofenac dose in the 24 hour period in mg	292.9 +/- 83	163.4 +/- 81	227.3 +/- 104	<0.0001
Time duration to administration of rescue analgesia	245.6 +/- 91	336.8 +/- 87	312.4 +/- 108	0.001

**Table-I. Various characteristics, Visual analog scale, and rescue analgesic use in the three groups.**

## DISCUSSION

According to the results of our study, we found that administration of 2mg betamethasone intrathecally is an effective, efficacious, safe and practical method to provide post-operative analgesia in patients undergoing cesarean section. The mechanism of action of the analgesic effect of steroid medications are still unclear, but according to established data, glucocorticoids block two pathways in the inflammatory cascade namely the cyclooxygenase and the lipooxygenase pathways, these medications have an effect in prostanoid and the eicosanoid systems.<sup>12</sup> According to a study by Johansson et al local administration of steroid methylprednisolone suppresses the transmission in thin unmyelinated nerve fibers at 30 min of application.<sup>13</sup> Various other studies also report analgesic effects of corticosteroids post-surgery.<sup>12</sup> While preoperative administration via different routes such as intramuscular, epidural, intra scalene and oral reduce the overall pain score and the requirement for analgesic medications with minimal side effects.<sup>5,8,14,15</sup> The beneficial effects of intrathecal betamethasone are not well studied.

According to a study by Bani Hashem et al in orthopedic surgery patients, they administered 8mg of dexamethasone with 15mg of bupivacaine, and found that the duration of sensory block increased significantly, without any change in time of onset and associated side effects.<sup>16</sup> According to Taguchi et al, they included in their study ten cancer patients and administered intrathecal betamethasone in small doses on a weekly basis, doing this they were able to achieve significant reduction in pain in 5 patients with no signs of any complications.<sup>18</sup> The role of epidural dexamethasone was studied by Siji et al who injected patients with 5mg dexamethasone after laparoscopic cholecystectomy and observed that the patients required less amount of morphine compared with the control group.<sup>15</sup> Aasboe et al recommend a 12mg dose of intramuscular betamethasone to be administered half an hour before a surgical procedure, which reduces pain and nausea after ambulatory surgery.<sup>14</sup> The results are similar to our study which also showed

a decrease use of rescue analgesia and VAS pain score at the 6 hour mark post operatively in patients who were administered betamethasone either intrathecally or intravenously. Which is due to effects of betamethasone as post-operative analgesic. This could be explained as inhibition of inflammatory mediators and prostaglandins.

Kroin et al did experiments with rats, and found that after bilateral incision of the foot, lumbar spinal COX-2 levels were increased after 3-6 hours post incision, while it normalized after that time as compared to the control group.<sup>17</sup> The results of which are similar to our study in which the highest pain relief was within 4 to 6 hours post operatively, which can be explained with the fact that the effect of betamethasone correlates with levels of COX 2. Whereas after 12 and 24 hours of surgery the COX 2 levels decrease, and also the effect of betamethasone decreases concomitantly, being similar to that of the control group. Betamethasone was selected in this study because it has a low mineralocorticoid effect, high anti-inflammatory properties and it is safe for intrathecal use.<sup>18</sup> Various studies showed no significant side effects of intrathecal betamethasone injection,<sup>19</sup> Langmayr et al observed no side effects in patients having lumbar disc surgery and Latham et al showed no pathologic effects in injected sheep with intrathecal betamethasone 5.7mg, but showed neurotoxicity at a dose of 11.4mg.<sup>20</sup> In our study we only injected 2mg of betamethasone which showed no significant side effects.

The antiemetic effects of corticosteroids have been attributed to the reduction of serotonin levels in the brain, inhibition of the prostaglandins and the changes in the blood brain barrier permeability. The chemoreceptor trigger zone (CTZ) is one of the areas that control the vomiting centre, and has dopamine, opioid, serotonin and muscarine receptors, which have an important role in transfer of impulses to the vomiting centre.<sup>21</sup> In our study we found that the nausea and vomiting in the Intravenous group was lower than that which was found in the intrathecal group, which can be explained by the peripheral antiemetic effects of corticosteroids.

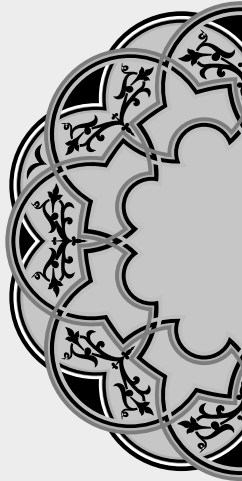
## CONCLUSION

According to the results of our study intrathecal betamethasone administration is an effective method of post-operative pain reduction in cesarean section surgeries and it also decreases the need for rescue analgesia required.

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*“Marriage is the only war in which you sleep with the enemy.”*

**Unknown**

#### **AUTHORSHIP AND CONTRIBUTION DECLARATION**

<b>Sr. #</b>	<b>Author-s Full Name</b>	<b>Contribution to the paper</b>	<b>Author=s Signature</b>
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3	Dr. Kamlaish	Data collection, write up, analysis, proof reading.	