Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/z0p08316

COMPARISON OF INTRATHECAL NALBUPHINE VERSUS DEXMEDETOMIDINE WITH LEVOBUPIVACAINE FOR POST-OPERATIVE ANALGESIA IN CAESAREAN SECTION: A PROSPECTIVE STUDY.

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Abstract

Background and Objectives: Various drugs have been used as an adjuvant with local anesthetics, to prolong the duration of spinal analgesia of single shot technique. This study aims at investigating and comparing the effects of intrathecal nalbuphine and dexmedetomidine as adjuvants to hyperbaric levobupivacaine in subarachnoid block.

Materials and Methods: 60 parturients undergoing elective Lower Segment Cesarean Section were allocated into 2 groups of 30 each to receive intrathecal administration of 10 mg of 0.5% hyperbaric Levobupivacaine with either 1 mg of Nalbuphine (Group N) or Dexmedetomidine 5µg (Group D).Characteristics of spinal anesthesia in terms of sensory analgesia and motor blockade, along with hemodynamic parameters and adverse effects, if any, were assessed. Data obtained was compiled and statistically analyzed with appropriate tests.

Results: Onset of sensory and motor blocks was faster in Group D (2.13±0.20 and 2.32±0.18 min) compared to Group N (4.08±0.16 and 5.37±0.22 min). Total duration of effective analgesia and total

duration of motor block were significantly prolonged in Group D (469.2±31.8 and 217.3±20.65 min) compared to Group N (294±17.4 and 119.8±15.26 min). There was no significant difference in the hemodynamic parameters and adverse effects between both the groups.
Conclusion: The intrathecal combination of 5µg dexmedetomidine and 0.5% hyperbaric levobupivacaine provides prolonged sensory and motor blockade with enhanced perioperative analgesia compared to nalbuphine 1mg.

Keywords: Levobupivacaine, Nalbuphine, Dexmedetomidine, Cesarean section.

Introduction:

Spinal anesthesia is universally accepted technique for both elective and emergency lower segment cesarean section (LSCS). Its ease of administration and quick onset enable the mother to remain awake and engage in the birthing process. Furthermore, it facilitates early mobilization post-surgery and may lower the risks of blood loss, the need for transfusions, venous thrombosis, pulmonary embolism, cardiac issues in high-risk patients, and respiratory depression.[1]
Levobupivacaine, the S (-) enantiomer of bupivacaine, is seen as a safer choice due to its lower cardiotoxicity and neurotoxicity. Adjuvants like nalbuphine, a semi-synthetic opioid, deliver analgesia and sedation by acting as an agonist at kappa receptors, while also minimizing side effects through mu receptor antagonism. This combination helps maintain hemodynamic stability and reduces the risk of respiratory depression.[2]
On the other hand, dexmedetomidine is a novel adjuvant that selectively activates α-2 adrenergic receptors, providing antinociceptive effects for both somatic and visceral pain.[3] This study aims to compare the efficacy, adverse effects, postoperative analgesia and neonatal outcomes of intrathecal nalbuphine and dexmedetomidine when used in combination with levobupivacaine for spinal anesthesia during LSCS.

Subjects and Methods:

A randomized, prospective, double blinded study of patients undergoing elective LSCS was conducted after institutional approval. Sample size of 60 was calculated by using OpenEpi software. We included parturients of 20-40 years of age, with gestational age of 37 to 40 weeks and ASA-II for the study and randomly divided them into two groups of 30 each, Group N (Nalbuphine) and Group D (Dexmedetomidine) by sealed envelope method.
Parturients, that refused to participate in the study, those undergoing emergency Caesarean section, having cardiac, endocrinal, hepatic, neurological or renal disorders, contraindications to regional anesthesia, allergic to local anesthetics, age <20 years and with American Society of Anesthesiologists grade >II, were excluded. After pre-anesthetic checkup, patients were kept fasting from previous night. Procedure of spinal anesthesia and the use of VAS scale were explained and informed written consent was obtained.
Patients' baseline parameters were recorded and preloading was done with Inj. Ringer Lactate 10ml/kg, 15minutes prior to induction. Routine monitors were attached and baseline pulse oximeter, non-invasive blood pressure, electrocardiogram and heartrate values were recorded. Oxygen (4L/min) was administered using a nasal cannula until the baby was delivered. After that, with all aseptic and antiseptic precautions; spinal anesthesia was performed in left lateral position at L3–L4 space using 23G Quincke spinal needle. After free flow of CSF, the drug was administered in each respective group, following which the patient was immediately positioned supine with left uterine displacement. Group N patients received Intrathecal Inj. Levobupivacaine heavy (0.5%) 2 ml + Inj. Nalbuphine (1mg) 0.5ml and Group D patients were given Intrathecal Inj. Levobupivacaine heavy (0.5%) 2 ml + Inj. Dexmedetomidine (5µg) 0.5ml. Time for onset and duration of sensory and motor blockade, time to achieve maximum sensory block level, two segment regressions time and duration of analgesia were observed. Sensory blockade was assessed by pin prick method, every 1min till first 5mins and then every 2mins till 10mins. Onset of sensory blockade (time interval from intrathecal injection to

L1 level), time for maximum sensory level (intrathecal injection to T6 level), and time for two segment regressions (from T6 to T8) were recorded. Motor blockade was assessed with Modified Bromage scale, every 1min till first 5mins and then every 2mins till 10mins. Onset of motor block (time interval from intrathecal injection to Bromage1) and duration of motor block (time interval from Bromage3 to Bromage0) were recorded. Intra-operatively HR, NIBP, SpO2 were recorded, every 2mins for the first 10mins, at 15mins and every 15mins till the end of surgery. Intra operative sedation was assessed every 15mins by using Modified Ramsay Sedation Scale. Side effects like hypotension, bradycardia, respiratory depression, nausea and vomiting were noted. Immediately, after the delivery, post neonatal examination by the standby pediatrician, Apgar score at 1min and 5 min was recorded. Maternal hypotension, defined as more than 20% decrease in baseline MAP, was promptly treated with bolus dose of 10 mg mephentermine IV and bolus IV fluid supplementation. Bradycardia defined as heart rate <60/min, was treated with 0.6mg atropine IV. Post-operative pain had been assessed every 30mins by VAS scale and when VAS≥4, injection Paracetamol 15mg/kg IV was given as rescue analgesic.

Observation and Results:

Demographic data in terms of age, height, weight and mean duration of surgery were comparable in both groups.

Table 1. Demographics and Duration of surgery

Variables	Group-N N=30	Group-D N=30	P value
	Mean ±SD		
Age (Years)	30.3±5.20	30.53±6.14	0.8776
Weight (Kg)	62.53±8.7	62.4±6.11	0.9468
Height (cm)	158.86±4.72	159±4.4	0.9058
Duration of surgery (min)	36.13±4.86	37.63±5.53	0.269

As seen in Table 1, the demographical profile which included patient's age, weight, height and duration of surgery were similar and not statistically significant. (p>0.05)

Table 2. Development and regression of Sensory block

Sensory Parameters	Group N		Group D		p-value	Remarks
	Mean	SD	Mean	SD		
Time to onset of Sensory Block at T10 (min)	4.08	0.16	2.13	0.20	<0.0001	HS
Time to reach T6 Sensory level (min)	8.20	0.56	5.90	0.47	<0.0001	HS
Time to Two Segment Regression(min)	122.9	7.10	172.06	15.99	<0.0001	HS
Time for Sensory Regression to S1 (min)	183.53	14.01	261.26	9.57	<0.0001	HS
Time of first rescue analgesic (min) (Duration of analgesia)	294	17.4	469.2	31.8	<0.0001	HS
Total number of doses of rescue analgesic required in 24 hours	2.2	0.47	1.6	0.48	<0.0001	HS

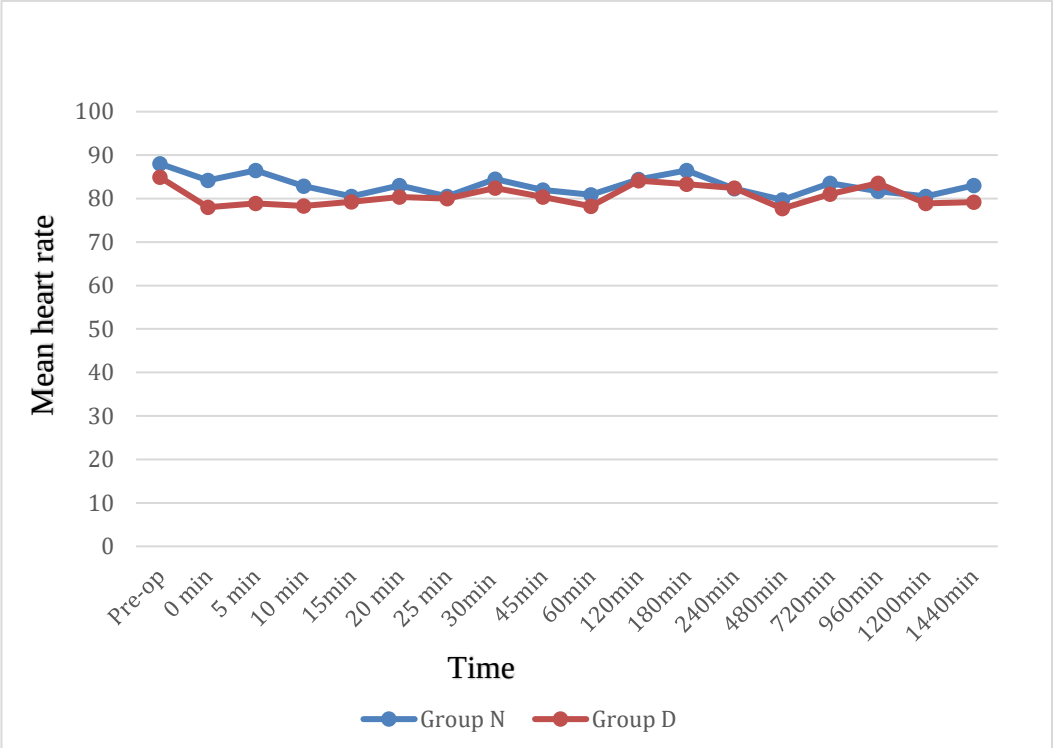
As per the table-2, Mean time for onset of sensory block, time to reach maximum level of sensory block (T6), time for two segment regression and time for sensory regression to S1 segment were extremely statistically significant in Group-D compared to Group-N. Mean time for 1st demand rescue analgesia was significantly longer in Group D compared to Group N. Mean number of Inj. Paracetamol doses required in 24 hours were significantly more in Group-N compared to Group-D. Analgesic (Inj. Paracetamol 15mg/kg) was given when VAS was ≥4. In Group-N, most patients experienced pain at mean time of 294±17.4 min, whereas in Group-D at 469.2±31.8 min, after surgery.

Table 3. Motor parameters in both study groups

Motor parameters	Group N		Group D		p-value	Remarks
	Mean	SD	Mean	SD		
Time onset of Motor block (min)	5.37	0.22	2.32	0.18	<0.0001	HS
Duration of Motor blockade (min)	119.8	15.26	217.3	20.65	<0.0001	HS

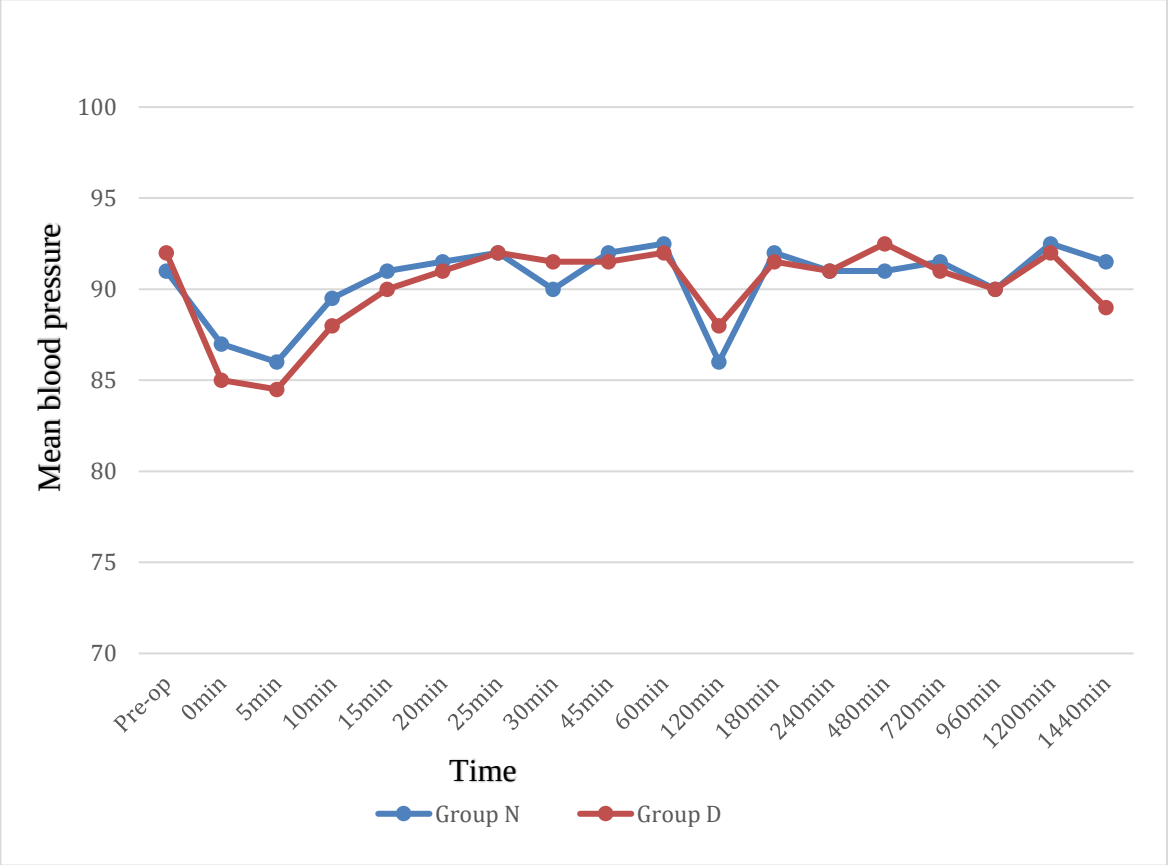
As per the table-3, Mean time for onset of motor block and duration of motor block showed highly significant difference in Group-D compared to Group N.

Figure 1. Heart rate changes in both groups



There was significant difference in heart rate at 0 and 5 min. In Group N and Group D, 3 and 2 parturients had bradycardia respectively, that was treated with Inj. Atropine 0.6 mg IV.

Figure 2. Mean arterial blood pressure (MAP) in both groups



A decrease in MAP, 5-15 minutes after intrathecal injection was observed in both groups. Intraoperative hypotension developed in 3 and 2 parturients of Group N and Group D, respectively, that was treated with increasing the rate of intravenous fluids and a single dose of Mephentermine 10 mg IV, when MAP reduced to less than 20% of baseline or <60mm Hg.

There were no statistically significant differences observed in hemodynamic parameters and associated adverse effects between both the groups. In both the groups, difference in the sedation score was statistically insignificant. None of the parturient was deeply sedated or had respiratory depression. Intraoperative and postoperative Spo_2 was maintained within normal limits in both the groups. No signs of fetal distress were observed, in neonates of both the groups, confirmed by Apgar score of more than 7 at 1min and 5min, in all the neonates.

Table 4. Comparative Incidence of Adverse Effects

Variables	Group –N	Group-D	p-value
Hypotension	3	2	>0.05
Nausea/vomiting	2	2	>0.05
Shivering	2	1	>0.05
Bradycardia	3	2	>0.05
Respiratory depression	0	0	-
Pruritus	0	0	-

The incidence of side effects like nausea and vomiting, hypotension, bradycardia, respiratory depression, shivering and pruritis were not significantly different in both the groups. No parturients had residual neurological deficit, postdural puncture headache or transient neurologic symptoms.

Discussion:

Spinal anaesthesia is the most commonly chosen method of regional anaesthesia due to its quick and straightforward induction, effective sensory and motor blockade, and minimal impact on the foetus.[4] The standard dose of levobupivacaine is linked to extended and profound sensory and motor block, along with significant sympathetic blockade, which may not be ideal for patients undergoing caesarean sections while, using a lower dose of levobupivacaine can restrict the spread of the spinal block, making it inadequate for prevention of visceral pain and nausea, particularly in the early stages.[5] Using appropriate adjuvants with intrathecal local anaesthetics enhances the quality of the block, extends the duration of analgesia, and decreases the necessary dose of local anaesthetics. This, in turn, reduces the risk of side effects associated with high doses, such as bradycardia, hypotension, nausea and vomiting.[6] Intrathecal opioids are carried supraspinally through the bulk flow of cerebrospinal fluid (CSF), where they influence descending inhibitory pain pathways. A small portion also diffuses into the epidural space, leading to systemic absorption that produces centrally mediated analgesia.[7] The addition of adjuvants like nalbuphine to bupivacaine in spinal anaesthesia has been shown to decrease the required dose of bupivacaine, leading to a lower incidence of side effects and a reduced analgesia requirement.[8] The optimal dosage of intrathecal nalbuphine remains a topic of discussion. It has been administered as an adjunct to bupivacaine intrathecally in various clinical contexts, with doses ranging from 0.8 mg to 2.4 mg.[9] Opioid receptors in the dorsal grey matter of the spinal cord, specifically in the substantia gelatinosa are activated by the intrathecal nalbuphine to alter the activity of afferent pain fibres.[2]

Dexmedetomidine, when used as an intrathecal adjuvant, is a novel and highly selective α2 receptor agonist. It provides extended sensory and motor block, enhances the quality of postoperative pain relief, and maintains stable hemodynamics with fewer side effects compared to nalbuphine.[2] Various authors concluded that a 5 µg dose of intrathecal dexmedetomidine results in protracted motor block and analgesia along with minimal hemodynamic changes and sedation, based on their studies on different dosing levels.[10-12] Lee yy et al compared 0.5 % isobaric levobupivacaine with 0.5 % isobaric bupivacaine and concluded that onset of time, duration of sensory and motor blockade, hemodynamic changes were similar in both groups.[13] In our study, we compared intrathecal nalbuphine (1mg) with intrathecal dexmedetomidine (5 µg) as adjuvant to 0.5% hyperbaric levobupivacaine for Caesarean section.

In our study, we observed extreme statistically significant difference between onset of sensory block with Nalbuphine (4.08±0.16 min) and Dexmedetomidine (2.13±0.20 min), mean time to reach T6 sensory level for Nalbuphine (8.20±0.56 min) and for Dexmedetomidine (5.90±0.47 min), mean time for two segment regression with dexmedetomidine (172.06±15.99 min) compared to nalbuphine (122.9±7.10 min) and sensory block regression (S1) with nalbuphine (183.53±14.01 min) as compared to dexmedetomidine (261.26±9.57 min), which correlates with the study of Ravi Paul Singh[6] and Arvind Khare[2]. In the study of Ravi Paul Singh et al[6], the onset of sensory block to T10 was faster (2.31 ± 0.35 min) with dexmedetomidine group compared to (4.33 ± 0.66 min) with nalbuphine group. In the study of Arvind khare et al[2], the mean time of onset of sensory block, was (3.07 ± 1.45 min) with nalbuphine and (2.50 ± 0.99 min) with dexmedetomidine. They also found time to reach T6 sensory level, prolonged in nalbuphine group (6.77±1.71 min) compared to (5.98±1.19 min) in dexmedetomidine and prolonged mean time for two segment regression (151.82±0.811 min) in dexmedetomidine group compared to (127.25±24.30 min) with nalbuphine. Michael RM et al[14], also concluded that mean duration of sensory block was significantly prolonged in dexmedetomidine (276.07±31.28 min) compared to nalbuphine, which is similar to our study. The Anjali Bhure et al study[11], compared intrathecal dexmedetomidine and fentanyl as an adjuvant to isobaric levobupivacaine for lower limb orthopedic surgery and found prolonged duration of effect with dexmedetomidine group (203.28±6.36 min), that may result from synergism between local anesthetic and alpha2 adrenoceptor agonist action. In our study, the mean duration of complete motor block was significantly longer with dexmedetomidine (217.3+20.65 min) compared to nalbuphine (119.8±15.26 min). Our study was further supported by the findings of Ahmed Basuni et al[15]. and Farhad Safari et al[16]., who reported similar prolongation of sensory and motor block with

dexmedetomidine. Additionally, pain and sedation scores were improved in patients receiving dexmedetomidine compared to those in the fentanyl and control groups, with patients appearing calmer and more sedated than those in the fentanyl group.[16] There was significant difference between onset of motor block with Nalbuphine (5.37±0.22 min) and Dexmedetomidine (2.32±0.18 min) in our study. In Ravi Paul Singh et al study[6], mean time for onset of motor block was also observed to be prolonged (7.00±0.43 min) with nalbuphine compared to (6.24±0.45min) with dexmedetomidine group. These results align with our findings, emphasizing that dexmedetomidine as an adjuvant to levobupivacaine not only reduces the mean onset time for sensory and motor block but also extends the overall duration of both. The prolonged effect of dexmedetomidine is attributed to its supraspinal action at the locus coeruleus and dorsal raphe nucleus.[3]

In our study, mean time for first demand rescue analgesia was (294±17.4 min) in group-N and (469.2±31.8 min) in group-D. Studies by Nirvana a.Elshalakany et al[10], Anjali Bhure et al[11] , Farhad safari et al[16] and Amir laique khan et al[17] showed similar results with dexmedetomidine group, evincing prolonged duration of first demand rescue analgesia along with reduced 24hour supplementary analgesic dose requirement, comparable with our study.

Duration of analgesia was longer in dexmedetomidine compared to nalbuphine group. Bhargav Vishnu ghantasala et al[18] study, also found extended duration of analgesia with dexmedetomidine (320±89 min) compared to nalbuphine (222±25.43min). Studies of Bhargav Vishnu ghantasala et al[18], Prasanna vadhanan et al[19] and Mukherjee et al[20] also demonstrated increased duration of analgesia compared to nalbuphine, which correlates with our study.

Hemodynamic parameters exhibited no statistically significant difference, similar to Ravi Paul Singh study.[6] Incidence of adverse effects was comparable between the groups. Hypotension and bradycardia developed in 3 parturients of Group N and 2 parturients of Group D, supported by Nirvana a.Elshalakany[10] and Abd Elhamid BM et al[12] studies. Two parturients with nalbuphine & one with dexmedetomidine had complaint of shivering but did not require medication. Several studies have demonstrated that dexmedetomidine mediated thermoregulatory inhibition, causes alleviation of shivering effects via widely distributed a2-adrenergic receptors in the hypothalamus.[21] Other studies confirmed that dexmedetomidine directly increased the temperature range without impacting thermoregulatory defenses, which contributed to a reduction in the incidence of shivering..[22] Nausea was observed in 2 parturients of both the groups but none of them developed vomiting. Al Ghanem at al[23], stated that 5% patients with dexmedetomidine developed nausea and vomiting. There was no documented respiratory depression and allergic reactions in both the groups. All parturients in group N had modified Ramsay sedation score of 2 in the immediate postoperative period. Mechanism of sedation in dexmedetomidine group is explained by its action on sleep promoting pathway.[11] As we have used minimal dexmedetomidine dose (5 µg), no parturient in group D was deeply sedated. Our study coincides with Michael & Mehta's study[14], and Arvind Khare's study[2], where the difference in the sedation score of both groups N and D was insignificant. All the new-borns had Apgar score more than 7 at 1 min, pointing to the added benefit of dexmedetomidine over other adjuvants, as supported by other studies.[24,25]

Limitations of study:

1. Our study was done only on parturients of age group 20-40 years of age.
2. Pain assessment by VAS is subjective and varies with the level of understanding between patient and anesthesiologist.
3. Only included ASA II parturient, further study required to investigate the efficacy of drug in ASA III and ASA IV and medically compromised patients.

Conclusion:

Levobupivacaine and dexmedetomidine combination not only enables faster onset of sensory and motor block, prolonged time for two segment regression and increased duration of sensory and motor blockade, but also increases the duration of analgesia hence, delaying the time for 1st demand rescue analgesic dose post-operatively. It offers better intraoperative and postoperative analgesia, arousable sedation without respiratory depression throughout the surgery, hemodynamic stability, minimal side

effects and no adverse effects on Apgar scoring, making it more attractive and better alternative to levobupivacaine and nalbuphine combination for intrathecal anesthesia and postoperative analgesia in LSCS.

References:

1. Mohamed h. Kamal, m.d.; jehan h. Ibrahim, m.d.; abeer a. Saaed, m.d.;marwa s. Zayed, m.d. and marianne magdy, M.Sc.Comparison of Intrathecal Dexmedetomidine and Fentanyl as Adjuvants to Levobupivacaine in Parturients Undergoing Elective Cesarean Sections. Med. J. Cairo Univ., Vol. 85, No. 2, March: 593-600, 2017
2. Khare, Arvind, et al. "A study to compare the efficacy of intrathecal dexmedetomidine versus nalbuphine as an adjuvant to 0.5% hyperbaricbupivacaine for postoperative analgesia in lower abdominal surgeries."Ain-Shams Journal of Anesthesiology 14.1 (2022): 1-9
3. Gupta R, Verma R, Bogra J, Kohli M, Raman R,Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesth Clin Pharmacol 2011; 27:339-43
4. Prabha P., Shreyavathi, Raghavendra Rao , Akshatha Rao Comparative Study of Intrathecal Bupivacaine and Levobupivacaine with Fentanyl for Caesarian Section Sch. J. App. Med. Sci., 2014; 2(4B):1255-1259
5. Yong-Hong Bi1, Xiao-Guang Cui1, Rui-Qin Zhang1, Chun-Yu Song1and Yan-Zhuo Zhang Low dose of dexmedetomidine as an adjuvant tobupivacaine in cesarean surgery provides better intraoperative somatovisceral sensory block characteristics and postoperative analgesia Oncotarget, 2017, Vol. 8, (No. 38), pp: 63587-63595
6. Singh RP**,** Kataria AP, Mahajan L, Arora HS, Kaur P. Comparison of Intrathecal Nalbuphine and Dexmedetomidine as Adjuvants to Levobupivacaine in Infraumbilical Surgeries. Int J Sci Stud 2021;8(12):54-59
7. Ahmed F, Narula H, Khandelwal M, Dutta D. A comparative study of three different doses of nalbuphine as an adjuvant to intrathecal bupivacaine for postoperative analgesia in abdominal hysterectomy. Indian J Pain 2016;30:23-8
8. Gurunath BB, Madhusudhana R. Postoperative Analgesic Efficacy of Intrathecal Fentanyl Compared to Nalbuphine with Bupivacaine in Spinal Anesthesia for Lower Abdominal Surgeries. Anesth Essays Res. 2018 Apr-Jun;12(2):535-538.doi: 10.4103/aer.AER_55_18. PMID:29962630; PMCID: PMC6020599
9. Jyothi B, Gowda S, Shaikh SI. A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopedicsurgeries. Indian J Pain 2014;28:18-23
10. Elshalakany NA, El-Shaer AN, Rabie AH, Moharram AA, Elsofy AM.Dexmedetomidine as adjuvant to hyperbaric bupivacaine in spinalanesthesia for inguinoscrotal surgery. Ain Shams J Anaesthesiol 2017;10:264-71
11. Anjali bhure 2019 Bhure A, Jagtap N. A comparison of intrathecal dexmedetomidine and fentanyl as an adjuvant to isobaric levobupivacaine for lower limb orthopaedic surgery. Indian J Clin Anaesth2019;6(1):89-96
12. Abd Elhamid BM, Ali HM. Comparison of 3 different dexmedetomidine doses and their effect on the duration of spinal anesthesia. J Anesth Clin Res 2017;8:762
13. Y Y Lee, K.Mucchal, C.K Chan: Levobupivacaine versus Bupivacainein spinal anesthesia for urological surgery. Anesth intensive care 2003;31:637-641
14. Michael RM, Mehta M (2016) Comparison between dexmedetomidineand nalbuphine as an adjuvant to bupivacaine in spinal anesthesia. Int. J Adv Res 3(1):1024 –1045
15. Basuni AS, Ezz HAA. Dexmedetomidine as supplement to low-dose levobupivacaine spinal anesthesia for knee arthroscopy. Egypt J Anaesth 2014;30(2):149–153
16. Safari F, Aminnejad R, Mohajerani SA, Farivar F, Mottaghi K, Safdari H. Intrathecal Dexmedetomidine and Fentanyl as Adjuvant to Bupivacaine on Duration of Spinal Block in

Addicted Patients. Anesth Pain Med. 2016Jan 31;6(1):e26714
17. Khan AL, Singh RB, Tripathi RK, Choubey S. A comparative study between intrathecal dexmedetomidine and fentanyl as adjuvant to intrathecal bupivacaine in lower abdominal surgeries: A randomized trial. Anesth essays Res 2015;9(2):139–148
18. Gantasala, Bhargav & Singam, Amol & Rallabhandi, Saranya & Chaubey, Kashish & Deulkar, Pallavi & Bansal, Ayush. (2020). Comparison of Intrathecal Dexmedetomidine and Nalbuphine as an Adjuvant in Hyperbaric Bupivacaine for Saddle Block and Postoperative Analgesia in Patients Undergoing Perianal Surgeries. Journal of Evolution of Medical and Dental Sciences. 9. 2028-2033. 10.14260/jemds/2020/442
19. Vadhanan P, Balakrishnan K. Comparison of postoperative analgesia with 0.8 mg and 1.6 mg intrathecal nalbuphine; a randomized controlled trial. Anaesth Pain & Intensive Care 2017;21(1):37-43
20. Mukherjee A, Pal A, Agarwal J, Mehrotra A, Dawar N. Intrathecal nalbuphine as an adjuvant to subarachnoid block: what is the most effective dose? Anaesth Essays Res 2011;5:171-5
21. Lewis SR, Nicholson A, Smith AF, et al. Alpha-2 adrenergic agonists for the prevention of shivering following general anaesthesia. CochraneDatabase Syst Rev
2015; 8: Cd011107. DOI: 10.1002/14651858. CD011107.pub 2
22. Bicer C, Esmaoglu A, Akin A, et al. Dexmedetomidine and meperidineprevent postanaesthetic shivering. Eur J Anaesthesiol 2006; 23: 149–153. DOI: 10.1017/s0265021505002061
23. Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, QudaisatIY, Qatawneh AM and Abu-Ali HM. Effect of Adding Dexmedetomidine versus Fentanyl to Intrathecal Bupivacaine on SpinalBlock Characteristics in Gynecological Procedures: A Double Blind Controlled Study. Am J Appl Sci 2009;6:882-7
24. Sun Y, Xu Y, Wang GN. Comparative evaluation of intrathecal bupivacaine alone, bubivacaine-fentanyl, and bupivacaine-dexmedetomidine in cesarean section. Drug Res (Stuttg). 2015;65:468-472. [PubMed] DOI: 1055/s-0034-1387740
25. Paech MJ, Pavy TJ, Orlikowski CE, Yeo ST, Banks SL, Evans SF, et al. Postcesarean analgesia with spinal morphine, clonidine, or their combination. Anesth Analg. 2004;98:1460-1466. [PubMed] DOI: 1213/01.ane.0000111208.08867.3c

Abbreviations:

LSCS	Lower Segment Caesarean Section
ASA	American society of Anesthesiologists
IV	Intravenous
mm Hg	Millimetres of Mercury
Inj.	Injection
min	Minute
BP	Blood pressure
MAP	Mean arterial pressure
RL	Ringer lactate
VAS	Visual analogue scale
SD	Standard deviation
CSF	Cerebrospinal Fluid
ml	Milli-litre
µg	Microgram
mg	Milligram

Kg	Kilogram
SpO_2	Peripheral oxygen saturation
HR	Heart Rate
NIBP	Non-Invasive Blood Pressure