Original Article

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Anaesthesia Section

Evaluation of the Effects of Doses of Dexmedetomidine as Adjuvants to Hyperbaric Bupivacaine in Subarachnoid Blocks for Elective Caesarean Sections: A Prospective, Randomised, Triple-blind Controlled Study

RAMANAREDDY VENKATA MOOLAGANI[1], MRUNALINI OWK[2], AMEENA BIBI SHAIK[3], KURMANADH KALLEPALLI[4], RAMANAPRASAD JAMMALA MADAKA[5], KAARTHIKA THOTTIKAT[6], HIMABINDU VENKATA ATTILI[7], SALIN KUMAR ADUSUMILLI[8]

ABSTRACT

Introduction: Since single-shot spinal anaesthesia for caesarean section operations provides limited postoperative analgesia, several adjuvants are employed to obtain the prolonged duration of sensory block. Dexmedetomidine (DMT) used as an adjuvant to 0.5% hyperbaric bupivacaine is found to provide a longer duration of analgesia.

Aim: To evaluate the block characteristics and neonatal effects of three doses of DMT 2.5 µg, 5 µg and 7.5 µg used as adjuvants to 0.5% hyperbaric bupivacaine (10 mg).

Materials and Methods: A prospective randomised multi arm triple-blind controlled study was conducted at the Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Andhra Pradesh, India from May 2020 to May 2022 on parturients who were assigned to four groups of 20 each. Parturients of Groups A, B and C were given 0.5% hyperbaric bupivacaine (10 mg) with DMT 2.5 µg (0.1), 5 µg (0.2) or 7.5 µg (0.3) mL, respectively as adjuvant and those in Group D were given 2 mL of 0.5% hyperbaric bupivacaine alone and the final volume was made 2.5 in all four groups by adding sterile normal saline (0.9% NaCl). Characteristics of the mother and neonate like age, height, body weight, Body Mass Index (BMI), gravida status etc., were recorded, the duration of analgesia, the total quantity of the analgesic medicine consumed during the 1st 24 hours of the postoperative period, duration of the motor and sensory blocks, changes in haemodynamic variables were also noted. Ramsay Sedation Scores (RSS), surgeon and patient satisfaction scores were recorded for statistical analysis. Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 20.0 and a p-value of ≤0.05 was considered statistically significant.

Results: Parturients of Groups A, B and C had an earlier onset of sensory block 4.3±0.8, 3.6±0.5, 2.7±0.5 minutes, respectively compared to control 5.7±0.6 minutes (p-value <0.001). They also had a longer duration of analgesia 203.6±14.4, 320.2±24.0, 340.0±14.4 minutes, respectively compared to those in control 150.1±7.1 minutes (p-value <0.0001) and consumed a lesser amount of analgesic medication; 165.0±14.4, 110.0±30.7, 100.0±0.0 mg, respectively compared to control 190.0±30.7 mg (p-value <0.001). Surgeon scores regarding the anaesthetic technique were satisfactory in a greater proportion/percentage of parturients in Groups A, B and C; 13 (65%), 16 (80%) and 18 (90%), respectively vs 9 (45%) in control p-value <0.01198. Patient scores regarding the anaesthetic technique were satisfactory in a greater proportion/percentage of parturients in Groups A, B and C; 14 (70%), 17 (85%), 19 (95%), respectively vs 10 (50%) in control p-value <0.00652.

Conclusion: On the basis of the results of the present study, it was concluded that 5 µg DMT added as an adjuvant to 10 mg of 0.5% hyperbaric bupivacaine intrathecally was the optimal drug combination to be used for spinal anaesthesia for caesarean section cases, whereas a higher dose of 7.5 µg DMT had resulted in greater fluctuations in Pulse Rate (PR) and Mean Arterial Pressure (MAP) and a lower dose of 2.5 µg DMT had resulted in a shorter duration of analgesia.

Keywords: α 2 receptor, Analysis of variance, Apgar score, Maternal, Neonate, Spinal

INTRODUCTION

Single-shot spinal block (spinal anaesthesia) is the most commonly employed anaesthetic technique with 0.5% hyperbaric bupivacaine (10 mg) as the most preferred local anaesthetic agent for caesarean section operations [1]. Clinical data supports the fact that caesarean surgeries performed under spinal anaesthesia had less maternal morbidity and mortality than surgeries done under general anaesthesia [2]. Spinal block is simple to perform and provides a rapid onset of reliable and adequate sensory and motor block besides being cost-effective and less likely to fail [3]. In contrast to general anaesthesia, it avoids the problems of a difficult airway, usage of multiple drugs and complications of aspiration pneumonia. Further, it also allows the parturients to be awake during the surgery and witness the process of delivery of the baby and enjoy the birth experience which is believed to promote maternal bonding with the baby besides having the advantage of causing minimal neonatal depression due to the use of minimal anaesthetic medications for the mother [4].

The optimum level of sensory block required for conducting caesarean surgery is believed to be T6 thoracic dermatome and this high level of sensory block is commonly associated with severe hypotension and decreased uteroplacental perfusion in the mother which adversely affects the foetal well-being [5]. Further, single-shot spinal anaesthesia provides only a fixed duration of block

and limited postoperative analgesia, necessitating the use of Non Steroidal Anti-inflammatory Drugs (NSAIDs) and opioids in the postoperative period, thereby exposing the mother and the neonate to the side-effects of these drugs. In the commonly used 10 mg dose, bupivacaine doesn't abolish the visceral pain associated with the handling of the gut and exteriorisation of the uterus during the course of the surgery [6].

Several adjuvants like fentanyl, morphine, neostigmine, midazolam, ketamine, clonidine and DMT are employed to obtain a prolonged block [7]. Though clonidine and DMT are established as the adjuvants of choice because of the unique benefits associated with their use, several studies indicate that during and after surgery DMT provides better quality analgesia and haemodynamic stability than clonidine [8-10].

The DMT is a more selective α 2 receptor agonist and was introduced into clinical practice as an adjuvant to local and general anaesthetics, as it was found to provide sedation, amnesia, anxiolysis and analgesia with better haemodynamic stability and minimal respiratory depression than other agents [11]. Further by its sympatholytic effects, DMT decreases heart rate, cardiac output, circulating catecholamines and shivering threshold in a dose-dependent manner resulting in reduced perioperative oxygen consumption and blunting of the sympathetic response to surgery contributing to better cardiac outcome [12]. The analgesic effect of DMT is mediated through the stimulation of the α 2C and α 2A receptors in the dorsal horn, thus directly suppressing pain transmission by reducing the release of substance P, glutamate and hyperpolarisation of interneurons [13].

The DMT is being safely used as an adjuvant for subarachnoid blocks in urological surgeries, orthopaedic procedures of the lower limb and lower abdominal surgical procedures but reports of its use in caesarean surgery are limited [14]. DMT does not cross the placenta and is reported to be retained within the placenta due to its high lipid solubility [15]. Some researchers using DMT for caesarean surgeries reported that they did not find any adverse effect of DMT on scores and umbilical blood gas levels of neonates [16].

Previous literature has revealed that 5 µg DMT is the optimum dose to be used as an adjuvant to 0.5% hyperbaric bupivacaine but the effect of doses like 2.5 µg and 7.5 µg are not much studied [17].

The aim of the study was to evaluate the effects of three doses of DMT i.e., 2.5 µg, 5 µg and 7.5 µg used as adjuvants to 0.5% hyperbaric bupivacaine (10 mg) in spinal anaesthesia for surgeries of elective lower segment caesarean sections.

MATERIALS AND METHODS

A prospective randomised multi arm triple-blind controlled study was conducted at the Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India from May 2020 to May 2022 on parturients. Institutional Ethical approval was obtained for conducting the study vide RC.No:GVPIHCMT/IEC/20201208/01 dated 08-12-2020, and the study was registered with the Clinical Trial Registry of India vide CTRI registration No CTRI/2020/12/030150.

Inclusion criteria: A total of 80 parturients of age between 20-40 years, height ranging from 145-170 cm who were of American Society of Anaesthesiologists (ASA) Grade-II [18], attending the medical college hospital with uncomplicated singleton pregnancies of more than 38 weeks of gestation for elective lower segment caesarean surgeries were enrolled in this study. Written Informed consent was obtained from all the participants after explaining in detail the study protocol and all the consequent risks and benefits in their mother tongue in the presence of two witnesses.

Exclusion criteria: Parturients with known allergies to study drugs, parturients refusing the local anaesthetic block, parturients suffering from neurological disorders, psychiatric disorders, uncontrolled hypertension and diabetes mellitus, coagulation or bleeding abnormalities, severe spinal deformity, infection at the spinal injection site and cases posted for emergency caesarean section were excluded from the study.

Sample size calculation: It was based on a pilot study (unpublished work) of two groups of parturients: (a) Bupivacaine-dexmedetomidine (7.5 µg) Group A and (b) Bupivacaine-dexmedetomidine (2.5 µg) group, with a sample size of 10 in each group (n=10).

Primary outcome measure of the study was duration of analgesia which was 4±1.6 hours (mean±SD) in Bupivacaine-dexmedetomidine (7.5 µg) Group A and 1.4±0.2 hours (mean±SD) in Bupivacaine-dexmedetomidine (2.5 µg) group.

The formula used for calculation of sample size was $N=Z^2 (SD^2)/d^2$ where,

N=sample size in each group (10 in the pilot study)

Z=Normal deviate or Unit normal deviate whose value is 1.96 and $Z^2=1.96*1.96=3.846$

SD^2=Pooled variance of the two groups under study which is given by the formula $SD^2=(n_1-1)(SD_1^2)+(n_2-1)(SD_2^2)/(n_1+n_2-2)$..... where n_1 and SD_1 are sample size and SD of Group-1; n_2 and SD_2 are sample size and SD of Group-2;

$SD^2=(10-1)(2.56)+(10-1)(0.04)/18$

$=(23.04+0.36)/18$

$=23.4/18$

$=1.3$

d=precision or allowable error which is usually taken as less than 20% of the difference of the means of the two groups.

d=20% of the difference of two means (M1-M2=4-1.4=2.6)

$=(20/100)*(2.6)$

$=0.52$

$d^2=0.52*0.52=0.2704$

Substituting the derived values in the formula $N=Z^2(SD^2)/d^2$

Sample size $N=(3.846*1.3)/0.2704=18.49$

N=18 (rounded off to 18)

With 80% power and 5% alpha error, a sample size of 18 patients per group was required and incorporating a compensation for a non responder's bias for an assumed attrition rate of 10% (1.84) it was calculated that a sample size of 20 (18+1.84=19.84, rounded-off to 20) patients in each group was required and it was believed to be adequate.

Study Procedure

Participants were randomly allocated to four groups of 20 each (n=20) by utilising a computer-generated random grouping software: and a sequentially numbered sealed opaque envelope method was utilised for allocating the individual patient to the respective study group. Parturients of groups A, B and C were given spinal block with 0.5% hyperbaric bupivacaine (10 mg) plus DMT 2.5 µg (0.1), 5 µg (0.2), and 7.5 µg (0.3) mL, respectively added as adjuvant. Parturients of the control group were given intrathecal 0.5% hyperbaric bupivacaine 10 mg alone without any adjuvant and the final volume of the spinal injection was made up to 2.5 mL for all parturients in all four groups by adding sterile normal saline (0.9% NaCl). Demographic characteristics of the parturient and the neonate like age, height, body weight, BMI, gravida status, period of gestation, duration of surgery, skin and uterine incision to baby delivery times were recorded.

The primary outcome variables studied were the differences in the duration of analgesia and the total quantity of the analgesic medicine consumed during the 1st 24 hours of the postoperative period. The secondary outcome variables studied were the differences in the

time to onset of the motor and sensory blocks, duration of the motor and sensory blocks (2-segment sensory regression), changes in haemodynamic variables like PR, MAP, RR, SaO_2, the quantity of vasopressor agent used, RSS and neonatal APGAR scores at one minute and five minutes after the delivery. The time interval between skin and uterine incision and the time of delivery of the baby, adverse drug effects and complications like Postoperative Nausea Vomiting (PONV), dryness of the mouth and shivering, incidence of PDPH and backache in the mother during the seven days postoperative period were noted for statistical analysis.

Before taking up for the surgery, all the parturients were examined in the clinic by a thorough history taking and physical examination and all the required investigations were carried out. Details of the technique of spinal anaesthesia and methods of examination regarding the evaluation of motor and sensory block and assessment of pain on a Verbal Numeric Rating Scale (VNRS) were explained to the parturients: (VNRS scale 0=no pain, scale10=worst pain imaginable) [19]. All the parturients were advised to fast for six hours for solids and two hours for liquids prior to the surgery and tablet ranitidine 150 mg and tablet metoclopramide 10 mg were given orally as premedication the night before the surgery. On the day of the surgery, all the parturients were provided preoperative aspiration prophylaxis with inj. ranitidine 50 mg intravenous (i.v.) and inj. metoclopramide 10 mg i.v. and 30 mL of 1/3 molar sodium citrate nonparticulate solution orally.

In the operation theatre, standard monitoring equipments were connected and PR, MAP, RR, Electrocardiogram (ECG) and SaO_2 were recorded at every five minutes interval throughout the surgery. A peripheral i.v. access was secured with an 18 G i.v. cannula and ringer lactate solution 10 mL/kg was infused as a preloading 20 minutes prior to administering the spinal block.

The spinal anaesthetic drugs were loaded into a syringe by an anaesthetist who was not associated with the assessment and monitoring of the parturients. Under strict aseptic precautions, spinal block was given keeping the parturient in the sitting position via a midline approach at L3-L4 or L2-L3 intervertebral space, using a 26 gauge Whitacre spinal needle and the drug was given over a period of 10 seconds after confirmation of clear and free flow of cerebrospinal fluid. Immediately after the block, the parturients were made to lie supine on the operation table kept in a horizontal position and a wedge was placed below the right buttock to have a 20° left lateral tilt for ensuring left uterine displacement to prevent aortocaval compression in the mother. The i.v. fluids were administered as required to attain stable haemodynamic parameters and supplemental O_2 was administered with a face mask if the maternal SaO_2 levels dropped below 95%. Sensory and motor block levels were assessed at every one-minute interval after completion of the spinal injection till a stable block level was obtained on two consecutive examinations. All the time intervals were calculated considering the time when the spinal injection was completed as zero reference point.

The onset of the sensory block (defined as the time elapsed to obtain sensory block at T6 dermatome level) and the time taken for 2-segment sensory regressions were recorded. Sensory block was tested using a pinprick method with a blunt 27G hypodermic needle at every one-minute interval till the onset of sensory block to T6 level was obtained and subsequently at every 10 minutes until 2-segment sensory regression was attained. Loss of pin-prick sensation at the T6 level was defined as the onset of a complete sensory block.

Grading for the motor block was done according to the modified Bromage scale [20] and attaining a motor block of Bromage Grade-4 was considered as satisfactory motor block and the time elapsed to attain this level of the block was noted. Parturients were considered ready for commencing surgery when the level of sensory block attained was T6 dermatome and attainment of motor block was of Bromage Grade-4. For assessing the time elapsed for the recovery of the block, the time to 2-segment regression from T6 sensory block and the time to motor recovery to Bromage Grade-1 with regards to the motor block were recorded.

Analgesia duration was taken as the time elapsed from attainment of satisfactory sensory block to the time of administration of Inj. diclofenac 75 mg intravenously as the rescue analgesic when parturients complained of pain of Grade-2 intensity on VNRS. Haemodynamic parameters of PR, MAP, RR, SaO_2 and ECG were recorded just before giving the spinal injection, then at every five minute-interval till the end of the surgery. The level of sedation attained was assessed by using the RSS [21]. Parturients were also observed for any adverse events like nausea, vomiting, dryness of mouth, desaturation, hypotension, bradycardia and allergic reactions. Postoperatively, the occurrence of pain was assessed using the VNRS score till the parturients complained of pain of Grade-2 intensity.

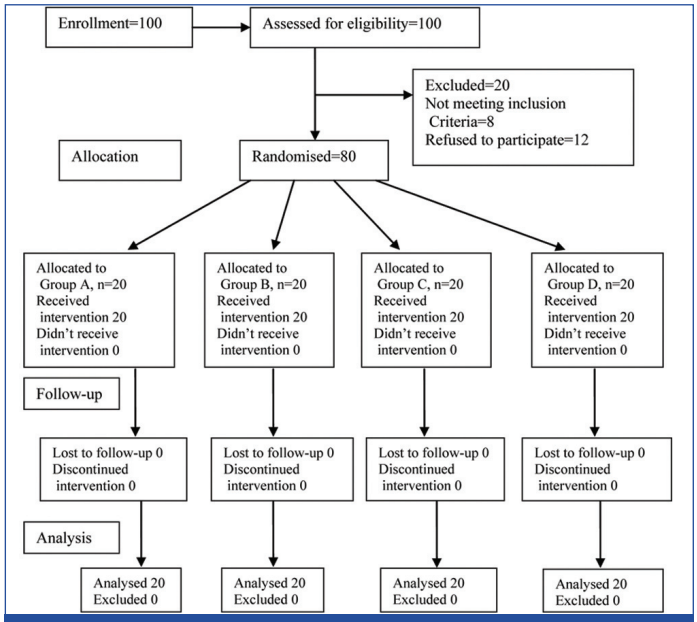
On the first postoperative day, parturients were enquired regarding their satisfaction level with the anaesthetic experience on a 3-point verbal rating score [22]. Surgeon satisfaction with the anaesthetic procedure was recorded at the end of the surgery by asking him to rate his satisfaction with the operating conditions, using a 3-points verbal rating score [23]. A score of 2 or 3 was taken as an acceptable satisfaction level both in the parturients and the surgeons.

STATISTICAL ANALYSIS

At the end of the study, data was compiled, and the parametric data were presented as mean±SD and the differences between the groups were analysed using the statistical test ANOVA and Tukey's posthoc test HSD Beta was used for comparison. Non parametric data were presented as numbers and percentages and the Chi-square test and Fisher's-exact test were used as applicable for the analysis of the differences between the groups. Statistical analysis was carried out using Microsoft excel 2007 and SPSS version 20.0 of IBM and a p-value of ≤0.05 was considered statistically significant.

RESULTS

The particulars of the parturients who were enrolled, screened and had gone through various study phases are shown as the flow diagram as per the guidelines of Consolidated Standards of Reporting Trials (CONSORT) [Table/Fig-1].



[Table/Fig-1]: Flowchart showing parturients progress through the study phases.
Group-A=Bupivacaine plus dexmedetomidine 2.5 µg; Group-B=Bupivacaine plus dexmedetomidine 5 µg
Group-C=Bupivacaine plus dexmedetomidine 7.5 µg; Group-D=Bupivacaine with no dexmedetomidine
{As per Consolidated Standards of Reporting Trials (CONSORT) guidelines}

The data of all 80 parturients were included in the statistical analysis as all of them completed the study. The demographic features like age, height, weight, BMI, parity and the duration of surgery are comparable in all four groups as shown in the table [Table/Fig-2].

Variables	Group A	Group B	Group C	Group D	p-value
Age (years) (mean±SD)	26.0±3.9	26.9±5.6	29.7±6.3	27.1±3.2	0.11
Height (cm) (mean±SD)	151.8±5.3	151.6±3.8	153.4±3.1	154.3±3.0	0.15
Weight (kg) (mean±SD)	58.7±5.7	57.0±3.9	56.2±4.7	56.0±4.5	0.90
BMI (kg/m^2) (mean±SD)	25.2±2.5	25.4±3.2	25.4±2.3	24.9±2.1	0.92
Gravida 1/Gravida 2/ Gravida 3 (numbers)	9/10/1	8/10/2	7/12/1	8/11/1	0.98
Surgery duration (min) (mean±SD)	54.2±5.7	57.0±3.9	56.2±4.7	56.0±4.9	0.31

[Table/Fig-2]: Demographic characteristics of the parturients across the groups.
SD: Standard deviation; BMI: Body mass index
Result not significant at p-value <0.05, Chi-square test: n=20 in all the four groups

The vital parameters like SaO_2, RR and ECG were comparable and within the clinically acceptable ranges in all the groups.

The fluctuations observed in the MAP and PR at baseline and in the intraoperative and postoperative periods are shown in [Table/Fig-3,4], respectively. Parturients of Group C had shown the greatest degree of fluctuations both in MAP and PR at time intervals of 5,10,15,20,25 and 30 and required more quantity of vasopressor medicines for attaining haemodynamic stability.

Time intervals	Group A	Group B	Group C	Group D	p-value
Starting	97	97	90	100	0.165
5 min	92	85	75	95	0.00001*
10 min	89	85	76	93	0.00001*
15 min	89	85	75	93	0.00001*
20 min	88	85	75	92	0.00001*
25 min	87	86	75	92	0.00001*
30 min	88	90	77	93	0.00001*
60 min	92	92	82	96	0.00001*
120 min	95	97	87	99	0.00001*

[Table/Fig-3]: Mean arterial pressure changes in millimetres of mercury (mm/Hg).
p-value <0.05 was considered significant; n=20 in all the four groups

Time intervals	Group A	Group B	Group C	Group D	p-value
Starting	89	87	88	93	0.009*
5 min	83	77	70	88	0.001*
10 min	84	75	70	87	0.001*
15 min	84	75	70	87	0.001*
20 min	85	75	71	87	0.001*
25 min	83	74	73	87	0.001*
30 min	85	75	77	88	0.001*
60 min	87	78	81	90	0.001*
120 min	89	82	84	93	0.001*

[Table/Fig-4]: Pulse rate changes in beats per minute (bpm).
p-value <0.05 was considered significant; n=20 in all the four groups

Parturients of groups A, B and C had an earlier onset of sensory block at T6 level and motor block of Bromage Grade-i.v. compared to the control Group D, with a statistically significant difference at p-value <0.001 [Table/Fig-5]. The time for 2-segment regression from the T6 level of the sensory block attained as well as the duration of motor block were prolonged in parturients of groups A, B and C in comparison to those of the Group-D with a statistically significant difference at p-value <0.001 [Table/Fig-5].

Variables (mean±SD) (min)	Group A	Group B	Group C	Group D	p-value
Onset of sensory block	4.3±0.8	3.6±0.5	2.7±0.5	5.7±0.6	<0.00001*
Duration of 2 segment sensory regression	136.5±11.9	205.8±11.9	313.0±14.9	75.7±6.5	<0.00001*
Onset of motor block	6.3±0.9	5.6±0.5	5.6±0.5	8.0±0.8	<0.00001*
Duration of motor block	291.0±19.4	325.2±22.0	459.0±21.2	136.6±7.6	<0.00001*
Duration of analgesia	203.6±14.4	320.2±24.0	340.0±14.4	150.1±7.1	<0.00001*
Pairwise comparisons					
Group A: Group B	203.6±14.4	325.2±22.0	....	....	<0.001*
Group A: Group C	203.6±14.4	....	340.0±14.4	....	<0.001*
Group A: Group D	203.6±14.4	....	....	150.1±7.1	<0.001*
Group B: Group C	....	320.2±24.0	340.0±14.4	....	0.00089*
Group B: Group D	....	320.2±24.0	....	150.1±7.1	<0.00001*
Group C: Group D	....	....	340.0±14.4	150.1±7.1	<0.00001*

[Table/Fig-5]: Characteristics of spinal block between the groups.
*Result significant at p<0.05, one-way ANOVA. **Result significant at p<0.05 (Chi-square test)
PDPH: Postdural puncture headache; SaO2=Percentage of peripheral arterial oxygen saturation
Values expressed as mean±SD and numbers (%); SD: Standard deviation

Parturients of groups A, B and C had a longer duration of analgesia compared to the control with a statistically significant difference at p-value <0.001 [Table/Fig-5]. The addition of DMT 7.5 µg, 5 µg and 2.5 µg doses to 0.5% bupivacaine heavy had groups statistically significant enhancement of the duration of analgesia; the effect being greater with 7.5 µg dose than with the lower doses i.e., 7.5 µg >5 µg >2.5 µg.

The pair-wise intergroup comparisons analysed by a posthoc Tukey's HSD (beta) test had shown a statistically significant difference between each pair; the groups with DMT added as an adjuvant showed a greater duration of analgesia than the control Group-D with statistically significant differences [Table/Fig-5].

Parturients of control group had consumed a greater amount of analgesic medication in the first 24 hours postoperative period than those in groups A, B and C and this difference in analgesic consumption was statistically significant at p-value <0.001 [Table/Fig-6]. Parturients of Group C required a greater amount of vasopressor medication for attaining haemodynamic control than those in groups A, B and D and this difference in vasopressor consumption was statistically significant at p-value <0.001 [Table/Fig-6].

The time elapsed between skin incision and delivery of the baby as well as the time elapsed between the uterine incision and delivery of the baby is shown in [Table/Fig-7] and the differences in the durations among the groups are not statistically significant. APGAR scores of the babies of the four groups recorded at 1-minute and 5-minute intervals are comparable as shown in [Table/Fig-7]. Parturients of groups A, B and C had satisfactory sedation levels measured on RSS at 15, 30, 45 and 60 minutes after the block with a statistically significant difference against the control Group D at p<0.05 as shown in the table [Table/Fig-7].

More cases in groups A, B and C had bradycardia and hypotension in comparison to cases of control with a statistically significant difference at p-values 0.024 and 0.039, respectively as shown in the table [Table/Fig-8]. A few cases in all four groups had complications like nausea and/or vomiting, dryness of mouth, shivering, Postdural Puncture Headache (PDPH) and backache and the differences

Variables (mean±SD)	Group A	Group B	Group C	Group D	p-value
Analgesic consumption (mg)	165.0±14.4	110.0±30.7	100.0±0.0	190.0±30.7	<0.00001*
Pairwise comparison A:B	165.0±14.4	110.0±30.7	.....	.....	0.00001*
Pairwise comparison A:C	165.0±14.4	.....	100.0±0.0	.....	<0.001*
Pairwise comparison A:D	165.0±14.4	.....	.....	190.0±30.7	0.08297
Pairwise comparison B:C	.....	110.0±30.7	100.0±0.0	.....	0.76927
Pairwise comparison B:D	.....	110.0±30.7	.....	190.0±30.7	<0.001*
Pairwise comparison C:D	.....	.....	100.0±0.0	190.0±30.7	<0.001*
Vasopressor consumption (mg)	10.8±4.1	16.5±4.2	28.2.0±5.5	2.7±3.0	<0.00001*
Pairwise comparison A:B	10.8±4.1	16.5±4.2	.....	.....	0.00052*
Pairwise comparison A:C	10.8±4.1	.....	28.2.0±5.5	.....	<0.001*
Pairwise comparison A:D	10.8±4.1	.....	.....	2.7±3.0	<0.001*
Pairwise comparison B:C	.....	16.5±4.2	28.2.0±5.5	.....	<0.001*
Pairwise comparison B:D	.....	16.5±4.2	.....	2.7±3.0	<0.001*
Pairwise comparison C:D	.....	.....	28.2.0±5.5	2.7±3.0	<0.001*

[Table/Fig-6]: Analgesic and vasopressor consumption of the parturients.
p-value <0.05 was considered significant; n=20 in all the four groups; SD: Standard deviation
*Result significant at p<0.05, One-Way ANOVA and Tukey's post hoc test HSD Beta (Honestly significant difference)
Group A=Bupivacaine plus dexmedetomidine 2.5 µg; Group B=Bupivacaine plus dexmedetomidine 5 µg; Group C=Bupivacaine plus dexmedetomidine 7.5 µg; Group D=Bupivacaine with no dexmedetomidine

Variables	Group A	Group B	Group C	Group D	p value
Skin incision to baby delivery time (min) (mean±SD)	8.8±1.3	8.75±1.0	8.75±1.4	8.8±1.4	0.998
Uterine incision to baby delivery time (min) (mean±SD)	2.5±0.6	2.5±0.7	2.6±0.7	2.4±0.6	0.896
Apgar scores at 1 min-N (S/US)	16/4	17/3	17/3	18/2	0.853
Apgar scores at 5 min-N (S/US)	19/1	18/2	19/1	19/1	0.887
RSS at 15 minutes-N (S/US)	8/12	14/6	16/4	6/14	0.003*
RSS at 30 minutes-N (S/US)	9/11	15/5	18/2	5/15	0.009*
RSS at 45 minutes-N (S/US)	10 /10	17/3	19/1	4 /16	0.001*
RSS at 60 minutes-N (S/US)	8/12	18/2	19/1	5/15	0.001*

[Table/Fig-7]: Apgar scores, skin and uterine incision to baby delivery times.
*The result is significant at p<0.05, Fisher's-exact test. S=Satisfactory, US=Unsatisfactory, N=numbers
RSS: Ramsay sedation score

among the groups did not show any statistical significance [Table/Fig-8]. Incidence of desaturation (SaO_2 <95%) was noted in more cases in groups A, B and C in comparison to those in control with a statistically significant difference at p-value=0.007 as shown in the [Table/Fig-8]. The fluctuations in RR are comparable in all four groups.

Surgeons expressed their satisfactory satisfaction levels about the anaesthetic technique in a higher percentage of cases in groups A, B and C than those in Group D and these differences among the groups were statistically significant at p-value <0.011 [Table/Fig-8]. More number of parturients in groups A, B and C had expressed their satisfaction levels about the anaesthetic technique than those in control and these differences among the groups were statistically significant at p-value=0.006 [Table/Fig-8].

Variables (numbers) (%)	Group A	Group B	Group C	Group D	p-value
Bradycardia	2 (10)	4 (20)	8 (40)	1 (5)	0.024*
Hypotension	6 (30)	12 (60)	16 (80)	4 (20)	0.039*
Nausea and/or Vomiting	4 (20)	5 (25)	7 (35)	3 (15)	0.490
Dryness of mouth	2 (10)	4 (20)	5 (25)	1 (5)	0.270
Shivering	4 (20)	6 (30)	8 (40)	2 (10)	0.148
PDPH	1 (5)	2 (10)	2 (10)	1 (5)	0.868
Desaturation (SaO_2 <95%)	2 (10)	4 (20)	9 (45)	1 (5)	0.007*
Back ache	2 (10)	4 (20)	3 (15)	2 (10)	0.762
Surgeon satisfaction scores	13 (65)	16 (80)	18 (90)	9 (45)	0.011**
Patient satisfaction scores	14 (70)	17 (85)	19 (95)	10 (50)	0.006**

[Table/Fig-8]: Comparison of side-effects, surgeon and patient satisfaction scores between the groups.
*Result was significant at p<0.05 (Fisher's-exact test)
**Result was significant at p<0.05 (Chi-square test)
Group-A=Bupivacaine plus dexmedetomidine 2.5 µg; Group-B=Bupivacaine plus dexmedetomidine 5 µg; Group-C=Bupivacaine plus dexmedetomidine 7.5 µg; Group-D=Bupivacaine with no dexmedetomidine; PDPH=Postdural puncture headache; SaO2=Percentage of peripheral arterial oxygen saturation

Gestational age and birth weight of the neonates at the time of caesarean surgery, the acid-base status of umbilical cord arterial and venous blood samples as measured by analysis of partial pressure of oxygen, partial pressure of carbon dioxide, plasma bicarbonate and base deficit are comparable with no statistically significant difference among the four groups [Table/Fig-9].

Variables mean (±SD)	Group A	Group B	Group C	Group D	p-value
Gestational age (week)	38.9±0.28	38.8±0.31	38.81±0.19	38.80±0.38	0.333
Birth weight (kg)	2.80±0.15	2.86±0.11	2.80±0.10	2.83±0.10	0.336
Umbilical arterial pH	7.28±0.01	7.27±0.01	7.28±0.01	7.29±0.01	0.058
PO_2 (mm/Hg)	15.44±0.70	15.61±0.59	15.66±0.75	15.60±0.68	0.763
PCO_2 (mm/Hg)	47.45±4.55	47.21±3.85	47.66±4.24	47.93±4.05	0.955
HCO_3 (mEq/L)	22.68±2.75	21.73±1.47	22.10±1.66	22.04±1.73	0.489
Base deficit (mEq/L)	(-)3.12±0.01	(-)3.12±0.01	(-)3.11±0.02	(-)3.11±0.03	0.124
Umbilical venous pH	7.30±0.01	7.31±0.02	7.30±0.03	7.31±0.04	0.682
PO_2 (mm/Hg)	25.02±2.40	24.47±2.91	24.85±3.39	25.12±3.09	0.832
PCO_2 (mm/Hg)	39.25±5.09	40.12±5.44	39.60±4.64	41.22±5.46	0.652
HCO_3 (mEq/L)	21.78±2.46	21.13±2.22	21.75±1.63	21.97±2.07	0.577
Base deficit (mEq/L)	(-)3.08±0.84	(-)3.07±1.21	(-)3.08±0.85	(-)3.09±0.85	0.999

[Table/Fig-9]: Neonatal data: gestational age, birth weight and umbilical arterial and venous acid base status.
Group-A=Bupivacaine with dexmedetomidine 2.5 µg; Group-B=Bupivacaine with dexmedetomidine 5 µg; Group-C=Bupivacaine with dexmedetomidine 7.5 µg; Group-D=Bupivacaine with no dexmedetomidine
PO_2=Partial pressure of oxygen; PCO_2=Partial pressure of carbon dioxide; HCO_3=Bicarbonate
pH=Power of hydrogen ion concentration (concentration expressed in a negative logarithmic scale)

DISCUSSION

Spinal anaesthesia is the preferred anaesthetic technique for caesarean deliveries due to its well-established benefits like increased maternal safety, better neonatal outcomes and technical simplicity with reliable and rapid production of ideal surgical conditions of dense sensory and motor block [24]. The local anaesthetic agent, hyperbaric bupivacaine

0.5% is commonly used in 2 mL volume (10 mg) for providing spinal anaesthesia in these cases, aiming to achieve a block level up to T6 thoracic dermatome [25]. For administering spinal anaesthesia, if only local anaesthetic agents are employed without any adjuvants, the duration of analgesia obtained is limited besides the increased incidence of nausea and vomiting and visceral pain while handling the gut and exteriorisation of the uterus during the course of the surgery [26].

Several adjuvants were used to enhance the block characteristics of bupivacaine and DMT is reported to be the most effective by virtue of its selective α 2-agonist activity and better haemodynamic stability. DMT is believed to produce its antinociceptive effect by acting at prejunctional and postjunctional receptors, thereby reducing neurotransmitter release and hyperpolarisation and reduction of impulse transmission in the nerve fibres [27].

The DMT is believed to have limited effects on uteroplacental blood flow, and minimal placental transfer based on studies on isolated perfused human placenta [28]. DMT was used for labour analgesia and caesarean delivery and was reported to have favourable maternal and foetal outcomes with no adverse effects having been recorded [29].

The optimum dose of intrathecal DMT to be used as an adjuvant to hyperbaric bupivacaine for spinal anaesthesia for elective caesarean section cases is reported to lie between 2.5 µg and 10 µg [30,31]. A dose of 5 µg DMT is reported to be the optimum dose to be used as an adjuvant to 0.5% hyperbaric bupivacaine but the effects of doses like 2.5 and 7.5 µg are not much studied [32]. In the backdrop of the above findings, to fill the knowledge gap in this field, the present study was undertaken to ascertain the optimum adjuvant dose to be used out of the three doses of DMT i.e., 2.5 µg, 5 µg and 7.5 µg with 2 mL of 0.5% hyperbaric bupivacaine (10 mg).

The study results had shown that DMT 2.5 µg, 5 µg and 7.5 µg added as adjuvants to 0.5% hyperbaric bupivacaine had shown better block characteristics than the control group having an intrathecal 0.5% bupivacaine alone by way of extending the duration of sensory and motor block, reducing the time to onset of the sensory and motor block and enhancing the duration of postoperative analgesia with negligible adverse effects on neonatal APGAR scores. The above-mentioned beneficial effects are directly proportional to the dose of DMT employed but the dose of 5 µg DMT appears to be the optimal dose to be used as there are minimal haemodynamic changes with this dose in comparison with the dose of 7.5 µg DMT where several instances of fluctuations in PR and MAP were noted necessitating frequent use of vasopressors for attaining haemodynamic stability; whereas a dose of 2.5 µg DMT had a shorter duration of analgesia compared to the other two doses.

A review of other studies on this subject had shown that Mishra VK et al., using 0.5% hyperbaric bupivacaine 9 mg+DMT 5 µg reported that the onset of sensory block (T10) was significantly faster in DMT Group-D (2.075±0.572 minutes) compared to the control Group-C (4.44±0.73) [33]. In the present study, faster onset of sensory block was observed in the groups A, B and C compared to the control Group-D, 4.3±0.8, 3.6±0.5, 2.7±0.5 vs 5.7±0.6 minutes respectively, but the durations noted in the present study are on the higher side compared to their study. This difference could be due to the higher level of T6 dermatome set as the optimum block level in the present study as against the T 10 level used in their study. They also reported that the time for two-segment sensory regression was significantly longer in DMT Group-D (130.33±10.9 minutes) than the control Group-C (79.67±11.05 minutes) and the results of the present study are in near agreement with their results. The time for rescue analgesia was reported as significantly prolonged in Group-D of their study (364.83±63.48 minutes) when compared to control Group-C (152.66±20.28 minutes) and the corresponding values in the present study are 320.2±24.0 and 150.1±7.1 in the Group-B and D, respectively which are in near agreement with their results.

Comparing hyperbaric bupivacaine 9 mg plus DMT 5 µg with a control group, Ranjan A and Horo V, reported that time for two-segment sensory regression, duration of motor block and time for the first analgesic request were significantly prolonged in their DMT group compared to the control group (140 vs. 44, 341 vs. 113 and 420 vs. 69 min) [34]. The corresponding values noted in the present study are 205 vs. 75, 325 vs. 136 and 320 vs. 150 and are in partial agreement with their results. They further stated that there was no significant difference in haemodynamic parameters, sedation and neonatal APGAR scores between the groups and concluded that the addition of 5 µg DMT as an intrathecal adjuvant to bupivacaine for caesarean section hastened and prolonged the sensory and motor block and provided better perioperative analgesia without significant maternal and neonatal adverse effects. The findings of the present study are in complete agreement with their observations.

Comparing 0.5% hyperbaric bupivacaine 9 mg plus DMT 5 µg vs. bupivacaine alone, Royzada B et al., reported that the use of intrathecal 5 µg DMT as an adjuvant to bupivacaine for caesarean section operations produced rapid and prolonged sensory and motor block and better perioperative analgesia without significant maternal and neonatal adverse effects. Findings of the present study are in total agreement with their observations [35].

Bi YH et al., reported that co-administration of DMT (3 µg and 5 µg) with intrathecal bupivacaine10 mg had prolonged the duration of motor and sensory block compared with bupivacaine (10 mg) alone and that there was no significant difference in APGAR scores, neonatal umbilical pH, oxygen pressure, carbon dioxide pressures and the side-effects (shivering, nausea and vomiting) among the groups [36]. They concluded that the use of DMT especially at the dose of 3 µg as an adjuvant to bupivacaine in caesarean surgery provides better sensory block characteristics and postoperative analgesia. Findings of the present study are in partial agreement with their observations except that 5 µg DMT added as an adjuvant to bupivacaine produced better results than a 2.5 µg dose.

Comparing the effect of adding DMT 10 µg or fentanyl to intrathecal bupivacaine in caesarean section cases, Noor El-Din T et al., stated that sensory and motor block onset times were shorter and the two-dermatome regression time and the postoperative analgesic effect were longer in their DMT group [37]. Similar results were obtained in the present study using 5 µg DMT instead of 10 µg of DMT.

Limitation(s)

As the sample size small in the present study, future studies with a larger sample size on a large-scale trials can throw more light on this subject.

CONCLUSION(S)

On the basis of the results of the present study, it can be concluded that 5 µg DMT dexmedetomidine added as an adjuvant to 10 mg of 0.5% hyperbaric bupivacaine (2 mL) intrathecally was the optimal drug combination for spinal anaesthesia for caesarean section cases, as it hastened the onset of sensory and motor block, prolonged the postoperative analgesia and provided adequate sedation and stable haemodynamic parameters in the parturients with adequate satisfaction levels in the surgeons and parturients regarding the anaesthetic technique and with no adverse neonatal effects; whereas a higher dose of 7.5 µg dexmedetomidine resulted in greater fluctuations in PR and MAP and a lower dose of 2.5 µg dexmedetomidine had resulted in a shorter duration of analgesia.

REFERENCES

[1] Traynor AJ, Aragon M, Ghosh D, Choi RS, Dingmann C, Vu Tran Z, et al. Obstetric anesthesia workforce survey: A 30-year update. Anesth Analg. 2016;122(6):1939-46.
[2] Kariya N, Tashiro C. Spinal anaesthesia for cesarean section--safe and effective anaesthetic management. Masui. 2010;59(3):311-18.
[3] Fettes PD, Jansson JR, Wildsmith JA. Failed spinal anaesthesia: Mechanisms, management, and prevention. Br J Anaesth. 2009;102(6):739-48.
[4] Chestnut DH, Wong CA, Tsen LC, Kee WDN, Beilin Y, Mhyre JM, et al. Anesthesia for cesarean delivery. Chapter 26. In: (Eds). Chestnut's Obstetric Anesthesia: Principles and Practice, Philadelphia: Elsevier Saunders. 2014;545-603.
[5] Kothari N, Bogra J, Chaudhary AK. Evaluation of analgesic effects of intrathecal clonidine along with bupivacaine in cesarean section. Saudi J Anaesth. 2011;5(1):31-35.
[6] Braveman FR, Scavone BM, Blessing ME, Wong CA. Obstetrical anesthesia. Chapter 40 In Barash P, Cullen BF, Stoelting RK, Cahalan M, Stock MC, & Ortega R. Clinical Anesthesia. 7th ed. Lippincott Williams and Wilkins; 2013;1144-1177.
[7] Berde CB, Strichartz GR. Local Anesthetics, Chapter 36. In: Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Weiner-Kronish JP, &Young WL. (Eds). Miller's Anesthesia. Philadelphia: Elsevier Saunders; 2015;8(1):1205-34.
[8] Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A novel sedative-analgesic agent. Proc (Bayl Univ Med Cent). 2001;14(1):13-21.
[9] Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J. 2009;30(3):365-70.
[10] 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(2):222-27.
[11] Teymourian H, Khorasanizadeh S, Ansar P, Nazari L, Dehkordy ME. Comparison of the effect of bupivacaine in combination with dexmedetomidine with bupivacaine plus placebo on neonatal APGAR score, bispectral index and sedation level of parturients women. Anesth Pain Med. 2018;8(5):e81947.
[12] Yazbek-Karam VG, Aouad MM. Perioperative uses of dexmedetomidine. Middle East J Anaesthesiol. 2006;18(6):1043-58.
[13] Shah A, Patel I, Gandhi R. Haemodynamic effects of intrathecal dexmedetomidine added to ropivacaine intraoperatively and for postoperative analgesia. Int J Basic Clin Pharmacol. 2013;2:26-29.
[14] Wu HH, Wang HT, Jin JJ, Cui GB, Zhou KC. Does dexmedetomidine as a neuraxial adjuvant facilitate better anesthesia and analgesia? A systematic review and meta-analysis. PLoS One. 2014;9(3):e93114.
[15] Sun Y, Xu Y, Wang GN. Comparative evaluation of intrathecal bupivacaine alone, bupivacaine-fentanyl, and bupivacaine dexmedetomidine in cesarean section. Drug Res. 2015;65(9):468-72.
[16] Palanisamy A, Klickovich RJ, Ramsay M, Ouyang DW, Tsen LC. Intravenous dexmedetomidine as an adjunct for labour analgesia and cesarean delivery anesthesia in a parturients with a tethered spinal cord. Int Journ Obstet Anesth. 2009;18(3):258-61.
[17] 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 Anaesthesiol Clin Pharmacol. 2011;27(3):339-43.
[18] Abouleish AE, Leib ML, Cohen NH. ASA provides examples to each ASA physical status class. ASA Monitor. 2015;79:38-39.
[19] Beilin Y, Hossain S, Bodian CA. The numerical rating scale labour epidural analgesia. Anaesth Analg. 2003;96:1794-98.
[20] Bromage PR, Burfoot MF, Crowell DE, Pettigrew RT. Quality of epidural blockade. I. influence of physical factors. Br J Anaesth. 1964;36:342-52.
[21] Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J. 1974;2:656-59.
[22] Moolagani VR, Burla SR, Neethipudi BR, Upadhyayula SM, Bikkina A, Arepalli NR. Ropivacaine plus lidocaine versus bupivacaine plus lidocaine for peribulbar block in cataract surgery: A prospective, randomized, double-blind, single-center, comparative clinical study. J Anaesthesiol Clin Pharmacol. 2019;35:498-503.
[23] Moolagani VR, Vigrahala P, Korra GN, Duba BK. Effects of intrathecal dexmedetomidine-bupivacaine versus intravenous dexmedetomidine plus intrathecal bupivacaine: A randomised triple-blind clinical study. J Clin Diag Res. 2022;16(7):UC20-UC26.
[24] Hawkins JL, Chang J, Palmer SK, Gibbs CP, Callaghan WM. Anesthesia-related maternal mortality in the United States: 1979-2002. Obstetric Gynecol. 2011;117:69-74.
[25] Danelli G, Zangrillo A, Nucera D, Giorgi E, Fanelli G, Senatore R, et al. The minimum effective dose of 0.5% hyperbaric spinal bupivacaine for cesarean section. Minerva Anesthesiol. 2001;67:573-77.
[26] Roofthooft E, Van de Velde M. Lowdose spinal anaesthesia for cesarean section to prevent spinal-induced hypotension. Curr Opin Anaesthesiol. 2008;21(3):259-62.
[27] Bajwa SJ, Kulshrestha A. Dexmedetomidine: An adjuvant making large inroads into clinical practice. Ann Med Health Sci Res. 2013;3(4):475-83.
[28] Ala-Kokko TI, Pienimaki P, Lampela E, Hollmen AI, Pelkonen O, Vahakangas K. Transfer of clonidine and dexmedetomidine across the isolated perfused human placenta. Acta Anaesth Scand. 1997;41(2):313-19.
[29] Jenkins JG, Khan MM. Anaesthesia for cesarean section: A survey in a UK region from 1992 to 2002. Anaesthesia. 2003;58(11):1114-18.
[30] Sushruth MR, Rao DG. Effect of adding intrathecal dexmedetomidine as an adjuvant to hyperbaric bupivacaine for elective cesarean section. Anaesth Pain & Intensive Care. 2018;22(3):348-54.
[31] Mahdy WR, Abdullah SI. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics and neonatal outcome in uncomplicated cesarean delivery: A randomized double blind placebo controlled. Menoufiya Med J. 2011;24(4):221-32.
[32] Xia F, Chang X, Zhang Y, Wang L, Xiao F. The effect of Intrathecal dexmedetomidine on the dose requirement of hyperbaric bupivacaine in spinal anaesthesia for cesarean section: A prospective double-blinded randomized study. BMC Anaesthesiol. 2018;18(1):74.
[33] Mishra VK, Ahmad S, Kumar S. A comparative study of perioperative effects of intrathecal fentanyl and dexmedetomidine with bupivacaine in elective JSCS. J Evolution Med Dent Sci. 2017;6(56):4206-10.
[34] Ranjan A, Horo V. Effect of adding intrathecal dexmedetomidine as anadjuvant to hyperbaric bupivacaine for elective cesarean section. Indian J App Res. 2019;9(2):06-09.
[35] Royzada B, Kujur S, Royzada A. Assessing the benefits of adding dexmedetomidine to intrathecal hyperbaric bupivacaine for cesarean section. J Evid Based Med Healthc. 2019;6(29):1949-53.
[36] 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):63587-95.
[37] Noor El-Din T, Hussein M, Abd El-galil A, Abdellatif AE. Intrathecal Fentanyl versus Dexmedetomedine as adjuvants to bupivacaine for cesarean section. IJMA. 2021;3(1):1083-87.

PARTICULARS OF CONTRIBUTORS:

1. Professor, Department of Anaesthesiology, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India.
2. Assistant Professor, Department of Anaesthesiology, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India.
3. Assistant Professor, Department of Anaesthesiology, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India.
4. Professor and Head, Department of Anaesthesiology, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India.
5. Professor, Department of Anaesthesiology, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India.
6. Assistant Professor, Department of Anaesthesiology, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India.
7. Assistant Professor, Department of Anaesthesiology, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India.
8. Associate Professor, Department of Anaesthesiology, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Marikavalasa, Visakhapatnam, Andhra Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Kurmanadh Kallepalli,
Door No. 8-1-97/2, Main Road, Pedda Waltair,
Visakhapatnam-530017, Andhra Pradesh, India
E-mail: kallenadhkurma@gmail.com

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