Original Article **Open Access**

Determining the Effect of Intrathecal Dexmedetomidine on Postoperative Pain Relief after Cesarean Section

Ayesha Shahid, Huda Shafqat, Salman Maqbool, Ahsan Ali, Rehana Feroze

ABSTRACT:

Objective: To analyze efficacy of intrathecal Dexmedetomidine as adjunct to hyperbaric Bupivacaine in terms of post-operative analgesia after caesarean section.

Study Design & Setting: This randomized controlled trial was conducted at Department of Anesthesia, Rawal Institute of Health Sciences, Islamabad from20th, October 2018 to 20thApril 2019 after taking Ethical board approval from the Institute. (letter no RIHS-REC/030/18, dated, 18th October 2018).

Methodology: Total n=120 patients having ASA status I, II undergoing elective cesarean section were randomly divided into 2groups (60 each) by lottery method. Group-A, was given hyperbaricBupivacaine (0.5%) 12mg alone and group-B, was given hyperbaricBupivacaine (0.5%) 12mg along with injection Dexmedetomidine 4ug in intrathecal space respectively. Patients were followed in postoperative period for onset of pain and requirement for rescue analgesia in first 6 hours.

Results: There was statistically significant difference in mean onset of postoperative pain among both the groups-A and B (178.18 ± 12.51 versus 364.07± 35.58min respectively with p value 0.000), as well as, postoperative analgesic requirement, in first 6 hours, 39 (65.0 %) versus 31 (51.7 %) with p-value 0.000 respectively. However, on stratification, considering effect modifiers, like age (20-30 years and 30-40 year and previous history of cesarean section), there was statistically significant difference in mean onset of pain in both groups, but no significant difference was found regarding rescue analgesic requirement in both groups.

Conclusion: Intrathecal Dexmedetomidine along with hyperbaric Bupivacaine was better than hyperbaric Bupivacaine alone in controlling postoperative pain in caesarean section.

Keywords: Cesarean section, Dexmedetomidine, Hyperbaric bupivacaine, Intrathecal space.

How to cite this Article:
Shahid A, Shafqat H, Maqbool S, Ali A, Feroze R. Determining the Effect of Intrathecal Dexmedetomidine on Postoperative Pain Relief after Cesarean Section. J Bahria Uni Med Dental Coll. 2022; 12(4):181-5. DOI: https://doi.org/10.51985/JBUMDC2021111

INTRODUCTION:

Caesarean sections are usually performed under neuraxial anesthesia. This practice was well established since beginning of 20th century. Its prevalence has been reported to be 32.5 % in African countries with 68.2 % cases performed under regional anesthesia.[1] As far as patient safety is concerned neuraxial anesthesia is a safe procedure as compared to general anesthesia.[2] It provides pain relief by blocking nociceptive transmission from peripheral to central nervous system. Since local anesthetics have got short half-life so they didn't provide long term pain relief in postoperative period. Increasing the dose of local anesthetic to achieve prolong analgesia in post operative period can result in systemic as well as potential neurotoxicity.[3] The analgesic effects of local anesthetic drug used in subarachnoid block can be increased by adding adjunct such as clonidine, opioids, ketamine, magnesium, dexamethasone, midazolam and tramadol. They not only enhance quality of block but also helps in keeping stable hemodynamics intraoperatively.[4] Pain after cesarean section is one of the most common postoperative problems, hence adequate postoperative analgesia is required for postpartum women. It not only increases patient satisfaction but also leads to earlier mobilization, decrease risk of thromboembolism, reduce hospital stay as well as hospital costs.[5]It also facilitate initiation of breast-feeding as hormonal changes and stress response due to pain may interfere with lactation. All these factors help to improve patient satisfaction in postpartum period.[6]

Ayesha Shahid *(Corresponding Author)*
Assistant Professor, Department of Anesthesia
Rawal Institute of Health Sciences, Islamabad
Email: Drayesha_kemu@hotmail.com

Huda Shafqat
Resident, Department of Anesthesia
Rawal Institute of Health Sciences, Islamabad

Salman Maqbool
Associate Professor, Department of Anesthesia
Rawal Institute of Health Sciences, Islamabad

Ahsan Ali
FCPS II Resident, Department of Anesthesiologist
CMH Lahore Medical College

Rehana Feroze
Assistant Professor, Department of Anesthesiology
CMH Lahore Medical College

Received: 29-Nov-2021
Accepted: 16-Sep-2022

Postoperative pain is usually treated with opioids that have their own side effects.[7] The side effects include pruritus, nausea, vomiting and respiratory depression.[8] Dexmedetomidine is one of the most common drugs that is being used as adjunct to bupivacaine in subarachnoid space. Dexmedetomidine has opioids sparing effect, therefore can be safely used as an adjunct for post operative pain relief.[5] It inhibits activation of spinal microglia and astrocytes to produce its antinociception effect. It also inhibits release of nociceptive substances that are triggered by painful stimuli.[3] In addition to its analgesic potency, it has got sedative, anxiolytic as well as sympatholytic properties.[9] Studies have shown that Dexmedetomidine when used alone is not a good analgesic , however when used as an adjunct in subarachnoid block, it improves onset of sensory and motor block, hemodynamic stability and prolongs the duration of analgesia.[10]In addition to its use as adjunct in subarachnoid space ,studies have shown that it has got synergistic effect with duration of subarachnoid block when given through intravenous route.[3]As Dexmedetomidine has recently been introduced contextually, thus existed data is limited at national level to evaluate the postoperative analgesic effect of intrathecal dexmedetomidine as an adjunct along with hyperbaric bupivacaine. Thus, the rationale of this study was to find better management for post-operative analgesia in caesarean section. This study was aimed to analyze the effect of intrathecal dexmedetomidine with hyperbaric bupivacaine on post operative analgesia in caesarean section.

METHODODOLOGY:

This study was conducted at Department of Anesthesia and critical care Rawal Institute of Health Sciences Islamabad from 20th, October 2018 to 20th April,2019 after taking Ethical board approval(letter no RIHS-REC/030/18, dated, 18th October 2018). Nonprobability consecutive sampling technique was well thought for this pilot study. Total n=120 patients with age 20-40 years, having ASA[11] status category I and II, planned for elective c- section were enrolled in this study. Patients with severe hypovolemia, coagulopathy, history of spinal stenosis, heart block and taking clonidine were excluded from study. Using WHO sample size calculator with following assumptions (confidence level=95%, Power of test=80%, population mean onset of pain in group 1=220.75mins, population mean onset of pain in group 2=1042.5mins [12]) sample size was calculated as 120 (60 cases placed into each group A and B by lottery method). All the patients gave informed written consent to participate in this trail. After standard 8 hours fasting, all patients were premedicated with injection metoclopramide 10 mg and inj. Dexamethasone 4mg intravenously. In the operation theatre, standard monitoring (ECG, BP, HR, pulse oximetry) was done and recorded. Group-A, patients were given inj. hyperbaric Bupivacaine (0.5%) 12mg and group B were given inj. hyperbaric Bupivacaine (0.5%) 12mg along with injection Dexmedetomidine 4ug in intrathecal space respectively. After completion of surgery, patients were transferred to recovery room and observed there for half hour. Patients were followed in postoperative period for onset of pain and analgesic requirement in first 6 hours. All findings were recorded on the specially designed proforma. Confidentiality of the record was maintained. SPSS version 21 was used.

RESULTS:

Mean age of patients was 32.12± 8.48 years in group A and 31.83 ± 8.84 years in group B respectively. There was statistically significant difference (P-value 0.000) in time for onset of pain in postoperative period in both groups as shown in table 1. Postoperative analgesic requirement was compared in terms of frequency in both groups. There was statistically significant difference (P- value 0.000) among both groups with 39 (65.0%) patients in group A, as compared to 31 (51.7%) patients in group-B, who demanded analgesia in first 6 hours postoperative period as shown in (table 1).

Effect modifier like age stratification was assessed by dividing patients in two age group (20-30yrs) and 30-40 years (as shown in table-2). There was statistically significant difference in time for onset of pain in groups-A and B, however when frequency of patients who needed rescue analgesia in first 6 hours was compared among groups-A and B, no significant difference was found, considering the patients in two age groups.

Similarly effect modifier like previous history of cesarean section stratification was done (as shown in table-3) and results were compared in both groups-A and B. There was statistically significant difference in time for onset of pain in groups-A and B, however when frequency of patients who needed rescue analgesia in first 6 hours was compared in groups A and B, there was no significant difference.

DISCUSSION:

Major limitation of sub-arachnoid block is relatively short duration of block and lesser postoperative analgesia.[13] The commonly used local anesthetic is Bupivacaine that has long duration of action however in terms of post-operative analgesia its duration is short.[14]So various adjuvants have been used intrathecally along with Bupivacaine. The aim is to enhance quality of intraoperative as well as postoperative analgesia.[15] The most commonly used intrathecal adjuvants are opioids.[16]Their side effects includes postoperative nausea and vomiting,pruritus, difficulty to void and delayed respiratory depression, so studies have been done to use

Table-1: Comparison of Onset of Pain (Min) and analgesia required in first 6 hours (both groups). (n=120)

	Group A	Group B	P-value
Onset of Pain (Min)	178.18 ±12.51	364.07 ±35.58	0.000
Postoperative Analgesic Requirement (Frequency)	39(65.0%)	31(51.7%)	0.000

Table-2: Effect modifiers like Age stratification with comparison of Onset of Postoperative pain & Postoperative Analgesic requirement in first 6 hours among both the groups. (n=120)

Age Group		GROUP A	GROUP B	p-value
20-30yrs	Mean Onset of postoperative pain (in minutes)	175.88 ± 10.55	359.55 ± 60.78	0.000
	Postoperative analgesic requirement (frequency)	11(68.8%)	7(35.0%)	0.044
30-40 years	Mean Onset of postoperative pain (in minutes)	180.32 ± 10.90	369.44 ± 11.96	0.000
	Postoperative analgesic requirement (frequency)	28(63.6%)	24(60.0%)	0.453

Table-3: Effect modifiers like previous history of cesarean section stratification with comparison of Onset of Postoperative pain & Postoperative Analgesic requirement in first 6 hours in both Groups. (n=120)

Effect modifier	Parameter	Group A	Group B	p- value
No history of previous cesarean section	Mean Onset of postoperative pain (minutes)	178.38 ± 11.92	364.25 ± 36.05	0.000
	postoperative analgesic requirement(frequency)	20(69.0%)	12(42.9%)	0.047
History of previous cesarean section	Mean Onset of postoperative pain (minutes)	178.00 ± 13.23	363.91 ± 35.73	0.000
	postoperative analgesic requirement (frequency)	19(61.3%)	19(59.4%)	1.000

non-opioid analgesics with lesser side effects in place of opioid analgesics.[17]The á$_2$-agonists when used as adjuvant in subarachnoid space have antinociceptive action both for somatic as well as for visceral pain. In addition to its analgesic effects, it also has sedative sympatholytic property, hence it not only stabilizes hemodynamics in intraoperative period but also reduces requirement of anesthetic agent for maintainance.[18]Therefore, these drugs have been commonly used as adjuvants to Bupivacaine in spinal anesthesia.[19]Among alpha-2 agonist, Dexmedetomidine and Clonidine are most used. Dexmedetomidine has ability to prolong postoperative analgesic effect of local anesthetics with minimal side effects.[20]Since Clonidine is partial agonist at alpha receptors, hence specificity of Dexmedetomidine is 7-8 times higher than Clonidine.[21] Being a lipophilic drug, dexmedetomidine rapidly gets absorbed into the CSF and binds to alpha 2 receptors of spinal cord and produce its analgesic effects. Irrespective of its route of administration, it has ability to prolong duration of sensory as well as motor blockade induced by local anesthetics.[22]

This study was performed in patients undergoing cesarean sections. Results of this study were comparable to another study done by Bi KH. et al[18] in patients undergoing cesarean section. Sixty patients were randomly divided in three groups. Patients undergoing cesarean section were given intrathecal bupivacaine alone or in combination with dexmedetomidine 3ug or 5ug. Results of this trial showed that addition of dexmedetomidine as adjunct to bupivacaine not only prolongs duration of sensory and motor block but also reduces requirement of analgesics in postoperative period as seen in our study. There was no significant difference regarding hemodynamics in three groups. Visual analog score for pain was also small in dexmedetomidine group. Reduced levels of cortisol and interleukin 6 in dexmedetomidine group supported the evidence that it also blunts stress response to surgery.[18]

Another study was done by Abdulkadir Y in patients undergoing hernia repair. He compared normal saline (group 1) ,2 ug (group 2) and 4 ug (group 3) of Dexmedetomidine used as an adjuvant to hyperbaric Bupivacaine in intrathecal space and compare the results. The mean time for onset of pain was 220.75±112.7 min in group 1 versus 371.5±223.5 min in group 2 and 1042.50±366.78 min in group 3. When compared, the time for first pain sensation in group 3 was significantly longer than in groups 1 and 2 with p value <0.001. So, the results of this study[12] were like our trial.

Ganesh M, et al;did a randomized prospective double-blind study to analyze effect of Clonidine and Dexmedetomidine on quality of subarachnoid block when used as an adjuvant to Bupivacaine. They compared onset of sensory and motor block as well as postoperative pain score in both groups. Onset of sensory block was low in both Clonidine and Dexmedetomidine group as compared to Bupivacaine alone however duration of motor block was highest in Dexmedetomidine group. Time for rescue analgesia was lowest in both Clonidine and Dexmedetomidine group and postoperative pain score was significantly low in both groups as compared to Bupivacaine alone group, so results of this study were comparable to our study as far as pain scoring and time for rescue analgesia was considered.[8]

Another study was carried out in patients undergoing infraumbilical surgeries. Group 1 was given intrathecal Bupivacaine alone while group 2 was given intrathecal Bupivacaine with Dexmedetomidine 5ug. Onset of sensory block (208.33±19.18 seconds in Group I versus 129.33±14.8 seconds in Group II with p value <0.001) as well as onset of motor block (320.33±29.81 minutes in group 1 versus 226.33±31.86 minutes in group 2 with p value <0.001)was significantly higher in Bupivacaine alone group as compared to Dexmedetomidine group.Total duration of sensory block(188±11.86 minutes in Group I versus 317.70±16.16

minutes in Group II with p value<0.001) as well as duration of motor block (166.5±12.11 minutes in Group I versus 286.33±15.15 minutes in group 11 with p value <0.001) was significantly low in Bupivacaine group as compared to Dexmedetomidine group. Duration of analgesia was 333.6±20.67 minutes in Dexmedetomidine group versus 193.67±7.06 minutes in Bupivacaine alone group.[23]So, these resultswere like our trial.

Literature review shows another trial done by KanaziGE, et al among patients undergoing prostate or bladder surgery under spinal anesthesia. Dexmedetomidine and Clonidine were used as an adjunct to Bupivacaine and their effect were analyzed in terms of duration of motor and sensory block, sedation score and hemodynamic variability. Time for onset of motor block was significantly reduced in Clonidine and Dexmedetomidine group as compared to Bupivacaine alone group. In contrast to onset of block, time for regression of sensory and motor block was significantly higher in these groups. However, there was no significant difference in sedation score in all three groups.[19]

Another comparative study was done in patients who were undergoing spinal saddle block. Intra-thecal hyperbaric Bupivacaine 5 mg(group A) was compared with hyperbaric Bupivacaine 5 mg with Dexmedetomidine 5 ug. Postoperative duration of analgesia was significantly prolonged in Dexmedetomidine group (group B, 501 ± 306 minutes versus group A, 284 ± 58 minutes) with less analgesic requirements in Dexmedetomidine group however, as compared to previous mentioned study done in infraumbilical procedures, there was no significant difference in peak sensory block as well as magnitude of motor block, and side effects in both groups.[24]

Another study was done in orthopedic patients undergoing lower limb surgeries. Dexmedetomidine 3 ug was compared with Dexmedetomidine 5 ug as adjuvant to hyperbaric Bupivacaine in intrathecal space. There was no difference in demographic profile, time interval to achieve sensory block, motor block, duration of surgery and intraoperative hemodynamics (p value 0.05). however, time for first rescue analgesia was significantly shorter in Dexmedetomidine 3 ug as compared to Dexmedetomidine 5 ug (206.47 min versus 271.33 min with p value <0.001).[25]

Further studies must be conducted at multiple setups at national level to emphasize adjuvant effect of intrathecal dexmedetomidine with hyperbaric bupivacaine on post-operative pain relief in caesarean section so that better management could be adopted in future.

Authors Contribution:
Ayesha: Concept & Design of Study, Drafting, Revisiting Critically, Data Analysis, Final Approval of version
Huda Shafqat: Concept & Design of Study, Drafting, Data Analysis
Salman Maqbool: Concept & Design of Study, Drafting, Revisiting Critically, Data Analysis, Final Approval of version
Ahsan Ali: Concept & Design of Study, Data Analysis
Rehana Feroze: Concept & Design of Study, Data Analysis

REFERENCES:

1. Shitemaw T, Jemal B, Mamo T, Akalu L. Incidence and associated factors for hypotension after spinal anesthesia during cesarean section at Gandhi Memorial Hospital Addis Ababa, Ethiopia. PLoS One 2020;15(8):e0236755. doi.org/10.1371/journal.pone.0236755
2. Moore DC, Bridenbaugh LD. Spinal (Subarachnoid) Block: A Review of 11,574 Cases.JAMA 1966;195(11):907– 912. Doi:10.1001/jama.195.11.907
3. Wu HH, Wang HT, Jin JJ, Cui GB, Zhou KC, Chen Y, Chen GZ, Dong YL, Wang W. Does dexmedetomidine as a neuraxial adjuvant facilitate better anesthesia and analgesia? A systematic review and meta-analysis. PLoS One 2014 ;9(3):e93114. doi: 10.1371/journal.pone.0093114.
4. Zahid F, Tarar HM, Tariq M. Intrathecal tramadol as an adjuvant in subarachnoid block to prolong the duration of analgesia. PAFMJ 2017; 67(4): 534-39.
5. Ahmed F, Khandelwal M, Sharma A. A comparative study of the effect of clonidine, fentanyl, and the combination of both as adjuvant to intrathecal bupivacaine for postoperative analgesia in total abdominal hysterectomy. J Anaesthesiol Clin Pharmacol 2017;33(1):102-106. doi:10.4103/0970-9185.202194
6. Bhardwaj S, Devgan S, Sood D, Katyal S. Comparison of Local Wound Infiltration with Ropivacaine Alone or Ropivacaine Plus Dexmedetomidine for Postoperative Pain Relief after Lower Segment Cesarean Section. Anesth Essays Res 2017;11(4):940-945. doi: 10.4103/aer.AER_14_17
7. Nie Y, Tu W, Shen X et al. Dexmedetomidine added to sufentanil patient-controlled intravenous analgesia relieves the postoperative pain after cesarean delivery:A prospective randomised controlled multicenter study. Sci Rep 2018; 8: 9952.
8. Ganesh M, Krishnamurthy D. A comparative study of dexmedetomidine and clonidine as an adjunct to intrathecal bupivacaine in lower abdominal surgeries. Anesth Essays Res 2018; 12: 539-545. DOI: 10.4103/aer.AER_54_18
9. Lee S. Dexmedetomidine: present and future directions. Korean J Anesthesiol. 2019;72(4):323-330. doi:10.4097 /kja.19259
10. Javahertalab M, Susanabadi A, Modir H, Kamali A, Amani A, Almasi-Hashiani A. Comparing intravenous dexmedetomidine and clonidine in hemodynamic changes and block following spinal anesthesia with ropivacaine in lower limb orthopedic surgery: a randomized clinical trial. Med Gas Res 2020;10(1):1-7. doi:10.4103/2045-9912.279977
11. Morgan GE, Mikhail MS. Clinical Anesthesiology.6th Edition. McGraw Hill Education 2018; 18:523.

12. Yektas A, Belli E. The effects of 2ug and 4ug doses of dexmedetomidine in combination with intrathecal hyperbaric bupivaineon spinal anaesthesia and its postoperative analgesic characteristics. Pain Res Manay 2014; 19(2):75-81. doi: 10.1155/2014/956825.

13. Boublik J, Gupta R, Bhar S, Atchabahian A. Prilocaine spinal anesthesia for ambulatory surgery: A review of the available studies.Anaesth Crit Care Pain Med 2016 ; 35(6):417-421. DOI: 10.1016/j.accpm.2016.03.005

14. Routray SS, Raut K, Pradhan A, Dash A, SorenM. Comparison of Intrathecal Clonidine and Fentanyl as Adjuvant to Hyperbaric Bupivacaine in Subarachnoid Block for Lower Limb Orthopedic Surgery.Anesth Essays Res .2017 ; 11(3): 589– 593.doi: 10.4103/aer.AER_91_17.

15. Qurban F, Qureshi SA, Hassan SI, Azeem Y. Determine the analgesic effectiveness of Dexmedetomidine with hyperbaric bupivacaine in spinal anesthesia for patients undergoing lower limb surgery. Pak J Med Health Sci 2020;14(2):1569-71

16. Farooq S, Rizvi MFA, Yousuf SMA, Dilshad R, Bashir G, Dilshad A. Comparing intrathecal dexmedetomidine and fentanyl as adjuvants to hyperbaric bupivacaine in elective casarian section, a study. Professional Med J 2022; 29(2):218-226. doi.org/10.29309/TPMJ/2022.29.02.6414

17. Chaney MA. Side effects of intrathecal and epidural opioids. Can J Anaesth1995; 42:891-903. doi: 10.1007/BF03011037

18. Bi YH, Cui XG, Zhang RQ, Song CY, Zhang YZ. Low dose of dexmedetomidine as an adjuvant to bupivacaine in cesarean surgery provides better intraoperative somato-visceral sensory block characteristics and postoperative analgesia. Oncotarget 2017;8(38):63587-63595.doi: 10.18632/oncotarget.18864.

19. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand 2006; 50:222-7.

20. Samantaray A, Hemanth N, Gunnampati K, Pasupuleti H, Mukkara M, Rao MH. Comparison of the effects of adding dexmedetomidine versus midazolam to intrathecal bupivacaine on postoperative analgesia. Pain Physician 2015;18(1):71–77

21. Bae HB. Dexmedetomidine: an attractive adjunct to anesthesia. Korean J Anesthesiol 2017;70(4):375-376. doi:10.4097/ kjae.2017.70.4.375

22. Naaz S, Ozair E. Dexmedetomidine in current anaesthesia practice- a review.J Clin Diagn Res 2014 ; 8(10):GE01-4.doi: 10.7860/JCDR/2014/9624.4946.

23. Patro SS, Deshmukh H, Ramani YR, Das G. Evaluation of Dexmedetomidine as an Adjuvant to Intrathecal Bupivacaine in Infraumbilical Surgeries. J Clin Diagn Res 2016;10(3): UC13-UC16.doi: 10.7860/JCDR/ 2016/ 17987.7379.

24. Gautam B, Lama SM, Sharma M. Effects of Adding Intrathecal Dexmedetomidine to Hyperbaric Bupivacaine for Saddle Spinal Block in Adults Undergoing Peri-anal Surgeries. J Nepal Health Res Counc 2018 ;16(1):43-48.

25. Rai A, Bhutia MP. Dexmedetomidine as an Additive to Spinal Anaesthesia in Orthopaedic Patients Undergoing Lower Limb Surgeries: A Randomized Clinical Trial Comparing Two Different Doses of Dexmedetomidine. J Clin Diagn Res 2017;11(4):UC09-UC12. doi: 10.7860/JCDR/ 2017/ 26241 .9654