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A Comparative Study of Fentanyl and Clonidine as an Adjuvant to Bupivacaine for Spinal Anesthesia

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Abstract

Background: Spinal Anesthesia is the regional anesthesia obtained by blocking spinal nerves in subarachnoid space, the aesthetic agents are deposited in the subarachnoid space and act on spinal nerve roots and not on substance of cord. Intrathecal opioids are synergistic with local aesthetic and intensity of sensory block without increasing motor block and offer Hemodynamic stability. Intrathecal opioids like fentanyl citrate is combined with local anesthetics which has milder side effects, also fentanyl citrate is lipophilic drugs. It has rapid onset compared lyophobic morphine. This property may affect onset of sensory block. When fentanyl citrate is added to bupivacaine hydrochloride for subarachnoid block. An intrathecal Clonidine has substantial antinociceptive effect by its action on α^2 Receptor in dorsal Horn of spinal cord and by adding Clonidine with Bupivacaine hydrochloride improves intraoperative analgesia and might prolong the duration of spinal Analgesia. We compared the effects of fentanyl and Clonidine as an adjuvant to Bupivacaine for spinal Anesthesia. *Methods:* The study was carried out by selecting the patients presenting for surgery of lower limb, perineal surgery, lower abdominal surgery etc. Study was done in 50 patients belonging to ASA 1 and 2 selected for the study. Group - BF: Inj. Bupivacaine Hydrochloride (20 mg) (0.5%) + inj. Fentanyl citrate 25 µg. Group - BC: Inj. Bupivacaine Hydrochloride (20 mg) (0.5%) + inj. Clonidine Hydrochloride 50 µg. Time at which sensory and motor blockade reached highest dermatome level & stabilized at highest level. Recording of vital signs was started from the point of injection of drug in CSF. Heart Rate, Blood Pressure, SpO_2, were noted every 1 min for first 10 min, then every 5 min till 30 min and then every 15 min till 60 min. Duration of total sensory and Motor Blockade is noted. Hypotension was defined as Systolic - Blood Pressure less than 90 mm HG or 30% decrease in Systolic Blood Pressure from Base line and Brady cardia was defined as Heart Rate less than 50 min. Patients were observed for following complication during procedure Hypotension, Bradycardia, Sedation, Respiratory depression, Nausea, Vomiting, Rigors, Pruritus. Duration of Motor & Sensory Blockade was noted. *Results:* We studied that mean time for onset of sensory block (sec) and motor block (sec) was shorter in Group - BF as compared to Group - BC. Total duration of motor and sensory block was longer in Group - BC as compared Group - BF. Changes in pulse rate, systolic BP and diastolic BP shows statistical significance in both Group. First analgesic requirement was more prolonged in Group - BC. Group - BF shows some complications like Nausea, Pruritus, and Hypotension. Group - BC shows complications like sedation, Hypotension + Bradycardia. *Conclusion:* Clonidine Hydrocloride caused intense sensory and motor blockade when injected with bupivacaine. Clonidine also didn't show side effects like respiratory depression, pruritus, urinary retention. Which were noted with the use of fentanyl. But onset of action was delayed with use of clonidine and increased chances of more bradycardia, hypotension and sedation compared to fentanyl which required more supportive care.

Keywords: Fentanyl; Clonidine; Bupivacaine; Spinal Anesthesia; Hemodynamic; Sensory and Motor blockade.

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Introduction

"For all the happiness mankind can give is not pleasure but in relief from pain" –Pain is extra ordinary complex sensation which is difficult to define and equally difficult to measure in an accurate objective manner. A Regional Anesthesia may be considered as Anesthesia of an anatomic part produced by application of chemical capable of blocking conduction in nerve tissue Associated with that part. Agent must not damage the tissue permanently and the functional derangement must be reversible" Spinal Anesthesia is the regional anesthesia obtained by blocking spinal nerves in subarachnoid space the anesthetic agents are deposited in the subarachnoid space and act on spinal nerve roots and not on substance of cord.

Spinal Anesthesia has been popular for short and intermediate duration of surgical procedures for decades. Lidocaine has been the local Anesthetics of choice for spinal Anesthesia in ambulatory surgical procedures.[1] This was based on drugs short duration of action which allows timely recovery and discharge, unfortunately recent reports of lidocaine neurotoxicity have created doubt of use of lidocaine. One study reported 37% incidence of "Radicular Symptoms" of pain and/or dysesthesias in buttocks, thigh or lower Limbs after spinal anesthesia with 5% lidocaine in 7.5% glucose for these reasons, Bupivacaine Hydrochloride has become popular for ambulatory short surgical procedure.[2]

Bupivacaine hydrochloride is a potent local Anesthetic. It has propensity to cause severe hypotension in geriatric patients. Intrathecal opioids are synergistic with local anesthetic and intensity of sensory block without increasing motor block and offer Hemodynamic stability. An intrathecal morphine is associated with higher incidence of side effects. So, newer opioids like fentanyl citrate is combined with local anesthetics which has milder side effects, also fentanylcitrate is lipophilic drugs. It has rapid onset compared lipophobic morphine. This property may affect onset of sensory block.

When fentanyl citrate is added to bupivacaine hydrochloride for subarachnoid block.[3] An intrathecal Clonidine has substantial antinociceptive effect by its action on α^2 Receptor in dorsal Horn of spinal cord and by adding Clonidine with Bupivacaine hydrochloride improves intraoperative analgesia and might prolong the duration of spinal Analgesia.[4]

"We compared the effects of fentanyl and Clonidine as an adjuvant to Bupivacaine for spinal Anesthesia."

Aims of Study

"A Comparative study of fentanyl and Clonidine as an adjuvant to Bupivacaine for spinal Anesthesia."

The parameters observed were:

1. To compare the onset of peak sensory blockade;
2. To compare the level of maximum motor blockade;
3. To compare the duration of sensory blockade;
4. To compare the duration of motor blockade;
5. Duration of postoperative analgesia and time to rescue analgesia;
6. Incidence of intraoperative & postoperative complication;
7. To compare adverse effects of procedure & drugs.

Materials and Methods

After getting approval from the ethical committee of our hospital. The study was carried out by selecting the patients presenting for surgery of lower limb, perineal surgery, lower abdominal surgery etc.

Study was done in Gujarat Cancer Research Institute in 50 patients study was done in ASA Grading I & II.

Exclusion Criteria

- Allergic to local Anesthetic;
- Patient refusal;
- Valvular heart disease;
- Surgery of longer duration;
- Bleeding tendency;
- Neurological problem;
- Infection at the site of injection.

Preanesthetic Assessment

All patients were examined preoperatively and history noted. All patients were tested for sensitivity to Bupivacaine by an intradermal skin test.

Investigation

HIV, HBSAG, Hemoglobin, total count, Platelet count, differential count, Renal function test, Serum Electrolytes, Liver function test, Urine

Analysis, Prothrombin time, Activated partial thromboplastin time, Electro–cardiogram, Chest X–Ray (P/A view).

Group allocation

50 Patients were randomly allocated in Two Group (n = 25)

Groups	
Group–BF	Inj. Bupivacaine Hydrochloride (20 mg) (0.5%) + Inj. Fentanyl citrate 25 μg.
Group–BC	Inj. Bupivacaine Hydrochloride (20 mg) (0.5%) + Inj. Clonidine Hydrochloride 50 μg

Premedication

Tab. Lorazepam 1 mg at 10.00 pm on previous night of surgery Tab. Diazepam 5 mg at 6.00 am on the day of surgery Spinal Anesthia is given for the surgeries in 50 patients were taken in operation room and monitoring devices, like Noninvasive Blood Pressure Monitoring Electrocardiography SpO_2. 18G Intravenous catheter was inserted in forearm peripheral vein followed by preloading 10 ml/kg of Injection Ringer lactate Solution. Patients were put in left lateral position followed by painting and draping of back taking aseptic precaution after local infiltration. Intrathecal space was identified and spinal needle introduced and drugs were given according to groups allowed. Patients were immediately turned supine. Sensory block was assessed by cotton gauze and level was confirmed. Motor Block was assessed at the time of reaching highest sensory block by bromate score

Bromage Score[5]

Grade–0 : No block full flexion of knee & feet;

Grade–I : Partial block just able to flex knee but full flexion of feet;

Grade–II : Almost complete block unable to flex knee but complete; Flexion of feet possible;

Grade–III : Complete block unable to flex knee & feet.

Time of the peak level of sensory and motor block was calculated. This was calculated from the time of drug injected intrathecal to time at which sensory and motor blockade reached highest dermatome level & stabilized at highest level. Level of dermatome block. Recording of vital signs was started from the point of injection of drug in CSF. Heart Rate, Blood Pressure, SpO_2, were noted every 1 min for first 10 min, then every 5 min till 30 min and then every 15 min till 60 min. Durationof total sensory and Motor Blockade is noted. Hypotension was defined as Systolic Blood Pressure less than 90 mm HG or 30% decrease in Systolic Blood Pressure from Base line and Brady cardia was defined as Heart Rate less than 50 min. Hypotension was treated by increasing the rate of Intravenous fluid, mephentermine 5 mg IV in Incremental doses. Brady cardia was treated by Inj. Glucopyrolate 0.2 mg IV. Patients were observed for following complication during procedure: Hypotension, Bradycardia, Sedation, Respiratory depression, Nausea, Vomiting, Rigors, and Pruritus.

Postoperative

Patient were shifted to postoperative ward and duration of Motor & Sensory Blockade was noted. Total duration of surgery and postoperative complications like headache, Urinary retention, diplopia, and backache was noted. Duration of postoperative first analgesic requirement was noted. Mean & Standard deviation were calculated for each parameter Statistical Analysis was done.

p - value < 0.05 were considered significant.

Results

There was no statistical significance difference between Two Groups (p > 0.05) with respect to age, sex, weight and height, as shown in (Table 1).

Table 1: Demographic details

	Group - BF	Group - BC	p - value
Age (mean ± SD)	50.6 ±14.4	54 ± 17.1	0.4507
Sex (M/F)	15:5	15:5	
Weight (mean ± SD)	51.5 ± 9.89	52.4 ± 7.98	0.7248
Height (mean ± SD)	168 ± 6.05	166 ± 5.65	0.2330

Table 2 shown that mean time for onset of sensory block (sec) was shorter in Group - BF as compared to Group - BC. p < 0.05 which is statistically significant. Peak height of sensory block was T6 in both Groups. Time to reach peak sensory level (min) showing no statistical significant difference in both Groups.

Table 2: Sensory block

Sr. No.	Sensory Blockade	Group - BF	Group - BC	*p* - value
1	Time of peak sensory height mean	T6	T6	
2	Time to reach peak sensory level (min) Mean ± SD	8.4 ±1.93	8.75 ±1.92	$p > 0.05$
	Motor Block			
3	Time of onset of sensory B. (sec)	36.25 ± 11.3	87 ± 25.7	$p < 0.05$
4	Time of onset of Motor Block (sec) mean ± SD	121.5 ± 59.67	156 ± 29.63	$p < 0.05$

Changes in pulse rate (min) showing $p < 0.05$ statistical significant difference in both Groups at 20 min, 25 min, 30 min, 45 min, shown as in (Table 3).

Table 3: Changes in pulse rate and min

Sr. No.	Time	Group - BF	Group - BC	*p* - value
1	Basal	96.5 ± 15.65	91.1 ± 13.2	0.1935
2	1 min	92.6 ± 21.1	92.2 ± 16.1	0.9402
3	3 min	95.7 ± 15	91.7 ± 16.3	0.3711
4	5 min	93.8 ± 15.1	89.1 ± 15.4	0.2813
5	10 min	91.2 ± 15.14	83.9 ± 16.64	0.1113
6	15 min	90.2 ± 14.89	82 ± 15.94	0.0662
7	20 min	87.9 ± 14.8	78.7 ± 17.3	$p < 0.05$
8	25 min	87.6 ± 14.6	74.8 ± 20	$p < 0.05$
9	30 min	87 ± 14.9	77.2 ± 16.7	$p < 0.05$
10	45 min	86.95 ± 14.48	77.85 ± 15.30	$p < 0.05$
11	60 min	84.95 ± 13.97	77.8 ± 14.37	0.0808

Table 4 shown, Systolic blood pressure changes (mm of Hg) showing $p < 0.05$ in both Group at 15 min, 20 min, 25 min, 30 min, 45 min. There was statistical significance. Difference in both Groups. Changes showing total duration of Motor and Sensory Block, shows in (Table 5). It Shows total duration of motor and sensory block was longer in Group - BC as compared Group - BF. $p < 0.05$ which is statistical significant difference in both Groups.

Table 4: Changes in blood pressure

Sr. No.	Time	Group - BF Systolic BP	Group - BC Systolic BP	*p* - value	Group - BF Diastolic BP	Group - BC Diastolic BP	*p* - value
1	Basal	131.15 ± 15.13	134 ± 11.4	0.4556	84.05 ± 9.13	85.55 ± 7.79	0.5350
2	1 min	126 ± 17.4	126 ± 13.9	1.0000	81.4 ± 9.9	80.1 ± 10	0.6462
3	3 min	122.65 ± 15.89	119 ± 13.7	0.3887	78.6 ± 8.75	75 ± 8.2	0.1399
4	5 min	121 ± 16.6	116 ± 15.5	0.2765	76.9 ± 9.26	73.2 ± 8.3	0.1434
5	10 min	116.9 ± 16.94	109.6 ± 15.02	0.1135	75.5 ± 9.8	70.7 ± 9.36	0.0829
6	15 min	116.5 ± 16.54	108.2 ± 14.41	$p < 0.05$	74.2 ± 10.3	68.3 ± 8.88	$p < 0.05$
7	20 min	114 ± 16.2	106 ± 14.2	$p < 0.05$	73.2 ± 10.4	67.8 ± 8.99	$p < 0.05$
8	25 min	114 ± 17.2	105 ± 16.9	$p < 0.05$	72.9 ± 10.6	66.35 ± 8.4	$p < 0.05$
9	30 min	114 ± 14	105 ± 14	$p < 0.05$	72.5 ± 10.3	67.3 ± 8.49	$p < 0.05$
10	45 min	116.6 ± 14.47	109.4 ± 11.21	$p < 0.05$	74.65 ± 10.4	68.75 ± 7.62	$p < 0.05$
11	60 min	118.6 ± 14.1	113.5 ± 11.07	0.1614	75.55 ± 10.2	72.3 ± 8.19	0.2202

Table 5: Duration of motor and sensory block

Sr. No.	Parameters	Group - BF	Group - BC	*p* - value
1	Total duration of Motor Blockade	177.5 ± 12.9	200 ± 18	$p < 0.05$
2	Total duration of Sensory Blockade	221 ± 20	234 ± 20.49	$p > 0.05$

First analgesic requirement was more prolonged in Group - BC as compared to Group - BF. $p < 0.05$ shows statistical significance between two Groups. Group – BF shows some complications like Nausea, Pruritus, and Hypotension. Group - BC shows complications like sedation, Hypotension + Bradycardia $p < 0.05$. There was statistical significant difference in both Groups in complications like Hypotension + Bradycardia, Sedation, Pruritus, as shown in (Table 6).

Table 6: 1st Analgesic requirement and duration of surgery

Sr. No.	Parameters	Group - BF	Group - BC	*p* - value
1	1st Analgesic Requirement	294 ± 10.32	344 ± 19	$p < 0.05$
2	Total duration of surgery	79 ± 49.96	100 ± 39.3	$p < 0.05$

Discussion

Spinal anesthesia is popular and commonly used worldwide. The advantages of an awake patient, minimal drug consumption, costs and rapid patient turn over has made this method of choice for many surgical procedures. Bupivacaine has been used as a spinal aesthetic since 1966 but has got longer duration of action. It has been well-documented that the combination of opioid with local anesthetics administered intrathecal has synergistic analgesic effect. Addition of fentanyl might potentiate the afferent sensory blockade, therefore, providing better surgical anesthesia. A Kararmaz, S Kaya et al.[6] Studied low-dose bupivacaine with fentanyl in spinal anesthesia for transurethral prostatectomy. Duration of analgesia was prolonged.

This study "A comparative study of fentanyl and clonidine as an adjuvant to bupivacaine in spinal anesthesia" was carried out in patients undergoing different surgical procedures like Lower-Limb Surgeries, Perineal Surgeries & Lower Abdominal Surgeries. This study was carried out in 50 adult patients of different age, sex, height and weight, ASA risk-status I and II, undergoing for lower limb, perineal region, lower abdominal surgeries. In this study, we divided patients into two Groups, having 25 patients in each Group.

Group - BF: Hyperbaric bupivacaine hydrocloride 20 mg + fentanyl citrate 25 μg;

Group - BC: Hyperbaric Bupivacaine Hydrocloride 20 mg + clonidine hydrocloride 50 μg;

Demographic Data

Mean age of patients in Group - BF was (50.6 ± 14.4) and Group - BC was (54 ± 17.1), All patients were of ASA status I/II having sex ratio in Group - BF was (M : F 15 : 5) and Group - BC was (M : F 15 : 5). They were scheduled for different surgical procedures. Mean weight of Group - BF was (51.5 ± 9.89) and Groub - BC was (52.4 ± 7.98). Mean height of Group - BF was (168 + 6.05) and Group - BC was (166 + 5.65). There was no statistical significant difference between Two Groups with respect to age, sex, weight and height ($p > 0.05$)

Ben-David et al.[7] Demonstrated that the use of diluted small dose bupivacaine for spinal blockade is inadequate to provide reliable anesthesia for longer duration of surgery. Addition of fentanyl was made it a reliable aesthetic. The added fentanyl provided an enhanced and increased duration of sensory analgesia without intensifying the motor blockade or prolonging analgesic effect.

Sensory Block

Onset of Sensory Block

In this study, onset of sensory block was earlier in Group - BF (36.25 + 11.3 sec) as compared to Group - BC (87 + 25.7 sec). There was statistically significant difference between Two Groups ($p < 0.05$). It is due to higher lipid solubility of fentanyl citrate thus allowing it to cross biological membranes rapidly and to be taken up by highly perfused tissues quickly. It crosses blood brain barrier so onset of action, sensory blockade was earlier in Group - BF

as compared to Group - BC Bano F, Sabbar S et al.[8] Studied that Intrathecal fentanyl as an adjuvant to Bupivacaine in spinal anesthesia for cesarean section. They concluded that addition of fentanyl to intrathecal bupivacaine results in earlier onset of Sensory Blockade.

Peak Sensory Level

In this study mean, height of Sensory Block was T6 level. It was due to addition of fentanyl citrate 25 μg or Clonidine hydrochloride 50 μg mixed with bupivacaine hydrochloride 20 mg. This increased the volume of injection to 4.5 cc. Pramod Patra, et al. (2003)[9] assessed the suitability of intrathecal spinal opioids plus bupivacaine for endoscopic urological surgeries and concluded that the addition of fentanyl to bupivacaine provided adequate surgical anesthesia and ideal peak sensory block height of T8 level.

Dobrydnjov, et al. (2003)[10] studied addition of bupivacaine 6 mg plus Clonidine 30 μg (Group - BC 30) diluted in 3 ml of saline. Which produced highest sensory block up to T6 level. Solokovic N et al. (2010).[11] Studied level of block and basicity of bupivacaine in spinal anesthesia. In (Group - BH) patients receiving hyperbaric bupivacaine (3 ml), highest level of block was upto T1 level in 3.33% of patients and lowest level of block was T7 level in 6.66% of patients. Time to achieve T6 level Sensory Block.

In this study mean, time (min) for onset of Sensory Blockade in Group - BF was (8.4 ± 1.9) and Group - BC was (8.75 ± 1.92). There was no statistical significant difference between both Groups (p > 0.05). Dobrydnjov et al. (2003)[10] studied addition of bupivacaine 6 mg plus Clonidine 30 μg (Group – BC 30) diluted in 3 ml of saline. Which produced highest Sensory Block up to T6 level.

Total Duration of Sensory Block

In this study, total duration of sensory blockade (min) in Group - BF was (221 ± 20) and Group - BC was (234 ± 20.49). There was no statistical significant difference between Two Groups (p > 0.05). Olfa Kaabachi et al. (2007)[12] studied Clonidine 1 μg/kg was safe and effective adjuvant to plain bupivacaine. They concluded addition of Clonidine to bupivacaine prolonged the duration of Sensory Block. Parvin Greval et al. (2003)[13] Did a double blind study, by injecting hyperbaric bupivacaine 15 mg plus fentanyl 25 μg intrathecal in 75 adult patients. Scheduled for lower limb and urological surgeries. They also concluded that duration of motor block is prolonged due to fentanyl administration.

Motor Block

Onset of motor blockade

In this study time (sec) for onset of motor blockade in Group - BF was (121.5 ± 59.67) and Group - BC was (156 ± 29.63). There was statistically significant difference between Two Groups (p > 0.05). Onset of motor block was earlier in patients receiving bupivacaine and fentanyl. It was due to fentanyl lipid solubility and onset of motor blockade was checked by Bromage Score. Bano F, Sabbar S, et al.[5,8] Studied that intrathecal fentanyl as an adjuvant to bupivacaine in spinal anesthesia for cesarean section. They concluded that addition of fentanyl to intrathecal bupivacaine results in earlier onset of motor blockade.

Total duration of motor block

Time (min) for total duration of motor blockade in Group - BF was (177 ± 12.9) and Group - BC was (200 ± 18). There was statistically significant difference between Two Groups (p < 0.05). Total duration of motor block was shorter in Group - BF. Parvin Greval et al. (2003)[13] Did a double blind study, by injecting hyperbaric bupivacaine 15 mg plus fentanyl 25 μg intrathecal in 75 adult patients, Scheduled for lower limb and urological surgeries. They also concluded that duration of motor block is prolonged due to fentanyl administration. Dobrydnjov et al. (2003)[10] addition of bupivacaine 6 mg plus Clonidine 30 μg (Group – BC 30) diluted in 3 ml saline produced prolonged motor blockade. The mean duration of motor block on the dependant side was significantly prolonged (Group – BC 30). Van Tuijl et al. (2006)[14] concluded that addition of 15 μg Clonidine to 5mg of intrathecal hyperbaric bupivacaine prolongs duration of motor block.

Hemodynamic changes

Systolic and Diastolic blood pressure changes

Spinal anesthesia causes hypotension by interruption of efferent sympathetic transmission. Which decreased peripheral resistance (decreased after load), venous dilatation, decreased venous return (decreased preload) & decreased cardiac output. Sympathetic preganglion nerve fibers exit the spinal cord from T1 to L2 level. Vasomotor tone is mediated by sympathetic fibers arising from T5 to L1 innervating arterial and venous smooth muscles. Sympathetic blockade level is two segments higher then analgesic blockade level.

In this study, Table 5 shows changes in systolic blood pressure (mm Hg). There was statistically

significant difference at 20 min, 25 min, 30 min, 45 min between both Groups as $p < 0.05$ after statistical analysis. Table 6 shows changes in diastolic blood pressure (mm Hg). Again, there was statistical significant difference at 20 min, 25 min, 30 min, 45 min between both Groups as $p < 0.05$ after statistical analysis. Olfa Kaabachi et al. (2007)[12] studied Clonidine 1 μg/kg intrathecal and found that it was a safe and effective adjuvant to plain bupivacaine. They concluded that during intrathecal anesthesia hypotension developed, which was more frequent in 29% patients of Clonidine Group compared to 17% patients of control Group. Merivitra et al. (2009)[15] studied a comparison between hyperbaric bupivacaine and bupivacaine + Clonidine. They concluded that patient receiving Clonidine needed more vasopressor. There was significant difference in systolic and diastolic blood pressure between Two Groups. Systolic and diastolic blood pressure being lower in patients receiving bupivacaine and clonidine. Erturk E et al. (2010)[16] studied 12 mg Ropivacaine or 8 mg Bupivacaine with fentanyl 20 µg in spinal anesthesia for major orthopedic surgeries. Study showed systolic and diastolic blood pressure was lower in patients receiving bupivacaine and fentanyl. Rajesh Mahajan et al. (2005)[17] studied 24 patients of pregnancy induced hypertension scheduled for cesarean section. Group - B and Group - BF showed mean arterial blood pressure was decreased in both Groups.

Pulse Rate

In this study of Table 3 shown, changes in pulse rate, p was < 0.05 after statistical analysis, suggesting significant difference between Two Groups at 20 min, 25 min, 30 min, 45 min. Bradycardia was expected after spinal anesthesia. Cardiac accelerating fibers are lying from T1 to T4 level. Clonidine cause stimulation of alpha 2 adrenergic receptors of the neurons in the tractus solitaries causes inhibition of the nucleus of sympathetic neurons in the medulla. By this mechanism, alpha adrenergic agonist reduce tonic activity of the bar reflex causing bradycardia. Bradycardia was noted in patients receiving bupivacaine with clonidine. Which was treated by inj. glycopyrolate (0.2 mg) intravenously. Eisenach et al.[18] Studied that bradycardia developed with use of caudal Clonidine in pediatric surgical patients during regional anesthesia. Olfa Kaabachi et al. (2007)[12] studied and found that Clonidine 1 µg/kg was a safe and effective adjuvant to plain bupivacaine. They concluded that the Clonidine 2 µg/kg added to bupivacaine frequently causes severe bradycardia. Incidence of bradycardia was reported in 21% patients. Erturk K et al. (2010)[16] studied comparison of 12 mg of ropivacaine or 8 mg bupivacaine, mixed with 20 µg fentanyl in spinal anesthesia for major orthopedic surgeries in geriatric patients. Heart rate was lower in patients receiving bupivacaine + fentanyl than in patients receiving bupivacaine + clonidine.

Complication

Hypotension developed in 5 patients in Group - BF and 3 patients in Group - BC intraoperatively. There was no statistical significant difference between Two Groups ($p > 0.05$). Olfa Kaabachi et al. (2007)[12] studied Clonidine 1 µg/kg & found that it was a safe and effective adjuvant to plain bupivacaine. They concluded that the addition of Clonidine tobupivacaine causes hypotension which was more frequent 29% of patients in Clonidine Groups and 17% patients in Control Groups.

Merivitra et al. (2009)[15] studied a comparison between hyperbaric bupivacaine and bupivacaine + Clonidine. They concluded that patients receiving Clonidine needed more vasopressor support compared to the Control Group. There was statistically significant difference between Two Groups. Hypotension was noted in patients receiving bupivacaine + Clonidine. Erturk E et al. (2010)[16] studied either 12 mg Ropivacaine or 8 mg Bupivacaine, mixed with fentanyl 20 μg in spinal anesthesia for major orthopedic surgeries. The study showed that systolic and diastolic blood pressure was lower in patients receiving bupivacaine and fentanyl. Rajesh Mahajan et al. (2005)[17] studied 24 patients of pregnancy induced hypertension scheduled for cesarean section. Mean arterial blood pressure decreased in both Groups within 4–6 min of spinal block as compared to baseline However, the fall in MAP was not statistically significant the decrease in MAP was 20% of base line in both Groups. In this study, 3 patients complained of pruritus in fentanyl Group. Pruritus was most common adverse effect in patient who received intrathecal fentanyl citrate. Pruritus was mild and did not require any treatment. Spencer Lui et al.[19] studied intrathecal lidocaine 5% with and without 25 μg fentanyl citrate in 8 volunteers. They concluded that patients receiving fentanyl pruritus was most common. Morgan G Ed Ward et al.[20] studied pruritus is a common complication with intrathecal opioid use, Most likely cause of spinal opioid induced pruritus was direct central effect on opioid receptor in substantia gelatinase.

Hypotension and bradycardia were noted in 5 patients receiving clonidine intrathecal. Olfa

Kaabachi et al (2007) (12) studied Clonidine 1µg/kg intrathecal and said that it was a safe and effective adjuvant to plain bupivacaine. They concluded that addition of Clonidine to bupivacaine leads to hypotension and bradycardia. Sedation was noted in 3 patients receiving clonidine. Lee et al.[21] studied Clonidine 2 µg/kg intrathecal showed longer duration of sedation in patients.

Postoperative analgesia

In this study, 1st analgesic requirement (min) in patients of fentatyl + bupivacaine was (294 ± 10.32) and in patients of clonidine + bupivacaine was (344 ± 19). This shows significant difference between Two Groups $p < 0.05$. Addition of Clonidine and fentanyl intrathecal caused prolonged postoperative analgesia. In this study, postoperative analgesic effect was more prolonged in Group - BC compared to Group - BF. I Van Tuijl (2006)[14] study also showed that addition of intrathecal Clonidine to hyperbaric bupivacaine prolonged the duration of spinal analgesia. I Dobrydnjov et al. (2003)[10] study also showed that addition of bupivacaine 6 mg plus Clonidine 30 μg (Group – BC 30) diluted in 3 ml saline prolonged duration of analgesia in inguinal herniorrhaphy. Levand Homme PM et al. (2009)[22] study also showed that intrathecal Clonidine 150 µg combined with bupivacaine caused prolonged postoperative analgesia. Parvin Greval et al. (2003)[13] studied "A double blind study on 75 adult patients scheduled for lower limb and urological surgeries by administration of intrathecal fentanyl 25 μg plus hyperbaric bupivacaine 15 mg." Fentanyl with low-dose bupivacaine prolonged the duration of analgesia. Rajesh Mahajan et al. (2005)[17] studied 24 patients of pregnancy induced hypertension scheduled for cesarean section. Group - B and Group - BF showed prolonged duration of analgesia without hemodynamic and neonatal compromise.

Onset of sensory and motor blockade was earlier in patients receiving fentanyl with bupivacaine compared to the patients receiving Clonidine with bupivacaine. Total duration of sensory and motor blockade was prolonged in groups of patients receiving Clonidine with bupivacaine. Systolic and diastolic blood pressure changes shows statistically significant difference between Two Groups. 1st analgesic requirement was prolonged in patients receiving clonidine with bupivacaine compared to patients receiving fentanyl with bupivacaine. Pruritus was noted in patients receiving fentanyl. Sedation, hypotension and bradycardia was noted in patients receiving clonidine with bupivacaine.

Conclusion

Clonidine hydrochloride caused intense sensory and motor blockade when injected with bupivacaine. Clonidine also didn't show side effects like respiratory depression, pruritus, urinary retention. Which were noted with use of fentanyl. But onset of action was delayed with use of clonidine and increased chances of more bradycardia, hypotension and sedation compared to fentanyl which required more supportive care.

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