IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 12 Ver. 6 (December. 2018), PP 10-16
www.iosrjournals.org

Comparative study of cardio respiratory stability and incidence of side effects after intra thecal administration of Bupivacaine with Ketamine vs Bupivacaine with Fentanyl for lower abdominal and lower limb surgeries".

Dr.T.D.Rambabu (MD Anaesthesia)
Assistant Professor Department of Anesthesiology Guntur Medical College, Guntur Andhra Pradesh.
Corresponding Author: Dr.T.D.Rambabu

Date of Submission: 05-12-2018 Date of acceptance: 21-12-2018

I. Introduction

In 1898, spinal anaesthesia as an anaesthetic technique for surgery was first used by AUGUST BIER since then the technique was evolved and now is a method of choice of anaesthesia for lower abdomen surgeries and lower limb surgeries. This is because of its efficacy, rapidity, minimal effects on mental status and reduction of blood loss. It also reduces the risk of vomiting and pulmonary aspiration in patients with full stomach and also it is useful in patients with chronic airway disease.

Subarachnoid block has some complications like hypotension, bradycardia, PDPH(Post dural puncture headache) as high as 25%. Spinal anaesthesia with hyperbaric bupivacaine is administered routinely for lower abdominal and lower limb surgeries.

An attempt was made to reduce the quantity of the local anaesthetic agent to limit the cardiovascular side effects and achieve the cardiovascular stability and to reduce the incidence of side effects.

Intrathecal opioids acts on the opioid receptors on the spinal cord and inhibit nociceptive afferent synaptic transmission via the A α and C fibers by opening pre synaptic K^+ channels to inhibit transmitter release thus reducing calcium influx. The use of opioids have been limited owing to the delayed respiratory depression caused by them.

Newer agents like fentanyl, a lipophilic opioid are not known to migrate intrathecally to the fourth ventricle to cause delayed respiratory depression and hence considered as safe alternatives.[33]

Ketamine (preservative free) a phencyclidine derivative is another adjuvant to intrathecal bupivacaine anaesthesia. Ketamine has been reported to interact with opioid receptors. Intrathecal ketamine produces a short period of analgesia with stable haemodynamics. Ketamine receptors have $GABA_A$receptor agonistic properties.

II. Aims And Objectives

Patient selection criteria

- ASA physical status 1 or 2
- Age 15-60 yrs
- Elective surgeries

Exclusion criteria

- Any contra indications to spinal anaesthesia.
- Patients with history of pruritus or allergy to opiods/local anaesthetics/ketamine.
- Patients who have received sedative medications in the last four hours. Patients on the anti-psychotic drugs.

Parameters studied are

- Onset of sensory level (checked at 30 secs interval with 24 gauge needle at T12 dermatome level by hot and cold saline).
- Maximum level of sensory blockade.
- Maximum intensity of motor blockade(bromage scale).
- Duration of analgesia. Haemodynamic changes like SBP, DBP, MAP Heart rate.
- Assess the respiratory rate changes and oxygen saturation(SpO_2).
- Incidence of side effects (nausea, vomiting, pruritis, shivering and nystagmus).

III. Methods And Materials

Study design: following ethical committee's approval the patient was subjected to a PAC and vital data was recorded. ASA 1 and ASA 2 physical status patients were included.

80 ASA physical status 1 or 2 patients scheduled to undergo elective lower abdominal and lower limb surgeries under subarachnoid block were included in the study following approval from the institute ethics committee. A written informed consent was obtained from each patient prior to study. Patients are allocated to group K (ketamine, n=40) or group F(fentanyl, n=40).

80 ASA 1 or 2 physical status patients in the age group of 15 to 60 years scheduled to undergo elective lower abdominal and lower limb surgeries under subarachnoid block included in the study. Any contraindication to spinal anesthesia, or patients with history of pruritus or allergy to opioids/local anaesthetics/Ketamine and patients who have received sedative medications in the last 4 hrs or patients on antipsychotic drugs were excluded. Patients are allocated to group K (25mg, preservative free ketamine, 0.5ml and 0.5% bupivacaine 2.0ml, n=40) or group F(25µg fentanyl, 0.5ml and 0.5% bupivacaine 2.0ml, n=40)..

Parameters studied are:

- Onset of sensory level(checked at 30 secs interval with 24 guage needle at T12 dermatome by hot and cold saline). Maximum level of sensory blockade.
- Maximum intensity of motor blockade as assessed by Bromage scale.
- Maximum intensity of motor blockade as assessed by Bromage scale.

Bromage Scale:

1. No impairment of movement of legs and feet.
2. Barely able to flex knees, no impairement in movement of feet.
3. Unable to flex knees, barely able to move feet.
4. Unable to move knee or feet.

- Duration of analgesia(four segment regression time).
- Haemodynamic changes(SBP, DBP, MAP and Heart rate).
- Respiratory changes(respiratory rate and saturation).
- Degree of sedation as assessed by Ramsay sedation scale.
- Incidence of side effects (nausea, vomiting, pruritis, shivering and nystagmus).

Ramsay sedation scale:

1. Anxious and agitated or restless or both.
2. Cooperative, oriented and calm.
3. Responsive to commands only.
4. Exhibiting brisk response to light glabellar tap or loud auditory stimulus.
5. Exhibiting a sluggish response to light glabellar tap or loud auditory stimulus.
6. Unresponsive.

After securing IV(18G) access and routine monitoring, patient placed in the lateral position and preloaded with 500ml of Ringer's lactate solution over 10min. A baseline recording of heart rate, NIBP, RR, SP02 were recorded. After ensuring the table in horizontal position 2.5 ml of study drug is injected over 15 sec in the L3-L4 interspace with 25G quinke's tip type spinal needle using standard sterile technique. Onset of sensory level, peak sensory level, and motor blockade are noted. NIBP, Heart rate, Respiratory rate & haeemoglobin oxygen saturation are recorded at 2, 5,10, 15, 20,30,60,90,120 min. sedation is assessed, using Ramsay sedation scale. Incidence of nausea, vomiting, shivering, pruritis, and nystagmus are noted. Intra operative fluid replacement is given as necessary, depending on the blood loss and haemodynamic parameters. All fluids used at room temperature and is used to provide warmth unless the patient complaints of shivering. Fluid balance and usage of vasopressors, atropine, opioids or perinorm recorded.

Table position will not be altered till 3 to 5 minutes after spinal anaesthesia. Parametric data were analyzed using Independent student's sample t-test and Non parametric data were analyzed using Mann Whitney U test. $P<0.05$ was considered significant. Systolic blood pressure <90mm of Hg is considered as hypotension.

Eighty patients who fulfilled the eligibility criteria were choosen and explained about the procedure and consent taken. Patients are divided into two groups: Group K(n=40) Group F(n=40).

After securing IV(18G) access and routine monitoring, patient placed in the lateral position and preloaded with 500ml of Ringer's lactate solution over 10min. A baseline recording of heart rate, NIBP, RR, SP02 were recorded. After ensuring the table in horizontal position 2.5 ml of study drug is injected over 15 sec

in the L3-L4 interspace with 25G quinke's tip type spinal needle using standard sterile technique. Onset of sensory level, peak sensory level, and motor blockade are noted. NIBP, Heart rate, Respiratory rate & haeemoglobin oxygen saturation are recorded at 2, 5,10, 15, 20,30,60,90,120 min. sedation is assessed, using Ramsay sedation scale. Incidence of nausea, vomiting, shivering, pruritis, and nystagmus are noted. Intra operative fluid replacement is given as necessary, depending on the blood loss and haemodynamic parameters. All fluids used at room temperature and is used to provide warmth unless the patient complaints of shivering. Fluid balance and usage of vasopressors, atropine, opioids or perinorm recorded.
Table position will not be altered till 3 to 5 minutes after spinal anaesthesia.
P<0.05 was considered significant. Systolic blood pressure <90mm of Hg is considered as hypotension.

IV. Results

80 ASA 1 or 2 patients scheduled to undergo lower abdominal and lower limb surgeries were allocated into group K(ketamine, n=40) and group F(fentanyl, n=40). After preloading with 500ml of lactated Ringer's solution, subarachnoid block was established with a 25 Guage spinal needle at L3-L4 interspace using 2ml of 0.5% hyperbaric Bupivacaine with 25 µg(0.5ml) of fentanyl in group F.
For group K 0.5% bupivacaine heavy with 25mg of ketamine (preservative free) is used.

Table 1: Physical characteristics of patients

Sl.No.	Parameter	Group K	Group F
1.	Age(Years)	40.6±11.8	37.75±13
2.	Weight(Kg)	54.4±6.7	54.7±6.4
3.	Height(Cm)	158.6±4.7	159.0±4.3

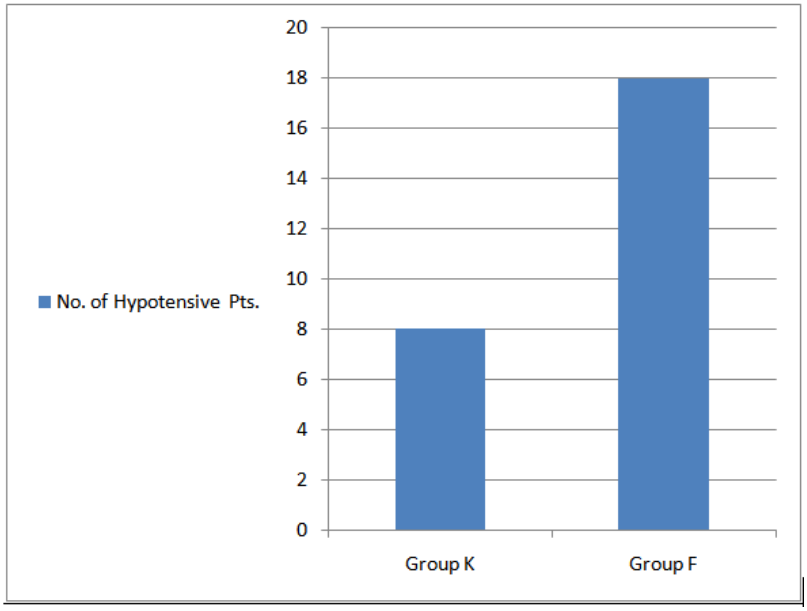
Table 2 :Baseline Parameters of patients

Sl.No.	Parameter	Group K	Group F
1	Systolic blood pressure(mmHg)	122.7±14.6	120.7±8.5
2	Distolic blood pressure(mmHg)	82±7.7	79.9±4.8
3.	Mean arterial pressure (mmHg)	95.5±9	93.5±4.7
4.	Heart rate(/min)	83.9±6.4	84.6±6.8
5.	Respiratory rate(/min)	17.8±1.6	17.8±1.6
6.	Haemoglobin Oxygen saturation	96-100%	96-100%

Table 3: Data of patients with significant Hypotension

	Group K (n=40)	Group F (n=40)
Pt's with significant hypotension	8	18
Pt's without significant	32	22
Total	40	40

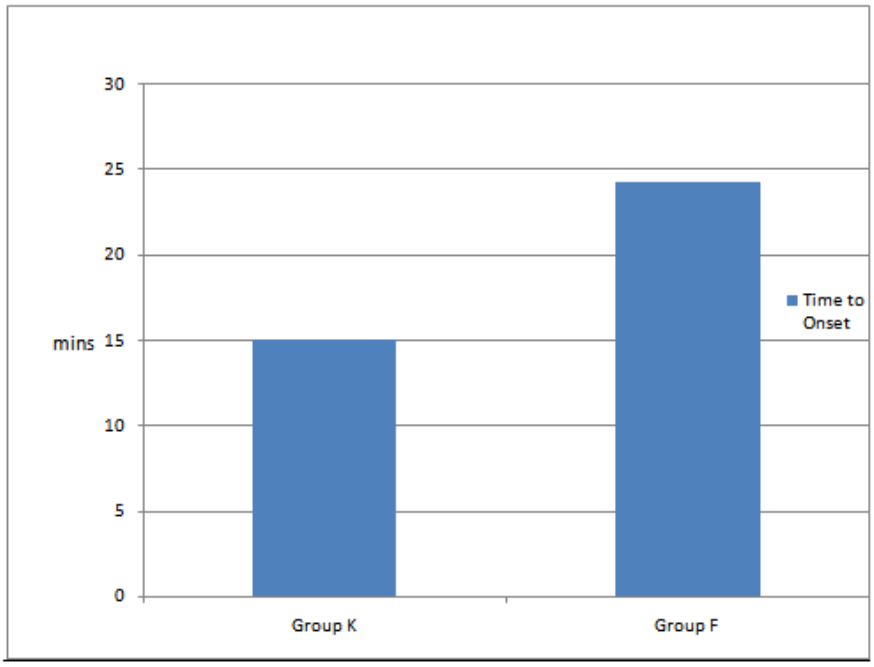
Chi-square value - 5.69
Degree of freedom - 1
P value = 0.01



Patients with Significant Hypotension

Table 4: Data of patients with significant hypotension

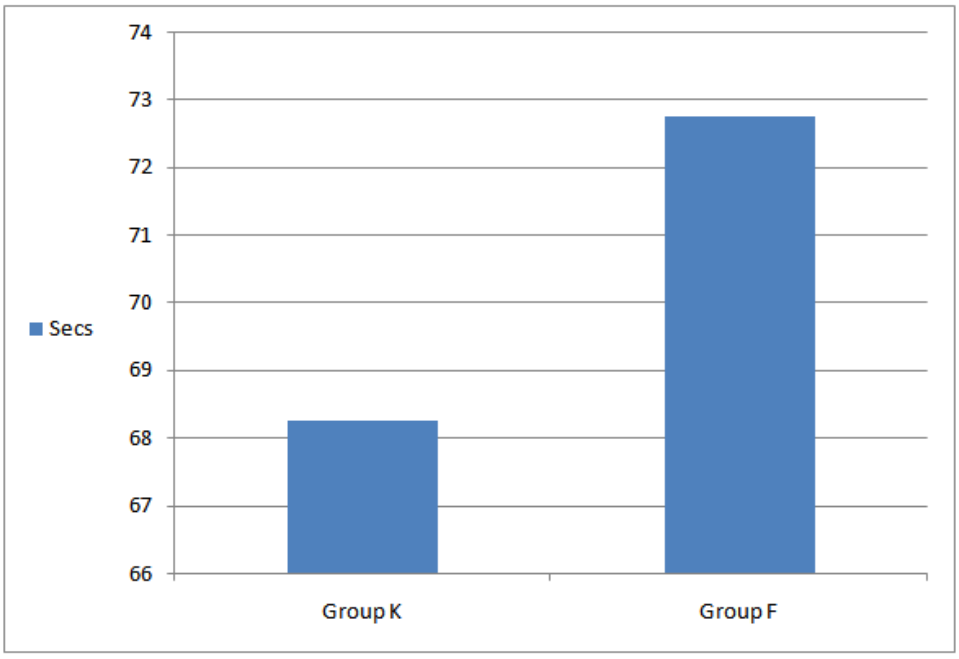
Sl.No.	Parameters	Group K (n=40)	Group F (n=40)
1.	Incidence	20%	45%
2	Time to onset(min) of hypotension	15.0±5.9	24.3±5.6
3	Fall in MAP (%)	23.0±2.9	25.9±6.1



Time to Onset of Hypotension

Table 5: Data of Sensory block

S.No.Sl. No.	Parameter	Group K (n=40)	Group F (n=40)
1.	Onset (Sec)	68.25 ±13.57	72.75±17.82
2.	Max. level of sensory blockade	T6(T4-T10)	T6(T4-T10
3.	Duration (min)	108.2±4.6	99.0±14.2
4.	Time for first analgesic(min)	168.3±12.8	150.2±5.5



Onset of Sensory Block

The onset of sensory block was earlier in group K than group F (68.25 sec Vs. 72.75 sec), P value <0.05. A median sensory level of T6 was observed in both groups.

The incidence of hypotension is markedly lower in group K when compared to group F (20% Vs. 45%), P<0.01. Among the hypotensive patients, the mean percentage change in MAP is similar in both the groups (23% Vs. 25.9%), but the time to maximum fall in MAP is earlier in group K than group F (15 minutes Vs. 24.3 minutes), P<0.05.

The statistically significant mean percentage fall in the heart rate occurred earlier in group F than group K (5^{th} minute Vs. 20^{th} minute) and the severity of the mean percentage fall in the heart rate was more in group F (30.25±1.64) than group K (26.33±1.46), but is statistically not significant.

The duration of sensory block is longer in group K than in group F (108.2 mins and 99 mins respectively), P<0.05.

The incidence of nystagmus was higher in group K (40%) than group F (10%), P=0.001, Chi-square=9.6, Degree of freedom=1.

The incidence of pruritis is higher in group F (30%) than group K (5%), P=0.003, Chi-square=8.6, Degree of freedom=1.

The incidence of vomiting is same in both the groups. The incidence of shivering was more in group F (20% Vs. 2.5%), P=0.01, Chi-square value=6.13, Degree of freedom=1.

V. Discussion

Ketamine, a phencyclidine derivative, popularly used as a general anesthetic has been used for spinal anesthesia with claims of advantages. It is widely accepted that intrathecal injection of ketamine is safe. In our study we evaluated the effect of ketamine and fentanyl as adjuvant for spinal anesthesia. Eighty patients posted for lower limb and lower abdominal surgery were included in the study following approval from the institute's ethics committee. They allocated to two groups of forty each. Patients belonging to Group K received 25mg (0.5ml) of preservative free ketamine and 2ml of 0.5% Bupivacaine heavy whereas patients belonging to Group F received 25µg(0.5ml) of fentanyl and 2ml of 0.5% Bupivacaine heavy.

The mean age in Group K was 40.6±11.8 years and 37.75±13.0 years in group F. The mean weight in group K was 54.4±6.7kg and group F was 54.7±6.4kg. The mean height in group K was 158.6±4.7 cm and group F was 159.0±4.3cm. The physical characteristics were comparable between the groups.

In the group K, there was statistically significant decrease in the heart rate compared to the baseline value from 20^{th} minute to 120^{th} minute (P<0.05). In the group F, there was statistically significant decrease in the heart rate compared to the baseline value from 5^{th} to 120^{th} minute (P<0.05). The statistically significant mean percentage fall in the heart rate occurred earlier in group F than group K (5th minute vs 20^{th} minute) and the severity of the mean percentage fall in the heart rate was more in group F(30.25±1.64) than group K (26.33±1.46), but was statistically not significant. When compared between the groups, the mean percentage fall in heart rate from the base line value was statistically significant in group F between the 2^{nd} and 20^{th}min P<0.001 following subarachnoid block. The decrease in the heart rate in both groups in our study was probably because of deeper level of sedation. These observations are similar to other studies.[10,13,27.]

In the group K, there was statistically significant decrease in the mean arterial blood pressure compared to the baseline value from 10^{th} minute to 30^{th} minute (P<0.05). In the group F, there was statistically significant decrease in the mean arterial blood pressure compared to the baseline value from 5^{th} minute to 120 minute (P<0.05). When compared between the groups, the mean percentage fall in the mean arterial pressure from the base line value was statistically significant in the group F at 2^{nd} min and from 15^{th} minute to 120^{th} minute (P<0.05) following subarachnoid block.

A significantly high incidence of hypotension was observed in group F (37.5%) when compared to group K (20%), P<0.05. Hypotension occurred at 15th minute and 24^{th} minute following the subarachnoid block in group K and group F respectively. The mean percentage change in mean arterial pressure was similar in both the groups. The lower incidence of hypotension in the ketamine group can be explained on the basis of property of ketamine to release catecholamine irrespective of the dose given.[10, 13, 27]

Fentanyl group showed a slight reduction in respiratory rate throughout the study period as compared to ketamine group which was not clinically significant, but change in respiratory rate was statistically significant at the 90^{th} min, P<0.05. This may be probably because of the central respiratory depressed action of intrathecal fentanyl[123]. The change in respiratory rate was not significant within the groups and there was no episode of desaturation during the study period.

Bion[27] also stated that intrathecal ketamine does not change the respiratory rate significantly. Other studies also confirm that there is no bradypnea with intrathecal ketamine.

In our study the onset of sensory block was earlier in group K(68.25±13.57sec), when compared to group F(72.75±17.82sec, P<0.05). Bansal et al[26] also reported similar onset of action. The duration of sensory

block (Four segment regression time) and duration of postoperative analgesia (time for first request of systematic analgesia) were longer in group K(108.2min and 168.3min respectively), when compared to group F(99.0min and 150.2min respectively), P<0.05. The axonal conduction block produced by the ketamine could be partly responsible for this effect[8]. The longer duration of action in the ketamine group may be explained on the basis of slow release of ketamine (liposomal impregnation)[10,28,29]. The addition of Ketamine to local anesthetic or other analgesics in peripheral or neuraxial anesthesia and analgesia improves or prolongs pain relief (Level II evidence)[14].

The median bromage scale and sedation scale are similar in both the groups. These observations are similar to other studies[10]. In our study the incidence of nystagmus was 40% in the ketamine group which is quite low as compared to the study of Bansal et al[26] (>80%). The incidence of nystagmus was 10% in the fentanyl group P-0.001, Chi-square-9.6, Degree of freedom-1. The decreased incidence is probably because of lower doses of ketamine used in our study. The high incidence of nystagmus observed in group K (40% as compared to group F (0% P<0.05) can be explained on the basis of central side effects of ketamine.

The incidence of pruritis in group F (30%) when compared to group K (5%, P=0.0=3) can be explained on the basis of side effects of intrathecal opioids. Pruritis induced by intrathecal opioid is likely due to cephaloid migration of the drug in the cerebro-spinal fluid and subsequent interaction with the trigeminal nucleus located superficially in the medulla. The opioid receptors are present in the trigeminal nucleus and the trigeminal nerve roots.

The incidence of vomiting was similar in both the groups whereas the incidence of shivering more in the fentanyl group (20%) than the ketamine group (2.5%), P=0.01.

VI. Summary

This is a comparative study designed to "**Compare the cardio respiratory stability and incidence of side effects after intrathecal administration of ketamine with bupivacaine and fentanyl with bupivacaine for lower abdominal and lower limb surgeries".**

Group K

2.0 CC of 0.5% bupivacaine heavy + 0.5ml(25mg) of ketamine (preservative free).

Group F

2.0 CC of 0.5% bupivacaine heavy + 0.5ml(25mg) of fentanyl.

The time taken for the onset of sensory level at T12 dermatome level were comparable in both the groups.

Maximum level of sensory block were comparable in both the groups. Maximum intensity of motor blockade (Bromage score) is same in both groups.

Duration of analgesia in minutes is more in group K compare with group F.

Adverse effects like bradycardia , hypotension, respiratory rate, oxygen saturation and degree of sedation were comparable in both the groups.

The incidence of pruritis and shivering are more in group F. The incidence of nystagmus is more in group K.

VII. Conclusion

In conclusion ketamine 25mg with 0.05% bupivacaine heavy intrathecally, maintains cardio respiratory stability compared to fentanyl with bupivacaine intrathecally with less incidence of side effects except nystagmus compared to fentanyl 25µg with 0.5% bupivacaine heavy intrathecally.

Bibliography

[1]. Malinovsky JM Cozian A, Lepage JY, Mussini JM, PinaudM,Soruon R : Ketamine and Midazolam Neurotoxicity in the Rabbit. Anesthesiology 1991; 75:91-95.

[2]. Malinovsky JM, Cozian A, Lepage JY, Mussini JM, Pinaud M, Souron R: Is Ketamine or its preservative responsible for Neurotoxicity in the Rabbit? Anesthesiology 1993; 78:109-115.

[3]. Borgbjerg FM, Svensson BA, Frigast C, Gordh T JR: Histopathology after repeated Intrathecal Injections of Preservative-Free Ketamine in the Rabbit; A Light and Electron Microscopic examination. Anesthesia and Analgesia 1994; 79:105-11.

[4]. Gabriella J,Horvath G, Klimscha W, Kekesi G, Dobos I, Szikszay M, Benedek G: The effects of Ketmine and its Enantiomers on the Morphine-or Dexmedetomidine-Induced Antinociception after Intrathecal administation in Rats. Anesthesiology 2000;93: 231-41.

[5]. Miyamoto H.Saitoy, Kirihara Y, Hara K, Sakura S and Kosaka Y: Spinal Coadministration of ketamine reduces the development of Tolerance to Visceral as well as Somatic Antiriociception during Spinal Morphine Infusion. Anesthesia Analgesia 2000l 90: 136-41.

[6]. Bhattacharya D, Banerjee A: A Comparative study of Clinical Effects of Intrathecal Hyperbaric Bupivacaine and Ketamine in Hyperbaric Solution. Indian Journal of Anaesthesia 2004;48:116-120.

[7]. Sabine H, Marcel D: Ketamine for perioperative Pain Management. Anaesthesiology 2005; 102:211-220.

[8]. Bernadette Veering: Focus on Adjuvants in regional Anaesthesia. Euro Anaesthesia 2005; 102:211-220.

[9]. Togel T etal. Efficacy of S+ ketamine added to bupivacaine for spinal anaesthesia for prostate surgery in elderly patients. European journal anaesthesia, 2004 by 21(3) : 193-197.

[10]. Ben-David B, Frankel R, Arzumonov T. et al. Minidose bupivacaine fentanyl spinal anesthesia for surgical repair of hip fracture in the aged. Anaesthesiology 2000;92:6-10.

[11]. M.S.Khanna, Ikwinder KJP Singh. Comparative evaluation of bupivacaine plain versus bupivacaine with fentanyl in spinal anaesthesia in geriatric patients. Indian J.Anaesth 2002;46(3):199-203.
[12]. Joel Griffith Hardman, Lee E.Limbird, Alfred G.Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th edition. NewYork: McGraw-Hill;2001.
[13]. Ummenhofer WC, Arends RH, Shen DD, Bernards CM. Comparative spinal distribution and clearance kinetics of intrathecally administered morphine, Fentanyl, Alfentanil and Sufentanil. Anesthesiology 2000;92:739-53.
[14]. Herman NL, Choi KC, Affleck PJ et al. Analgesia, pruritus and ventilation exhibit a dose – response relationship in parturients receiving intrathecal fentanyl during labour. Anesth Analg 1999; 89:378-83.
[15]. Shendi D, Cooper GM, Bowden MI. The influence of IV fentanyl on the characteristics of subarachnoid block for caesarean section. Anaesthesia 1998; Jul 53(7): 706-10.

Dr.T.D.Rambabu. "Comparative study of cardio respiratory stability and incidence of side effects after intra thecal administration of Bupivacaine with Ketamine vs Bupivacaine with Fentanyl for lower abdominal and lower limb surgeries". " IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 12, 2018, pp 10-16.