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ORIGINAL ARTICLE

A COMPARATIVE CLINICAL STUDY OF EFFECT OF ADDING 5µg DEXMEDETOMIDINE VERSUS 50µg CLONIDINE TO INTRATHECAL 12.5mg OF 0.5%HYPERBARIC BUPIVACAINE ON SPINAL BLOCK CHARACTERISTICS IN PATIENTS UNDERGOING ELECTIVE LOWER ABDOMINAL SURGERIES

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ABSTRACT: Uncontrolled postoperative pain may produce a range of detrimental acute and chronic effects. Spinal Anaesthesia provided by bupivacaine may be too short for providing postoperative analgesia. The present study is conducted to evaluate and compare the efficacy of intrathecal Dexmedetomidine or intrathecal clonidine as an adjuvant to hyperbaric bupivacaine with regards to the onset and duration of sensory and motor blockade, as well as postoperative analgesia and adverse effects. **METHODS:** Ninety patients aged 20-60 years of either sex were randomly divided into three groups. Each group consisting of 30 patients of either sex belonging to ASA class I and II posted for elective lower abdominal surgeries were given spinal anaesthsia using bupivacaine 0.5% heavy 2.5ml with either normal saline 0.5ml (Group B) or 50µg preservative free clonidine (Group C) or 5µg of preservative free Dexmedetomidine (Group D). Assessment of the sensory and motor blockade were done at the end of each minute till the maximum level achieved. Measurement of blood pressure, pulse rate, respiratory rate and arterial oxygen saturation were obtained. Postoperatively the patients were observed for the duration of analgesia, time taken for complete regression of sensory blockade to S1 and time taken for complete recovery of motor power. **RESULTS:** The results showed a statistically highly significant prolongation of sensory and motor blockade, time taken for sensory regression by two segments and postoperative analgesia in the Dexmedetomidine and clonidine group compared to the control group. In Dexmedetomidine group seven out of thirty patients, in clonidine group seven out of thirty patients and in control group two out of thirty patients developed hypotension. In Dexmedetomidine group five out of thirty patients, in clonidine group four out of thirty patients and in control group one out of thirty patients developed bradycardia. **CONCLUSION:** Dexmedetomidine 5µg or clonidine 50µg when added to intrathecal bupivacaine 0.5% heavy prolongs the duration of sensory and motor blockade, time taken for sensory regression by two segments and duration of post-operative analgesia.

KEYWORDS: Post-operative analgesia, Sensory and motor block, bupivacaine heavy 0.5%. Intrathecal clonidines, intrathecal Dexmedetomidine, spinal anaesthesia, lower abdominal surgeries.

INTRODUCTION: Regional anaesthesia is the preferred technique of choice for lower abdominal and lower limb surgeries. It allows the patient to remain awake, minimizes or completely avoids the problem associated with airway management. With spinal anesthesia, the technique is simple to perform; the onset of anaesthesia is more rapid, avoids poly pharmacy and provides postoperative analgesia.

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For decades lignocaine had been the local anesthetic of choice for spinal anaesthesia. Its advantages are rapid onset of action and good motor block manifested as good muscle relaxation. Its use is limited by its short duration of action and has been implicated in transient neurologic symptoms and cauda equina syndrome following intrathecal injection.[1,2]

Bupivacaine is three to four times more potent than lignocaine 4 and has longer duration of action. Its disadvantages are slow onset of action and decreased motor block. Hyperbaric bupivacaine 0.5% is extensively used in India for spinal anaesthesia. Though the duration of action of bupivacaine is prolonged compared to lignocaine, it is not enough in prolonged surgeries of more than 2 hours.

Hence another adjuvant is required for producing prolonged post-operative analgesia. The discovery of opioid receptors and endorphins in spinal and supraspinal regions led to the use of spinal opiates as adjuvant along with local anaesthetics. Morphine was the first opioid administered intrathecally to augment neuraxial blocks. But morphine can produce serious side effects like late and unpredictable respiratory depression, post-operative nausea and vomiting, pruritus and urinary retention.[3,4,5]

Recently α-2 adrenoreceptor agonists' clonidine and Dexmedetomidine have been used as adjuvants to local anesthetic agents because of their sedative, analgesic and haemodynamic stabilizing effect.[6] They have been found to prolong the duration of spinal block following intrathecal administration. Addition of intrathecal clonidine to bupivacaine prolongs the duration of analgesia and has antihypertensive properties.

It has been shown to result in prolongation of the sensory blockade and decreases the dose of local anesthetic agent required to produce post-operative analgesia.[7] Clonidine also has the ability to prolong the motor blockade produced by bupivacaine. Dexmedetomidine also a α-2 adrenoreceptor agonist is pharmacologically related to clonidine and is a highly specific and selective alpha-2 adrenoreceptor agonist with 8 times more affinity for alpha-2 adrenoreceptor than clonidine.

The ratio of alpha-1: alpha-2 receptor binding selectivity for Dexmedetomidine is 1:1620 compared to 1:220 for clonidine.[8] While clonidine has been used as an adjuvant to local anesthetic agents for intrathecal purposes with successful results, there are only a few studies available for Dexmedetomidine for such studies.

Since it has been recently introduced in India and not many studies are available regarding its use as an adjuvant to local anesthetic agents for intrathecal purpose, hence there is a need to study its effectiveness for spinal anaesthesia. Hence the present study was undertaken to evaluate and compare the effects of adding clonidine versus Dexmedetomidine with intrathecal hyperbaric 0.5% bupivacaine in patients scheduled for lower abdominal surgeries.

METHODOLOGY: The study entitled "A Comparative Clinical Study of Effect Of Adding 5µg Dexmedetomidine Versus 50µg Clonidine To Intrathecal 12.5mg OF 0.5% Hyperbaric Bupivacaine On Spinal Block Characteristics In Patients Undergoing Elective Lower Abdominal Surgeries" was undertaken in Krishna Rajendra hospital attached to Mysore Medical College & Research Institute, Mysore after obtaining ethical committee clearance as well as informed consent from all the patients.

Ninety patients in the age group of 20 to 60 years of either sex belonging to ASA Class 1and 11 posted for elective lower abdominal surgeries without any co-morbid diseases were grouped randomly into three groups (n=30). Randomization was done using simple sealed envelope technique.

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Group B (Control group): Received 12.5mg of 0.5% hyperbaric bupivacaine with 0.5ml of normal saline. Group C (Clonidine group): received 12.5mg of 0.5% hyperbaric bupivacaine with 50 µg clonidine Group D (Dexmedetomidine group): Received 12.5mg of 0.5% hyperbaric bupivacaine with 5µg of Dexmedetomidine.

The doses of Dexmedetomidine and clonidine were chosen according to a 1:10 ratio found to be equipotent and would produce similar effects on the characteristics of bupivacaine spinal anaesthesia.44

INCLUSION CRITERIA: Adult patients of either sex, aged between 20 and 60 years, belonging to ASA class 1 and 11 without any co-morbid diseases scheduled for elective lower abdominal surgeries.

EXCLUSION CRITERIA:

Patients belonging to the following classes:

- Age group less than 20 years and more than 60 years.
- Patients belong to ASA class 111, IV and V.
- Pregnant females.
- Patients posted for emergency surgeries.
- Patients with morbid obesity.
- Patients having any absolute contraindications for spinal anaesthesia like raised intracranial pressure, severe hypovolaemia, bleeding diathesis and local infection.
- Patients with co-morbid diseases like diabetes, hypertension and any other are excluded from the study.

Pre-operative assessment will be done for each patient and written informed consent is taken. Patient will be kept NPO for solids 6to8hours and premeditated on the night before surgery with tablet Ranitidine 150mg and tablet Alprazolam 0.5mg. Intravenous line obtained with 18gauge cannula and preloaded with ringer lactate 500ml half an hour before institution of spinal anaesthesia. Monitoring will be done using multiparameter monitor having pulse oximetry, ECG & NIBP (Star plus of LARSEN & TOURBO) Patients will be placed in flexed lateral position. Under aseptic precautions spinal block will be performed at level of L3-L4 through a midline approach using 25G Quincke spinal needle and study drug will be injected with operative table kept flat. Patient will be turned to supine posture immediately and supplemental oxygen given.

The test drugs are prepared by the senior anesthesiologist who is not involved in the study, Clonidine (Cloneon 150µg/ml of Neon laboratories) is diluted to 1.5 ml with normal saline and 0.5 ml (50µg) of it will be added to 2.5ml of 0.5% hyperbaric bupivacaine. Dexmedetomidine (Dexem 50µg/0.5ml of Thames Laboratories) 0.5 ml is diluted to 5 ml with normal saline and 0.5ml of this is added to 2.5ml of 0.5% hyperbaric bupivacaine. The observer and the patient are blinded for the study drug.

The following parameters are noted:

- Onset of Sensory and Motor blockade.
- Maximum level of sensory blockade attained and time taken for the same will be noted.
- Maximum lever of motor blockade attained and time taken for the same will be noted.
- Two segments sensory regression time will be noted.
- Total duration of analgesia will be noted.

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- Total duration of sensory blockade and motor blockade will be noted.
- Sensory blockade will be tested using pinprick method with a blunt tipped 27G needle at every minute for first 5 minutes and every 5 minutes for next 15 minutes and every 10 minutes for next 30 minutes and every 15 minutes till the end of surgery and thereafter every 30 minutes until sensory block is resolved.
- Quality of motor blockade will be assessed by modified Bromage scale.
- Level of sedation noted.
- Total duration of surgery and if any side effects will be noted.

Haemodynamic monitoring will be done during the block every 5minutes for first 15minutes and every 10minutes for the next 30minutes and once in 15minutes till the end of surgery and post operatively every hourly employing multiparameter monitor which displays heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, ECG and SpO2hourly.

ADVERSE EFFECTS: Patients will be monitored for any cardiovascular side effects like changes in blood pressure, heart rate and rhythm, central nervous system depression, respiratory depression and any hypersensitivity reactions for drugs.

STATISTICAL ANALYSIS: The pilot study done revealed the required sample to be 30 in each group. Analysis was done by SPSS 17 statistical method. Descriptive statistics, mean and standard deviation were calculated. Independent- Samples "t" test to measure the difference between two groups i.e. inter group comparison. Paired "t" test was done to measure the difference within the groups i.e. intra group comparison. Repeated measures ANOVA (Group v/s sessions together) and Contingency table analysis (For association between the rows and columns)

RESULTS.

Sensory block characteristics:

Mean time taken for sensory onset in minute:

Time taken for sensory onset in minutes	Group B	Group C	Group D	P Value B vs C	P Value B vs D	P Value C vs D
Mean ±SD	2.80±.664	1.43 ±.504	1.17 ±.379	0.000	0.000	0.024
Minimum	2	1	1			
Maximum	4	2	2			

Mean time taken for maximum sensory blockade in minutes:

Time taken for maximum sensory block in minutes	Group B	Group C	Group D	P Value B vs C	P Value B vs D	P Value C vs D
Mean ±SD	7.41 ± 1.102	5.9 ±.504	5.2 ± 0.714	0.000	0.000	0.001
Minimum	6	5	4			
Maximum	9	7	7			

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Motor block characteristics.

Time taken for onset of motor blockade:

Time taken for motor block onset in minutes	Group B	Group C	Group D	P Value B vs C	P Value B vs D	P Value C vs D
Mean ±SD	4± 0.695	1.63 ± 0.49	1.13 ± 0.346	0.000	0.000	0.000
Minimum	3	1	1			
Maximum	5	2	2			

Time taken for maximum motor block attained

Time taken for maximum motor blockade in minutes	Group B	Group C	Group D	P Value B vs C	P Value B vs D	P Value C vs D
Mean ±SD	6.57± 0.935	6.43 ± 1.04	5.2 ± 0.887	0.000	0.000	0.000
Minimum	5	5	4			
Maximum	9	8	7			

Mean duration of Motor blockade

Duration of motor block in minutes	Group B	Group C	Group D	P Value B vs C	P Value B vs D	P Value C vs D
Mean ±SD	166.16± 20.95	279 ± 24.68	303 ± 35.95	0.000	0.000	0.003
Minimum	135	240	240			
Maximum	210	330	360			

Mean duration of analgesia

Duration of analgesia in minutes	Group B	Group C	Group D	P Value B vs C	P Value B vs D	P Value C vs D
Mean ±SD	191± 22.94	342.333± 28.12	369.33 ± 34.13	0.000	0.000	0.001
Minimum	150	300	300			
Maximum	240	390	420			

RESULTS OBTAINED

Spinal block characteristics	GROUP B	GROUP C	GROUP D
Time taken for onset of sensory block	2.8±0.6 mins	1.43±0.5 mins	1.17±0.379 mins
Time taken for maximum sensory block	7.4±1.1 Mins	5.9±0,8 mins	5.2±0.71 mins
Time taken for regression of sensory block by two segments	79.46±10.1 Min	136.33±10,9 mins	136.33±11.59 mins
The time taken for sensory block to regress to S1	203.33±42.41 Mins	365±24.6 mins	396.16±30.6 mins

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Duration of Analgesia	191±22.9 Mins	343.33±28.12 mins	369.33±34.13 mins
Onset of motor blockade	4±0.69 Mins	1.63±0.49 mins	1.13±0.346 mins
Time taken for maximum motor block	6.57±0.9 Mins	6.43±1.04 mins	5.2±0.88 mins
Duration of motor block.	166.16±20.95 Mins	279±24.68 mins	303.66±35.95 mins

From the present study it is found that in Dexmedetomidine group and Clonidine group there is an early onset of both sensory and motor blockade and a higher level of sensory blockade compared to control group and duration of sensory, motor blockade and duration of analgesia is significantly prolonged in the Dexmedetomidine group and Clonidine group compared to Control group.

Haemodynamic were preserved both intraoperatively and postoperatively. However, there were a small percentage of patients who developed significant fall in blood pressure and bradycardia which were easily managed without any untoward effect.

Seven patients each in Dexmedetomidine and clonidine group and two patients in control group developed hypotension requiring treatment. Five patients in Dexmedetomidine group, four patients in clonidine group and one patient in control group developed bradycardia requiring treatment.

More number of patients in the Dexmedetomidine group and clonidine group were sedated and easily arousable. No patient had any respiratory depression, nausea, vomiting or shivering in either of the groups.

DISCUSSI0N: The aim of good post-operative analgesia is to produce a long lasting continuous effective analgesia with minimum side effects. Commonly used local anaesthetics for intrathecal anaesthesia are Lignocaine and Bupivacaine in India. Bupivacaine 0.5% heavy has more prolonged duration of action compared to Lignocaine Heavy, but the post-operative analgesic duration is limited. Other method of prolonging analgesia is using a continuous epidural analgesia, which is technically more difficult and more costly.

Hence an intrathecal additive to these local anaesthetics forms a reliable and reproducible method of prolonged post-operative analgesia and to prolong the duration of anaesthesia. This technique being simple and less cumbersome has gained a wide acceptance. A number of adjuvants to local anaesthetics for spinal anaesthesia like opioids (Fentanyl and buprenorphine), benzodiazepines (Midazolam), Ketamine and neostigmine have been used.[9,10,11]

The most common agents used are opioids and they have formed a cornerstone option for the treatment of post-operative pain. Spinal opiates prolong the duration of analgesia, but they do have drawbacks of late and unpredictable respiratory depression, pruritus, nausea, vomiting and urinary retention. Which requires constant post-operative monitoring and urinary catheterization.[11,12] Hence there is a requirement of an adjuvant to be used along with local anaesthetics which can produce prolonged analgesia without the above said side effects.

Intrathecal alpha 2 agonists are found to have antinociceptive action for both somatic and visceral pain.[13] So in this context alpha2 agonists may be a very useful drug along with the local anesthetic Bupivacaine 0.5% heavy for spinal anaesthesia. Clonidine is a selective partial

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alpha-2 adrenergic agonist. It is known to potentiate both sensory and motor block of local anaesthetics.[4,5]

The analgesic effect of clonidine is mediated spinally through activation of post synaptic alpha-2 receptors in substantia gelantinosa of spinal cord. It also activates the descending inhibitory pathways (Medellospinal pathways) and there by decreases the release of nociceptive substances from substantia gelatinosa.[14,7]

Various authors have studied clonidine for its analgesic action when it is used as an adjuvant along with local anaesthetics without the side effects of opioids. Clonidine has found a definitive place as an adjuvant to bupivacaine spinal anaesthesia to prolong the duration of analgesia.

Dexmedetomidine also an alpha-2 adrenergic agonist, pharmacologically related to clonidine and is the most recent agent in this group approved by FDA in 1999 for the use in humans as short term medication (<24hrs) for analgesia and sedation in intensive care unit.[8] Dexmedetomidine is a highly selective alpha-2 agonist with 8 times more affinity for alpha-2 receptors than clonidine.[15]

The ratio of alpha1: alpha2 receptor affinity for Dexmedetomidine is 1:1620 and for clonidine is 1:220.[8,15] Clonidine is commonly used for premedication and as an adjuvant to general anaesthesia. It reduces opioid and inhalational anesthetic requirements. While clonidine has been used as an adjuvant to local anesthetic agents for intrathecal purposes with successful results, there are only a few studies available for Dexmedetomidine for such studies. Dexmedetomidine has been recently introduced in India and hence there is a need to compare its effectiveness as a spinal adjuvant to bupivacaine.

CONCLUSION: In the present study the efficacy of intrathecal Dexmedetomidine and Clonidine were compared and we noticed that intrathecal Dexmedetomidine was better than clonidine with regards to onset and duration of both sensory and motor blockade as well as duration of analgesia. Hence Dexmedetomidine is a better neuraxial adjuvant compared to clonidine for providing early onset of sensory and motor blockade, adequate sedation and prolonged post-operative analgesia.

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