A COMPARATIVE STUDY OF INTRATHECAL DEXMEDETOMIDINE AND FENTANYL AS ADJUVANTS TO BUPIVACAINE

Gollapalli Hanumanth Rao[1], Gottipati Rajendra[2], Mekala Priyadarsini[3], Bais Deepraj Singh[4], Srikanth[5]

[1]Assistant Professor, Department of Anaesthesia, MGM/KMC Hospital, Warangal, Telangana.
[2]Associate Professor, Department of Anaesthesia, Government Medical College, Nizamabad, Telangana.
[3]Senior Resident, MGM Hospital, Warangal, Telangana.
[4]Professor, Department of Anaesthesiology, Osmania Medical College, Hyderabad, Telangana.
[5]Senior Resident, Department of Anaesthesia, Government Medical College, Nizamabad, Telangana.

ABSTRACT

INTRODUCTION

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. This study is conducted to evaluate the efficacy of intrathecal fentanyl and intrathecal dexmedetomidine 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. Hundred patients aged 18-55 years were randomly divided into two groups, each group consisting of 50 patients of either sex belonging to ASA class I and II posted for elective lower abdominal surgeries were given spinal anaesthesia using bupivacaine 0.5%, heavy 2.5 ml with either fentanyl 25µg (group F) 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

Our results showed a statistically highly significant prolongation of sensory and motor blockade, and postoperative analgesia in the dexmedetomidine group compared to the fentanyl group. In dexmedetomidine group four out of fifty patients, and in fentanyl group two out of fifty patients developed hypotension. In dexmedetomidine group five out of fifty patients, and in fentanyl group two out of fifty patients developed bradycardia. Incidence of pruritis is significantly high in fentanyl group.

KEYWORDS

Bupivacaine, Intrathecal, Fentanyl, Dexmedetomidine, Lower abdominal surgeries.

HOW TO CITE THIS ARTICLE: Rao GH, Rajendra G, Priyadarsini M, et al. A comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. J. Evid. Based Med. Healthc. 2016; 3(12), 380-387. DOI: 10.18410/jebmh/2016/90

INTRODUCTION: The ease of practice and relative predictability of neuraxial anaesthesia, coupled with its potential to provide multiple benefits to patients in the perioperative period has led to its widespread popularity. Nevertheless, concern of potential failed blocks and untoward effects still limits the acceptance of these techniques. Much effort has been put forth to minimize these undesirable events and optimize the patient experience. The addition of adjuvant medication to local anaesthetic preparation has been one avenue pursued to attain these goals.

Since the identification of opioid receptors in the spinal cord, the potent analgesic effects of neuraxial opioids have been exploited to improve perioperative analgesia and reduce the supraspinal side effects of sedation and respiratory depression seen with systemic opioids.[1]

Submission 06-01-2016, Peer Review 21-01-2016,
Acceptance 29-01-2016, Published 11-02-2016.
Corresponding Author:
Dr. B. Deepraj Singh,
#1-7-145/15, Musheerabad,
Hyderabad-500020, Telangana.
E-mail: drdeepraj@gmail.com
DOI: 10.18410/jebmh/2016/90

The lipophilic opioids are more suitable for intra operative use in the intrathecal space due to their rapid onset and modest duration. Additionally, with more timely clearance from the CSF, the risk of delayed respiratory depression from these drugs is much lower than morphine. Addition of 10 to 25 mcg fentanyl to low dose lidocaine and bupivacaine spinal anaesthesia dramatically improves anaesthetic success, improves the quality of intraoperative and early postoperative subarachnoid block without delaying achievement of discharge criteria for ambulatory patients.[2,3,4]

This technique is still limited by dose dependent pruritis; nausea, and urinary retention.[5,6] Nevertheless, fentanyl remains one of the most useful analgesic adjuvants for spinal anaesthesia.

Recently-2 adrenoceptor agonists have been gaining popularity in the field of regional anaesthesia as adjuvants to local anaesthetic agents because of their sedative, analgesic and haemodynamic stabilizing effects without the concerns of pruritis and respiratory depression seen with opioids. Clonidine was first injected intrathecally in humans in 1984, but other alpha-2 agonists had been used in veterinary anesthesia for many years.

Dexmedetomidine is a highly specific and selective alpha-2 adrenoceptor agonist with 8 times more affinity for alpha-2 adrenoceptor than clonidine. The ratio of alpha-2 receptor binding selectivity for Dexmedetomidine is 1:1620 compared to 1:220 for clonidine.[7] It is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects.

Till date, there are very few studies comparing intrathecal dexmedetomidine and fentanyl as adjuvants to hyperbaric bupivacaine, although various studies have compared dexmedetomidine and fentanyl with isobaric bupivacaine.

Hence, we have undertaken this study to evaluate and compare the effects of adding Dexmedetomidine versus Fentanyl with intrathecal hyperbaric 0.5% bupivacaine in patients scheduled for elective lower abdominal surgeries.

AIMS AND OBJECTIVES: The aim of my study is to compare and evaluate the efficacy of intrathecal dexmedetomidine 5µg versus intrathecal fentanyl 25µg as an adjuvant to 0.5% bupivacaine heavy 2.5 ml (12.5 mg) for spinal anesthesia with regard to,

1. Time taken for onset of sensory blockade.
2. Duration of analgesia.
3. Total analgesic requirement in first 24 hrs. post-operative period.
4. Adverse effects.

METHODOLOGY: The study entitled " A Comparative study of Intrathecal Dexmedetomidine (5g) and Fentanyl (25 g) as adjuvants to intrathecal 0.5% hyperbaric Bupivacaine" was a randomized, prospective, observational study done in the Department of Anaesthesiology at Maharajah's Institute of medical sciences, Nellimarla, Vizianagaram from November 2011 to October 2013.

The study was undertaken after obtaining Hospital Ethics Committee clearance as well as written, informed consent from all patients after explaining and reassuring about the spinal procedure.

A total of 100 patients of both sexes scheduled for elective lower abdominal surgeries under spinal anaesthesia, in the age group of 18 to 55 years and belonging to American society of Anaesthesiologist (ASA) Physical Status I & II were enrolled for the study.

The enrolled patients were randomized to one of the two groups of equal sized prospective, comparative study group using an open protocol design.

Group F (n=50) received 2.5mL volume of 0.5% hyperbaric bupivacaine with 25g fentanyl intrathecally and Group D (n=50) received 2.5mL volume of 0.5% hyperbaric bupivacaine and 5gdexmedetomidine intrathecally (dexmedetomidine 100 g/mL was diluted in 10 ml preservative-free normal saline).

Routine pre-anaesthetic check-up of all the patients was done to exclude co-existing medical conditions and to assess airway and spine. Routine investigations like haemoglobin%, blood group and typing, urine examination etc., were done.

Inclusion Criteria: Adult patients of either sex, aged between 18 and 55 years, belonging to ASA grade I and II scheduled for elective lower abdominal surgeries.

Exclusion Criteria:

1. ASA III, IV and V patients.
2. Age <18 and >55 years.
3. Pregnant females.
4. Body weight more than 100 kg.
5. Height less than 150 cm.
6. Patients using alpha 2 receptor antagonists, calcium channel blockers and angiotensin converting enzyme inhibitors.
7. Heart block/Dysrhythmia by ECG.
8. Contraindication to spinal anaesthesia (patient refusal, allergic to drug, coagulation disorder, infection at puncture site, increased intracranial tension and hypotension).
9. The use of any opioid or sedative in the week prior to surgery.
10. Patients with psychiatric illness and neurologic disease.

Investigations Required:

- Hb%, TC, DC, ESR, BT, CT.
- Urine routine.
- RBS, Blood urea and serum creatinine.
- Chest x-ray, ECG.

Standard pre-operative preparation consisted of: NPO for solids 6 hrs and to clear liquids 2 hrs before surgery, Premedication with Tab. Alprazolam 0.5mg and Tab. Ranitidine 150 mg PO given at 22:00 hrs. night before surgery. Preload with 500ml of Ringer lactate solution IV 30 minutes before surgery with 18G IV cannula.

Preoperative pulse, BP, respiratory rate and oxygen saturation were recorded.

MATERIALS:

Study Agents:

- 0.5% hyperbaric bupivacaine ampoule.
- 2ml fentanyl (50µg/ml) ampoule.
- 1ml Dexmedetomidine (100µg/ml) ampoule.

Monitors:

- Pulse oximeter.
- Non-invasive blood pressure monitor by sphygmomanometer on the upper limb.
- ECG monitoring.

Technique: With the patient in lateral decubitus position the skin over the back was prepared with iodine containing sterilizing solution, spirit and draped with a sterile towel. The procedure was done under full sterile precautions, including gown, mask and gloves. As per protocol the interspace chosen was L_3-L_4. If the attempt at this level failed the L_{2-3} level was the next choice.

A 25G Quincke spinal needle was introduced into the L_2 –L_3 or L_3 –L_4 intervertebral space gently in the midline until it reached the subarachnoid space. The position of the needle in the subarachnoid space was confirmed by dripping of cerebrospinal fluid through the needle freely. After aspirating 0.2ml of cerebrospinal fluid into the syringe, the study drug 2.5ml of 0.5% hyperbaric bupivacaine with 0.5ml (25µgm) of Fentanyl, or 2.5ml of 0.5% Hyperbaric Bupivacaine with 0.5ml (5µg) of Dexmedetomidine (100µgm/1ml diluted to 10 ml with normal saline) was injected into the subarachnoid space slowly at the rate of 0.25ml/sec. with the bevel cephalad. The needle was withdrawn and the patient turned supine. 100% oxygen via face mask (at the rate of 4 L/min) was administered.

The following parameters are noted:

- Onset of sensory blockade and motor blockade.
- Total duration of analgesia noted.
- Side effects if any are noted.

Haemodynamic monitoring was done during the block every 5 mins for first 15 mins and every 10 mins for next 30 mins and once in 15 mins till the end of surgery and post operatively every hourly employing multi parameter monitor which displays heart rate (HR), systolic blood pressure (SBP) diastolic blood pressure (DBP), mean arterial pressure (MAP), ECG and SpO2 hourly.

Onset of Sensory Blockade: is defined as time taken from the completion of the injection of study drug till the patient does not feel the pin prick at T10 level.

Time Taken for Maximum Sensory Blockade: is defined as the time taken from the completion of the injection of the study drug to the maximum sensory blockade attained.

Duration of Analgesia: is defined as the time taken from the completion of the injection of the study drug till the patient requests for rescue analgesic in the post-operative period.

Assessment of degree or intensity of sensory block was done using Visual Analogue Scale Score on a 10cm scale:

Grade 0:0	No pain.
Grade 1:1–2.5	Mild Pain.
Grade 2:2.6–5	Moderate Pain.
Grade 3:5.1–7.5	Severe Pain.
Grade 4:7.6–10	Worst possible pain.

Duration of Sensory Blockade: is defined as the taken from the time of injection till the patient feels the sensation at S1 dermatome.

Duration of Motor Blockade: is defined as the taken from the time of injection till the patient attains complete motor recovery.

Assessment of Sedation Score: Sedation score described by Culebras et al was used to assess sedation.

1. Awake and alert.
2. Sedated, responding to verbal stimulus.
3. Sedated, responding to mild physical stimulus.
4. Sedated, responding to moderate or severe physical stimulus.
5. Not arousable.

Hypotension is defined as reduction of systolic blood pressure more than 30% below baseline value and it will be treated with increased rate of intravenous fluids and if needed injection mephentermine 3mg increments given.

Bradycardia is defined as heart rate less than 60/minute and will be treated with injection atropine 0.6mg iv.

The side effects recorded during and after surgery are: Nausea and Vomiting, Hypotension, Bradycardia, Drowsiness, Pruritus, Shivering, Respiratory depression, Postural puncture headache, and Urinary retention.

After surgery, cardiovascular (pulse and blood pressure) and respiratory parameters (respiratory rate and oxygen saturation) and clinical evaluation of sensory and motor profiles were noted and the patient was transferred to the post-operative ward. Continuous monitoring and recording at regular intervals was done until the complete return of sensory and motor function.

Postoperatively, the pain score was recorded by using visual analog pain scale (VAS) between 0 and 10 (0=no pain, 10=most severe pain), initially every 1h for 2h, then every 2h for the next 8 h and then after every 4h till 24h. Diclofenac 50mg was given intramuscularly as rescue analgesia (RA) when VAS was >4.

OBSERVATION AND RESULTS: The study entitled " A Comparative study of Intrathecal Dexmedetomidine (5g) and Fentanyl (25g) as adjuvants to intrathecal 0.5% hyperbaric Bupivacaine" was a randomized, prospective, observational study done in the Department of Anaesthesiology at Maharajah's Institute of medical sciences, Nellimarla, Vizianagaram from November 2011 to October 2013. The study was undertaken after obtaining Hospital Ethics Committee clearance as well as written, informed consent from all patients after explaining and reassuring about the spinal procedure.

A total of 100 patients of both sexes scheduled for elective lower abdominal surgeries under spinal anaesthesia, in the age group of 18 to 55 years and belonging to American society of Anaesthesiologist (ASA) Physical Status I & II were enrolled for the study.

The enrolled patients were randomized to one of the two groups of equal sized prospective, comparative study group using an open protocol design.

Group F (n=50) received 2.5mL volume of 0.5% hyperbaric bupivacaine with 25g fentanyl intrathecally and Group D (n=50) received 2.5mL volume of 0.5% hyperbaric bupivacaine and 5gdexmedetomidine in 0.5mL of normal saline intrathecal (dexmedetomidine 100g/mL was diluted in 10ml preservative-free normal saline).

The minimum age in group F is 19 years and in group D if 18 years. The maximum age in both the groups is 55 years. The mean age in group F is 39.80±10.7 years, and group D is 36.80±10.2 years. There is no significant difference between the two groups as per the student t-test value (1.44) and its corresponding P-value (0.154) is greater than 0.05, the level of significance

Time taken for sensory onset in mins	Groups	
	Group F	Group D
Mean	1.84	1.68
S.D	0.710	0.71 2
Minimum	1 min	1 min
Maximum	3 min	3 min
P-value		0.263(p>0.05)
Decision		Not significant

Table 1: Mean time taken for sensory onset in minutes

The mean time of onset of sensory blockade in group F (Fentanyl group) is 1.84±0.710mins, in group D (Dexmedetomidine group) is 1.68±0.7 12mins.There is no clinical significance between group F and group D regarding mean time taken for onset of sensory blockade, with P value=0.263 (p>0.05).

Duration of analgesia in mins	Groups	
	Group F	Group D
Mean	169.9	354.6
S.D	17.1	35.8
Minimum	145 min	280 min
Maximum	210 min	420 min
T-value		-32.92
P-value		0.000
Decision		Significant

Table 2: Mean duration of analgesia

The mean duration of analgesia is 169.9 ± 22.94 mins in group F (Fentanyl) and 354.6±35.8 mins in group D (dexmedetomidine group). There is a statistically highly significant difference between group F and group D (p=0.000).

HR	Group	Mean	S.D	P-value	Decision
Basal	Fentanyl	79	7.08	0.565	Not significant
	Dexmedetomidine	79	7.69		
0 mins	Fentanyl	80	7.37	0.539	Not significant
	Dexmedetomidine	80	8.05		
2 mins	Fentanyl	77	6.91	0.076	Not significant
	Dexmedetomidine	75	5.35		
5 mins	Fentanyl	73	7.11	0.132	Not significant
	Dexmedetomidine	70	8.83		
10 mins	Fentanyl	71	6.04	0.060	Not significant
	Dexmedetomidine	69	7.92		
20 mins	Fentanyl	71	5.71	0.14	Not significant
	Dexmedetomidine	68	4.64		
30 mins	Fentanyl	71	5.81	0.36	Not significant
	Dexmedetomidine	70	5.10		
40 mins	Fentanyl	72	5.79	0.521	Not significant
	Dexmedetomidine	71	5.28		
50 mins	Fentanyl	73	5.95	0.89	Not significant
	Dexmedetomidine	71	5.84		
60 mins	Fentanyl	73	6.27	0.60	Not significant
	Dexmedetomidine	72	5.82		
90 mins	Fentanyl	74	5.95	0.82	Not significant
	Dexmedetomidine	72	6.14		
120 mins	Fentanyl	74	6.61	0.33	Not significant
	Dexmedetomidine	72	5.75		
180 mins	Fentanyl	76	6.62	0.31	Not significant
	Dexmedetomidine	74	5.73		

Table 3: Mean heart rate in bpm at various intervals

In the group F (Fentanyl group) the basal value of mean heart rate is 79±7.08 bpm and we observed a decrease in mean heart rate which is maximum of 8 bpm from basal value at 20th min (10.12% decrease from basal value).

In the group D (dexmedetomidine group) the basal value of mean heart rate is 79±7.69 bpm and we observed a decrease in mean heart rate which is maximum of 11 bpm from basal value at 20th min (13.92% decrease from basal value).

Though a greater reduction in mean heart rate is observed in Group D, there is no statistically significant difference between the groups (Group F vs. Group D).

MAP	Group	Mean	S.D	T-value	P-value	Decision
Basal	Fentanyl	97.62	2.59	1.8505	0.067	Not significant
	Dexmedetomidine	96.78	2.80			
0mins	Fentanyl	97.68	2.06	1.960	0.0527	Not significant
	Dexmedetomidine	96.48	6.88			
2mins	Fentanyl	94.56	2.18	1.978	0.0537	Not significant
	Dexmedetomidine	93.34	6.78			
5mins	Fentanyl	88.77	5.13	2.1405	0.0347	Not significant
	Dexmedetomidine	86.85	4.023			
10mins	Fentanyl	88.14	2.84	1.756	0.082	Not significant
	Dexmedetomidine	86.74	2.88			
20mins	Fentanyl	87.48	2.89	1.693	0.093	Not significant
	Dexmedetomidine	86.02	2.98			

30mins	Fentanyl	90.80	3.83	4.270	0.000	significant
	Dexmedetomidine	88.46	3.18			
40mins	Fentanyl	90.90	3.25	3.171	0.002	significant
	Dexmedetomidine	89.22	2.50			
50mins	Fentanyl	91.48	3.22	3.1742	0.002	significant
	Dexmedetomidine	89.28	3.10			
60mins	Fentanyl	92.48	3.53	2.898	0.004	significant
	Dexmedetomidine	89.68	3.42			
90mins	Fentanyl	93.24	3.59	1.5617	0.1216	Not significant
	Dexmedetomidine	91.72	3.089			
120mins	Fentanyl	93.70	3.50	1.5123	0.133	Not significant
	Dexmedetomidine	92.80	3.15			
180mins	Fentanyl	94.12	3.27	1.5855	0.1161	Not significant
	Dexmedetomidine	93.04	3.08			

Table 4: Mean MAP at various time intervals in mm Hg

In the group F (Fentanyl group) the basal value of mean MAP is 97.62±2.594 mmHg and we observed a fall in mean MAP which is maximum of 10.14 mmHg from mean basal MAP at 20th min (10.38% fall from basal MAP).

In the group D (dexmedetomidine group) the basal value of mean MAP is 96.78±2.80 mmHg and we observed a fall in mean MAP which is maximum of 10.76 mmHg from mean basal MAP at 20 th min (11.11% fall from basal MAP).

The mean MAP from basal to 20th minute recording is statistically not significant between group F and group D. The mean MAP from 30th to 60th minute recording is statistically highly significant between group F and group D.

No. of RA in post-op 24 hrs	Groups	
	Group F	Group D
Mean	3.5	1.98
S.D	1.265	0.713
Minimum	1	1
Maximum	5	3
Total analgesic dose	175mg ± 63.25mg	99mg ± 35.65mg
P – value	0.000	
Decision	Significant	

Table 5: Number of rescue analgesics in post-op 24 hours

The mean no. of RA required in first 24 post-op hrs in group F (Fentanyl) is 3.5±1.265. In group D (dexmedetomidine) mean no. of RA required in first 24 post-op hrs is 1.98±0.713. Total analgesic dose required in first 24hrs in Group F (Fentanyl) is 175mg±63.25mg where as in Group D (Dexmedetomidine) is 99mg±35.65mg.There is a statistically highly significant difference between group F and group D (p=0.000).

Group Vs. Hypotension	Absent	Present	Total
Fentanyl	48(96%)	2(4%)	50(100%)
Dexmedetomidine	46(92%)	4(8%)	50(100%)
Total	94(94%)	6(6%)	100(100%)

Table 6: Incidence Hypotension & Bradycardia

Pearson Chi-Square=0.709, P-Value=0.400 Not significant

Group Vs. Bradycardia	Absent	Present	Total
Fentanyl	48(96%)	2(4%)	50(100%)
Dexmedetomidine	45(90%)	5(10%)	50(100%)
Total	93(93%)	7(7%)	100(100%)

Table 7

Pearson Chi-Square=1.382, P-Value=0.240 Not significant

In Group F, two out of 50 and in Group D, four out of 50 patients developed hypotension which is statistically not significant (p>0.05). All the patients who developed hypotension could be easily treated with intravenous fluids and vasopressor. In Group F, four out of 50 and in Group D, five out of 50 patients developed bradycardia which is statistically not significant (p>0.05). All the patients who developed bradycardia were treated by single dose of 0.6 mg of atropine.

Pruritis	Groups			
	Group F		Group D	
	No. of Pts	%	No. of Pts	%
Present	9	18%	0	0%
Absent	41	82%	50	100%
Total	50	100%	50	100%
Pearson chi-square	9.890			
P – value	0.002			
Decision	Significant			

Table 8: Incidence of Pruritis

In Group F (Fentanyl), nine out of 50 patients i.e. 18% of patients had developed pruritis where as in Group D (Dexmedetomidine) none of the patients developed pruritis. There is a statistically highly significant difference in the incidence of pruritis between group F and group D (p=0.002)

DISCUSSION: 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 action compared to Lignocaine, 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.

The use of opioids in conjunction with local anaesthetic for spinal anaesthesia has been associated with decreased pain scores and reduced analgesic requirement in

The post-operative period intrathecal Fentanyl is a lipophilic -receptor agonist opioid. Intrathecally, fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of spinal cord and may have a supraspinal spread and action. Fentanyl is established to provide post-operative analgesia following SAB. Results of previous studies have demonstrated that intrathecal fentanyl not only enhance analgesia when added to subtherapeutic doses of local anaesthetics but also do not prolong recovery.

The mechanism by which intrathecal $_2$-adrenoceptor agonists prolong the motor and sensory block of local anaesthetics is not well known. They act by binding to presynaptic C-fibres and postsynaptic dorsal horn neurons. Their analgesic action is a result of depression of the release of C-fibre transmitters and hyperpolarisation of postsynaptic dorsal horn neurons. Local anaesthetic agents act by blocking sodium channels. The prolongation of effect may result from synergism between local anaesthetic and $_2$-adrenoceptor agonist, while the prolongation of the motor block of spinal anaesthetics may result from the binding of $_2$-adrenoceptor agonists to motor neurons in the dorsal horn. Intrathecal $_2$-receptor agonists have been found to have antinociceptive action for both somatic and visceral pain.

Dexmedetomidine, an-2 adrenergic agonist is 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 (<24 hrs) for analgesia and sedation in intense care unit. Dexmedetomidine is a highly specific and selective alpha-2 adrenoceptor agonist with 8 times more affinity for alpha-2 adrenoceptor than clonidine. The ratio of alpha-1: alpha-2 receptor binding selectivity for dexmedetomidine is 1:1620 compared to 1:220 for clonidine.

Hence, we have undertaken this study to evaluate and compare the effects of adding fentanyl versus dexmedetomidine with intrathecal hyperbaric 0.5% bupivacaine in patients scheduled for elective lower abdominal surgeries.

A total of 100 patients of both sexes scheduled for elective lower abdominal surgeries under spinal anaesthesia, belonging to American society of Anaesthesiologist (ASA) Physical Status I & II were randomized into two groups (group F and group D) of equal sized prospective, observational study group using an open protocol design.

Demographic Data: The demographic data compared among the two groups were the age, sex, height, weight. The differences in the mean values of these parameters were not statistically significant (>0.05) among the two groups.

Hypothesis done Before the Study: It was hypothesised that intrathecal bupivacaine and dexmedetomidine mixture provides longer duration of sensory blockade and superior analgesia (with lesser requirement for rescue analgesia) compared to the intrathecal bupivacaine and fentanyl.

Onset of Sensory Blockade: In our study the mean time taken for onset of sensory block is 1.84±0.710 mins in the fentanyl group and 1.68±0.712 mins in the dexmedetomidine group. There is no statistical significant difference in the onset of sensory blockade between fentanyl group and the dexmedetomidine group.

Duration of Analgesia: The mean duration of analgesia ie., time to rescue analgesia in our study is 169.9±22.94 mins in group F (Fentanyl) and 354.6±35.8 mins in group D (Dexmedetomidine group). There is a statistically highly significant difference between group F and group D (p=0.000)

In studies conducted by Gehan A et al.,[8] Gupta R et al.[9] and Hala EA Eidet al.,[10] authors observed a statistically significant increase in the mean duration of analgesia in Group D when compared with Group F.

Hemodynamic Effects: Mean Arterial Blood Pressure: In the group F (Fentanyl group) we observed a fall in mean MAP which is maximum of 10.14 mmHg from mean basal MAP at 20th min (10.38% fall from basal MAP) and in group D (Dexmedetomidine group) a fall in mean MAP which is maximum of 10.76 mmHg from mean basal MAP at 20th min (11.11% fall from basal MAP).

The mean MAP from basal to 20th minute recording is statistically not significant between group F and group D. The mean MAP from 30th to 60th minute recording is statistically significant between group F and group D. No significant difference is observed in mean MAP at 120 min and at 180 min between the two groups. However the mean MAP is significantly lower at 180 min when compared to basal values in both the groups.

In a study conducted by Gehan A et al.,[8] authors observed no significant difference between the two groups in mean MAP at 120 min and at 180 min but significantly lower when compared with the basal values, which concurs with our study results.

Heart Rate: In the group F (Fentanyl group) the basal value of mean heart rate is 79±7.08bpm and we observed a decrease in mean heart rate which is maximum of 8 bpm from basal value at 20th min (10.12% decrease from basal value) where as in the group D (Dexmedetomidine group) the basal value of mean heart rate is 79±7.69 bpm and we observed a decrease in mean heart rate which is maximum of 11 bpm from basal value at 20th min (13.92% decrease from basal value).

Though a greater reduction in mean heart rate is observed in Group D, there is no statistically significant difference between the groups (Group F vs Group D).

In a study conducted by Gehan A et al., authors observed changes in heart rate at various intervals ie., at basal, 120 min, and 180 min to be 85±22, 91±15 and 84±10 in BF group and 88±14, 88±8 and 79±9 in BD group with no significant difference between the groups, which concurs with our study.

Our study is consistent with the studies done by Al-Ghanem SM et al.[11] who observed that there was no significant difference in mean value of heart rate throughout the intraoperative and postoperative period.

Rescue Analgesic Dose in First 24 Hrs: In our study the mean no. of RA required in first 24 post-op hrs in group F (Fentanyl) is 3.5±1.265. In group D (Dexmedetomidine) mean no. of RA required in first 24 post-op hrs is 1.98±0.713. Total analgesic dose required in first 24 hrs in Group F (Fentanyl) is 175mg±63.25mg where as in Group D (Dexmedetomidine) is 99mg±35.65mg.There is a statistically highly significant difference between group F and group D (p=0.000)

In a study conducted by Gupta R et al.[9,10] the total analgesic dose in first 24hrs is 180±70 mg in Group F and 80±67 in Group D, which concurs with our study.

Incidence of Complications: Hypotension and Bradycardia: In our study, in Group F two out of 50 and in Group D four out of 50 patients developed hypotension which is statistically not significant (p>0.05). All the patients who developed hypotension could be easily treated with intravenous fluids and vasopressor.

In Group F four out of 50 and in Group D five out of 50 patients developed bradycardia which is statistically not significant (p>0.05). All the patients who developed bradycardia were treated by single dose of 0.6 mg of atropine.

In a study conducted by Al-Ghanem SM et al.[11] authors observed that the hypotension (fall in MAP of>30% of pre-induction value) was mild to moderate in both dexmedetomidine and fentanyl group. 4/38 patients in dexmedetomidine group and 9/38 patient in fentanyl group had hypotension but it did not reach a significant difference.

Similarly in a study conducted by Gehan A et al., authors observed 15% incidence of hypotension in both the groups and incidence of bradycardia of 5% in BF group and 10% in BD group with no statistical significance between the groups.

Pruritis: In our study, in Group F (Fentanyl) nine out of 50 patients i.e., 18% of patients had developed pruritis where as in Group D (Dexmedetomidine) none of the patients developed pruritis. There is a statistically highly significant difference in the incidence of pruritis between group F and group D (p=0.002). Pruritis in fentanyl group is mild in nature and did not require any treatment.

Pruritis is the commonest side effect of intrathecal opioids.[12] In earlier studies on spinal anaesthesia for ambulatory knee arthroscopy, the combination of bupivacaine with fentanyl was associated with an instance of pruritis ranging from 48 to 75%compared with the groups receiving bupivacaine alone.[13] Ackerman et al.[14] have also reported that opioids that stimulated-receptors following epidural administration exhibited significantly less pruritis than pure -receptor opioids administered similarly.

Nausea, Vomiting and Respiratory depression: In our study none of the patients developed nausea and vomiting as hypotension is treated promptly and effectively. We did not observe any evidence of respiratory depression.

In our study none of the patients came back to us with backache, buttock pain or leg pain or any neurological deficit. This was confirmed with most of the studies.

CONCLUSION: From the present study it can be concluded that intrathecal dexmedetomidine in the dose of 5 microgram along with 2.5ml bupivacaine, 0.5% heavy when compared with intrathecal fentanyl in a dose of 25 microgramμ along with 2.5ml bupivacaine, 0.5% heavy, in patients undergoing elective lower abdominal surgeries,

- Produces prolonged postoperative analgesia.
- Produces prolonged sensory blockade.
- Produces prolonged motor blockade.
- Produces sedation in which more patients were asleep and easily arousable.
- Produces haemodynamic changes comparable with fentanyl group which could be easily managed.
- Reduced total analgesic dose requirement in first 24 hrs post-op.
- Not associated with significant side effects like pruritis as observed in fentanyl group.

Since dexmedetomidine (5μg) when used intrathecally along with 0.5% bupivacaine heavy significantly prolonged the duration of analgesia and reduced total analgesic dose requirement in first 24 hrs post-op with stable hemodynamic parameters hence can be an attractive alternative for opioids for prolonging spinal analgesia.

SUMMARY: The study entitled "A Comparative study of Intrathecal Dexmedetomidine (5μg) and Fentanyl (25μg) as adjuvants to intrathecal 0.5% hyperbaric Bupivacaine" was undertaken to evaluate the efficacy and the safety of fentanyl or dexmedetomidine as adjuvant to intrathecal hyperbaric 0.5% bupivacaine.

It is found from our study that duration of sensory, motor blockade and duration of analgesia is significantly prolonged in the dexmedetomidine group.

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

Four patients in dexmedetomidine group and two patients in fentanyl group developed hypotension requiring treatment. Five patients in dexmedetomidine group, and two patients in fentanyl group developed bradycardia requiring treatment.

More number of patients in the dexmedetomidine group were sedated and easily arousable.

Total analgesic dose requirement is significantly less in dexmedetomidine group.

Pruritis is not observed in any of the patients in dexmedetomidine group.

No patient had any respiratory depression, nausea, vomiting or shivering in either of the groups.

REFERENCES:

1. Etches RC, Sandler AN, Daley MD. Respiratory depression and spinal opiods. Can J Anaesth 1989;36:165-85.
2. Liu S, Chiu AA, Carpenter RL, et al. Fentanyl prolongs lidocaine spinal anaesthesia without prolonging recovery. Anesth Analg 1995;80:730-34.
3. Ben-David B, Solomon E, Levin H, et al. Intrathecal fentanyl with small dose dilute bupivacaine: Better anaesthesia without prolonging recovery. Anesth Analg 1997;85:560-65.
4. Hunt CO, Naulty JS, Bader AM, et al. Perioperative analgesia with subarachnoid fentanyl-bupivacaine for cesarean delivery. Anesthesiology 1989;71:535–40.
5. Morgan M. The rationale use of intrathecal and extradural opiods. Br J Anaesth 1989;63:165-88.
6. Crone L-AL, Conly JM, Clark KM, et al. Recurrent herpes simplex virus labialis and the use of epidural morphine in obstetric patients. Anesth Analg 1988;67:318-23.
7. Ralph Getler, Clieghton H Brown, Mitchel H, et al. Dexmedetomidine: a novel sedative analgesic agent. Baylor University Medical Centre Proceedings 2001;14(1):13-21.
8. Gehan A Tarbeeh, Ayman A Mohamed. Effects of intrathecal bupivacaine–fentanyl versus bupivacaine–dexmedetomidine in diabetic surgical patients. Egyptian Journal of Anaesthesia 2013;29(1):13-18.
9. Rajni Gupta, Reetu Verma, Jaishri Bogra, et al. A comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. J Anaesthesioly Clin Pharmacoly 2011;27(3):339–43.
10. Rajni Gupta, Hala E A Eid, Mohamed A Shafie, et al. Dose-Related prolongation of hyperbaric bupivacaine spinal anesthesia by dexmedetomidine. Ain Shams Journal of Anesthesiology 2011;4(2).
11. Subhi M Al-Ghanem, Islam M Massad, Mahmoud M Al-Mustafa, et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures. American Journal of Applied Sciences 2009;6(5):882-87.
12. Chaney MA. Side effects of intrathecal and epidural opioids. Can J Anaesth 1995;42:891-903.
13. Nair GS, Abrishami A, Lermitte J, et al. Systemic review of spinal anaesthesia using bupivacaine for ambulatory knee arthroscopy. Br J Anaesth 2009;102:307-15.
14. Ackerman WE, Juneja MM, Kaczorowski DM, et al. A comparison of incidence of pruritis following epidural opioid administration in parturient. Can J Anaesth 1989;36:388-91.