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Original Research Article

A Comparative Study of Anesthetic and Analgesic Effect of Clonidine with Bupivacaine and Fentanyl with Bupivacaine Combinations for Infra Umbilical and Lower Limb Surgeries

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Conflict of interest: Nil

Abstract:

Background: A comparative study between spinal adjuvants, clonidine 30µg or Fentanyl 25µg along with 0.5% hyperbaric bupivacaine 15 mg for their anesthetic and analgesic properties in patients undergoing infraumbilical & lower limb surgeries.

Objectives of the study: Primary objective: To compare the onset time of sensory block, onset time of motor block, duration of sensory blockade, duration of motor blockade and duration of analgesia of clonidine bupivacaine combination and fentanyl bupivacaine combination intrathecally.

Secondary objective: To compare hemodynamic change by clonidine bupivacaine combination and fentanyl bupivacaine combination intrathecally.

Materials and Methods: This study comprised of 60 patients, of ASA grades I– II, between the age group 18 and 60 years belonging to ASA Grade I and II. Standard procedure for sub arachnoid block with a fixed dose of 0.5% hyperbaric bupivacaine 15mg with either clonidine 30µg or fentanyl 25 µg as per randomization. All vital and study parameters were recorded and monitored till 180 min. Any intra operative complications were managed. The time until patient requested for pain relief or when VAS score was more than 3 was taken as the duration of analgesia.

Results: Time in seconds for onset of sensory blockade with clonidine 102.06±16.1, with fentanyl 100.733±10.46 (p=0.027); time in seconds to onset of motor blockade with clonidine 123.13±13, with fentanyl 126.3±14.77(p=0.946); Time in minutes for peak of sensory blockade with clonidine 8.5±0.75, with fentanyl 7.015±0.41(p=0.031);Two segment regression time in minutes for sensory blockade with clonidine 125.9±17.04, with fentanyl 111.06±8.87 (p=0.651): duration of analgesia in minutes with clonidine 248.17±29.93, with fentanyl 201.0±34.09 (p< 0.001).

Conclusion: Hence clonidine 30µg as an adjuvant has more advantages in terms of duration of analgesia and fentanyl 25 µg as an adjuvant has faster sensory onset based on our study.

Keywords: Fentanyl, Clonidine, bupivacaine, infra umbilical and lower limb surgeries.

CTRI: REF/2019/03/024407.

Introduction

Hyperbaric bupivacaine 0.5% is the drug of choice in regional anaesthesia. Studies have shown associated hemodynamic instability with higher volumes of some local anesthetics, hence the use of adjuvant like morphine, fentanyl, ketamine, clonidine and magnesium sulphate are used. [1]

After discovery of adrenergic pain modulating system in spinal cord, α_2 adrenergic agonists like clonidine has been used for neuraxial block for peri-operative analgesia. Intrathecal clonidine potentiates post-operative analgesia by hyperpolarising Aδ and C fibre in the substantia gelatinosa of the spinal cord. [2] Low-dose clonidine has good analgesic efficacy with a low incidence of adverse effects(sedation). [3]

Fentanyl being highly lipid soluble opioid diffuses into the spinal cord and binds to dorsal horn receptors rapidly when administered intrathecally.

This produces a rapid onset of analgesia with minimal cephalic spread. [4]

The addition of adjuvant to the routine spinal aesthetic can help reduce overall medications required to produce a good operative and post-operative outcomes including pain control.

Numerous studies have been conducted just to achieve this goal of effective anaesthesia in respect to onset, duration and quality during and after surgery with minimal side effects and minimum or no compromise on the core factors of anaesthesia.

In this study we have compared spinal adjuvants, clonidine 30µg and Fentanyl 25µg along with 0.5% hyperbaric bupivacaine 15 mg and assessed their anesthetic and analgesic properties in patients undergoing infraumbilical & lower limb surgeries.

Materials and Methods

Study Area: Department of Anaesthesiology, General hospital Jayanagar.

Study Population: Consenting patients of General hospital Jayanagar for study.

Study Design: Randomised comparative cross sectional single blinded clinical study.

Study Period: from January 2019 to Mar 2020

Source of Data: All consented patients total of 60 who underwent surgery in the infra umbilical and lower limb region, consented patients belonging to ASA I, II.

Inclusion Criteria

1. Patients consent
2. Elective infra umbilical, lower limb surgeries (planned: spinal anaesthesia)
3. Patient belonging to ASA I and II
4. Age between 18-60 years
5. Height of patient between 120 to 180 cm
6. weight 50 -80 KG

Exclusion Criteria

1. Patients refusal for study.
2. Patients with contraindication for spinal anaesthesia
3. Patients posted for emergency surgeries
4. Patients designated ASA III, IV, V and VI
5. Patients with history of allergy to bupivacaine/ clonidine/ Fentanyl.

Sample Size

Patients will be randomly assigned to group A (Clonidine 30µg (0.2ml) making to 0.5ml with 0.9% normal saline and hyperbaric bupivacaine 0.5% 3ml) group B (Fentanyl 25µg (0.5ml) with hyperbaric bupivacaine 0.5% 3ml) with a total of 30 patients in each of the group.

Randomization and Blinding

The study was designed as a simple random comparative double blinded clinical study. Participants were allocated into two equal groups of 30 each using computer generated random number list of hospital inpatient numbers. The Anaesthesiologist administering the injections and observing the effects received serially numbered sealed envelopes indicating the C or F codes for the anesthetic mixture to be administered. The C and F syringes were loaded with drugs by another anaesthesiologist not involved in administering the drugs and further evaluation of the patients. All observations were also recorded in a blinded manner.

Spinal anaesthesia was performed with landmark guided blind technique. Premedication was limited only for indicated patients.

Group A received 3ml of hyperbaric Bupivacaine 0.5% with clonidine 30µg (0.5ml).

Group B received 3ml of hyperbaric Bupivacaine 0.5% with fentanyl 25 µg (0.5ml)

Method of Data Collection

Preoperative interview, assessment & consent were obtained before the study, all of them were preloaded with 500ml Ringer Lactate (RL), basal readings were recorded.

Procedure of Spinal Anaesthesia: In lateral decubitus, patients were positioned with their back parallel to the long side of the operation table. Thighs were flexed up and neck was flexed forward. Preferably L3-L 4 interspace was marked and local infiltration given, after local infiltration with lignocaine 2%, a 25-gauge Quincke spinal needle was inserted in the middle of space in cephalad direction with bevel parallel to the longitudinal fibers of Dura. Slowly advancing the needle till subarachnoid space. And the needle position was confirmed by the CSF flow and aspiration. The spinal anesthetic was injected at the rate 0.2mL/Second. The patient was not informed about the allotted adjuvant. The patient was then positioned supine and waited for the drug to fixate, required study parameters were noted and later the position was adjusted as required while hemodynamic changes were monitored and recorded.

Routine spinal anaesthesia was performed and the baseline hemodynamic was monitored. Monitoring consisted of non-invasive blood pressure, pulse oximetry. Sedation was avoided where possible. Blood pressure, heart rate and oxygen saturation were monitored and recorded every 5 minutes for

first 15 min and every 15 minutes for next 45 min and later every 30 minutes up to 3 hours and then till regression of block completely or first analgesia request. Dose of vasopressors like mephentermine or ephedrine was recorded. Time of onset of sensory block and maximum level achieved were assessed by eliciting pain by pin prick method and attainment of complete motor blockade using modified Bromage scale.

The motor block is assessed by using modified Bromage[5] three-point score

0= normal motor function with full flexion and extension of knees, and feet.

1=decreased motor strength with in ability to raise extended leg; able to move knees and feet

2= Inability to raise extended leg and move knee; able to move feet.

3 = complete motor block

The time of onset of motor blockade was noted.

The time of onset of sensory block is defined as the elapsed between the injection of drug and complete loss of pin prick perception, while onset of motor blockade was defined as the time elapsed from injection of drug to Bromage 2.

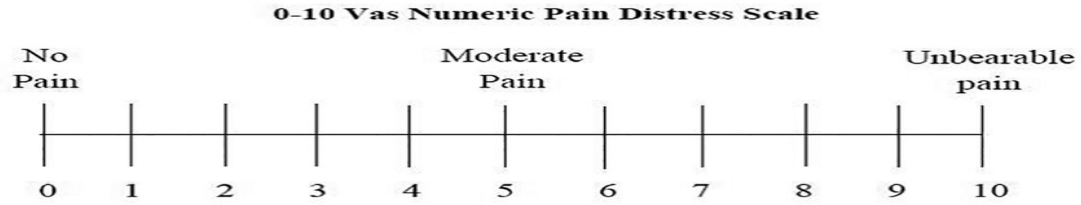
Maximum Sensory level was monitored every 30 minutes interval until they have regressed by two segments assessed by pin prick method.

Duration of motor block is considered time interval between completion of injection of local anesthetic to patients' ability to raise the extended leg as assessed by modified Bromage scale.

Ramsay Scale	
Level	**Clinical Description**
1	Anxious and agitated
2	Cooperative, oriented, tranquil
3	Responds only to verbal commands
4	Asleep with brisk response to light stimulation
5	Asleep without response to light stimulation
6	Non- responsive

Any sedation during the procedure is assessed using the Ramsay sedation scale.

Duration of analgesia was the time from spinal anaesthesia administration till the first request of analgesic or VAS >3. Pain score was assessed using visual analogue scale (VAS) [6] in Post anaesthesia care unit.
Any patient reporting VAS >3 was given analgesic.



Statistical analysis

Descriptive and inferential statistical analysis has been carried out in the present study. The results were analysed by using SPSS version 18 (IBM Corporation, SPSS Inc., Chicago, IL, USA). Results on categorical measurements are presented in percentages (%) and continuous variables as Mean±SD. Inferential statistics like independent t test and Chi-square test/Fischer-exact test was used to check statistically significant difference between the two groups. P value less than 0.05 was considered to be statistically significant.

Results

The study groups were mostly middle aged and all cases were selected based on the criteria established, as shown in table 1,2a and 2b. Age and gender distribution were almost equal between the two groups: the mean age of Clonidine group (CB) is 52.97±9.8 and Fentanyl group (FB) is 47.6± 6.785 in years.

Table 1: Age Distribution

Age (yrs)	Clonidine		Fentanyl	
	Number	Percentage	Number	Percentage
≤ 30	1	3.3	1	3.3
31 – 40	2	6.7	4	13.3

41 – 50	8	26.7	12	40.0
51 – 60	19	63.3	13	43.3
Total	30	100.0	30	100.0

Table 2a. Age distribution among the groups in years

Study group	Mean	SD
Clonidine	52.97	9.796
Fentanyl	47.63	6.785

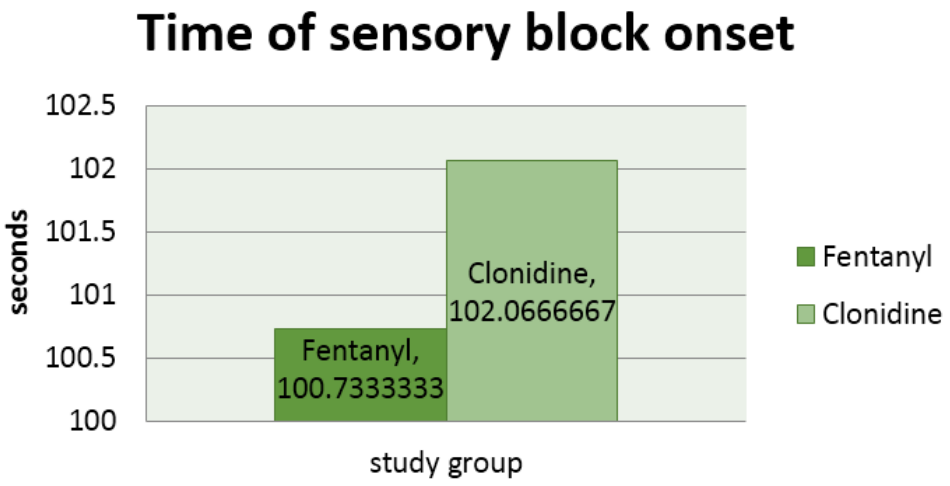
Table 2b. Gender distribution between the groups

Gender	Clonidine		Fentanyl	
	Number	Percentage	Number	Percentage
Male	14	46.7	12	40
Female	16	53.3	18	60.0
Total	30	100.0	30	100

There is slightly raised female preponderance in the study.

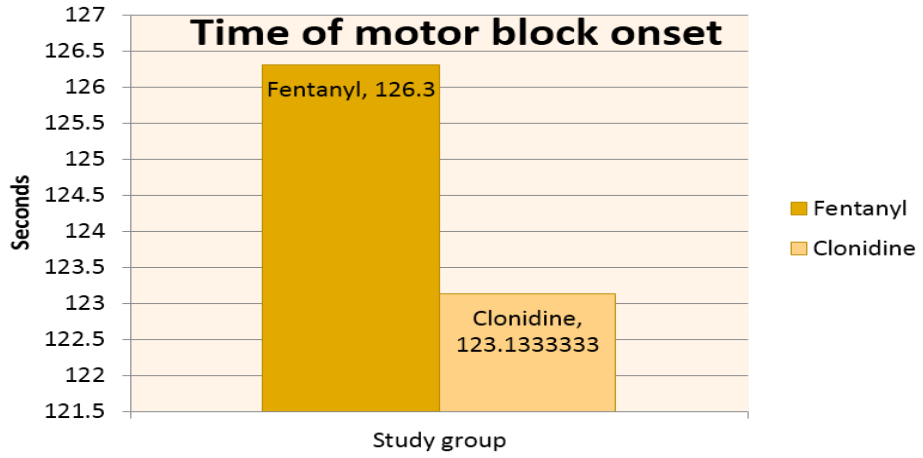
The comparison of main parameters of the study along with intra operative and post operative findings are depicted below

Comparison between the Time of onset of sensory blockade in secs.

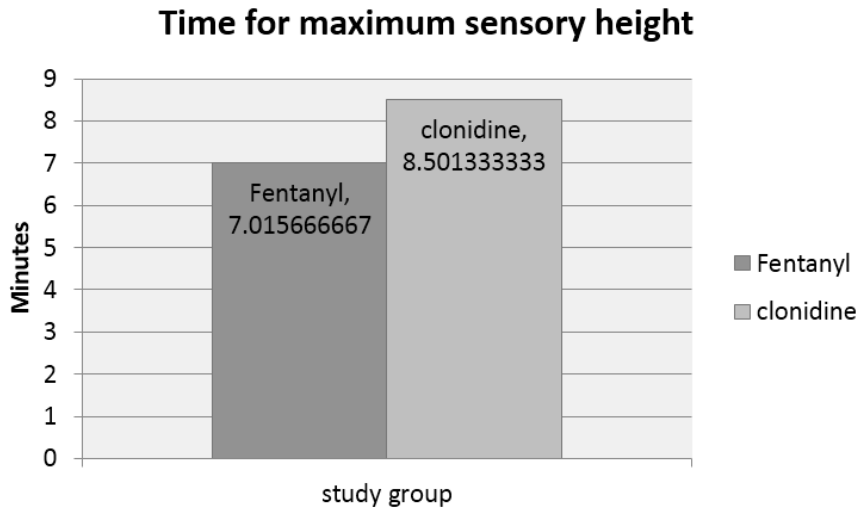


Graph 1: Time of sensory block onset among the study groups

Comparison of time of onset of motor blockade among groups in secs.

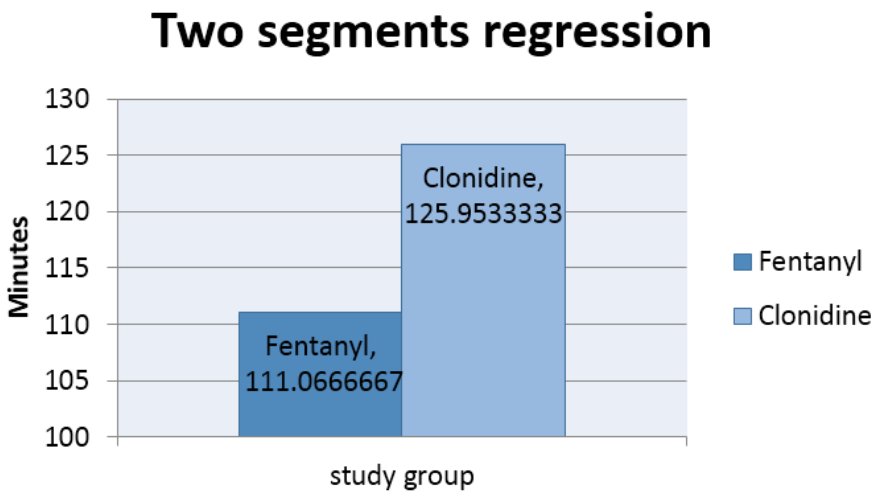


Graph 2: Time of motor block onset after obtaining bromage score of 2 And above Time in min for peak of sensory blockade



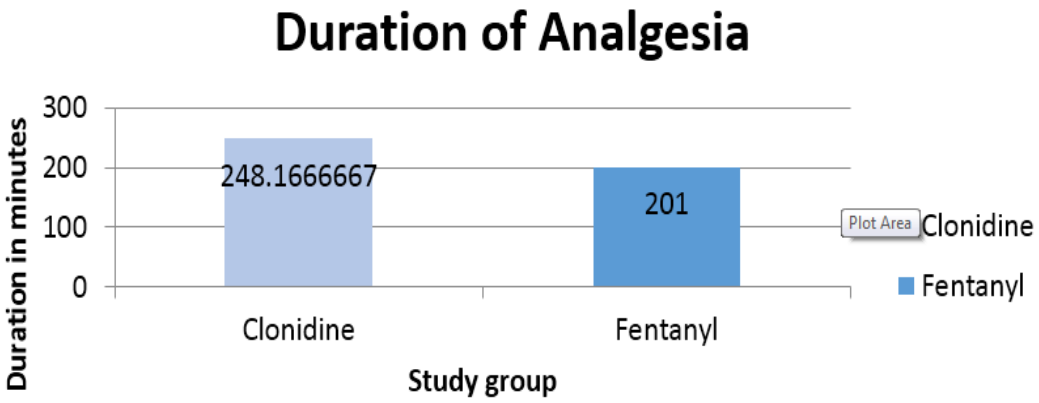
Graph 3: Time for maximum sensory height obtained after no change in height for more than two readings five minutes apart

Two segments regression for sensory blockade



Graph 4: Two segments' regressions is the time noted at which the sensory blockade had declined from its maximum height

Duration of Analgesia among the study group



Graph 5: Duration of analgesia among study groups

Table 3: Dermatomal levels among the groups throughout the study

Time	Dermatome	Clonidine	Fentanyl
5 minutes	T4	4	2
	T6	16	6
	T8	10	22
10 minutes	T4	19	9
	T6	11	21
15 minutes	T2	1	2
	T4	22	16
	T6	7	12
30 minutes	T2	1	2
	T4	23	18
	T6	6	10
45 minutes	T2	1	2
	T4	19	9
	T6	10	19
60 minutes	T2	1	2
	T4	19	9
	T6	10	19
90 minutes	T4	18	7
	T6	6	8
	T8	6	15
120 minutes	T4	16	0
	T6	8	11
	T8	6	18
	T10	0	1
180 minutes	T6	18	6
	T8	5	7
	T10	7	15
	T12	0	1
	L1	0	1

Table 4: Parameters with statistical value(p)

Parameters	Mean± SD		P value
	Clonidine group	Fentanyl group	
Time in **sec** to onset of sensory blockade	102.06±16.1	100.733±10.46	0.027
Time in **sec** to onset of motor blockade	123.13±13	126.3±14.77	0.946
Time in min for peak of sensory blockade	8.5±0.75	7.015±0.41	0.031
Two segment regression time in min for sensory blockade	125.9±17.04	111.06±8.87	0.651
Duration of Analgesia in min	248.17±29.93	201.0± 34.09	0.001

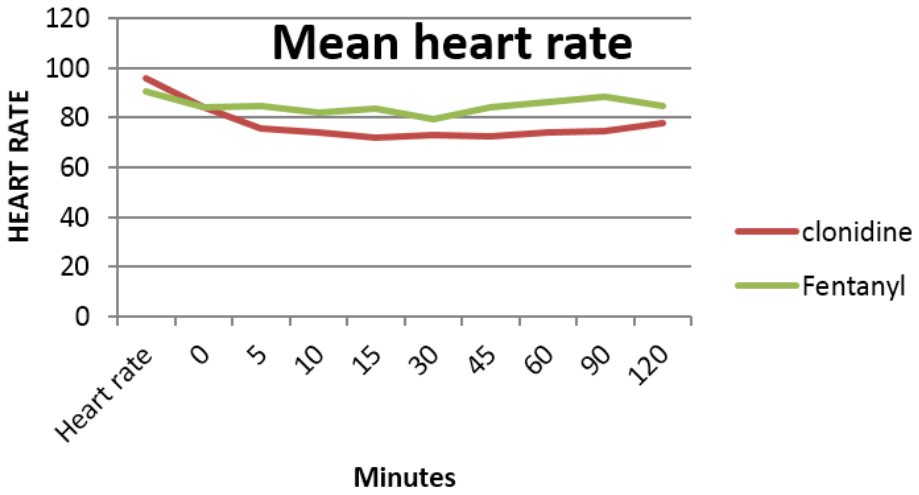
Hence from the comparison of above parameters, clonidine 30µg as an adjuvant has more advantages in terms of duration of analgesia and fentanyl 25 µg as an adjuvant has faster sensory onset than clonidine as adjuvant from our study.

Table 5: Heart rate (HR) monitiored and recorded among the study groups

HR	Study group	Mean	SD	t – value	P – value
0 minute	Clonidine	95.73	11.15	1.669	0.100
	Fentanyl	90.63	12.48		
5 minutes	Clonidine	84.47	15.51	0.921	0.361
	Fentanyl	87.93	13.57		
10 minutes	Clonidine	75.97	11.54	3.048	0.003
	Fentanyl	84.97	11.33		
15 minutes	Clonidine	73.97	10.95	4.105	P < 0.001
	Fentanyl	84.80	9.43		
30 minutes	Clonidine	72.00	9.36	4.210	P < 0.001
	Fentanyl	82.37	9.71		

45 minutes	Clonidine	73.17	9.54	4.118	P < 0.001
	Fentanyl	83.53	9.96		
60 minutes	Clonidine	72.63	8.98	3.205	0.002
	Fentanyl	79.40	7.29		
90 minutes	Clonidine	73.90	10.60	4.324	P < 0.001
	Fentanyl	84.40	8.03		
120 minutes	Clonidine	74.77	11.13	4.192	P < 0.001
	Fentanyl	86.40	10.36		
180 minutes	Clonidine	77.93	11.94	3.667	0.001
	Fentanyl	88.48	10.03		

The heart rate variation was minimal in Fentanyl group than compared to the clonidine which was statistically significant from 10 minutes onwards till 180 min.

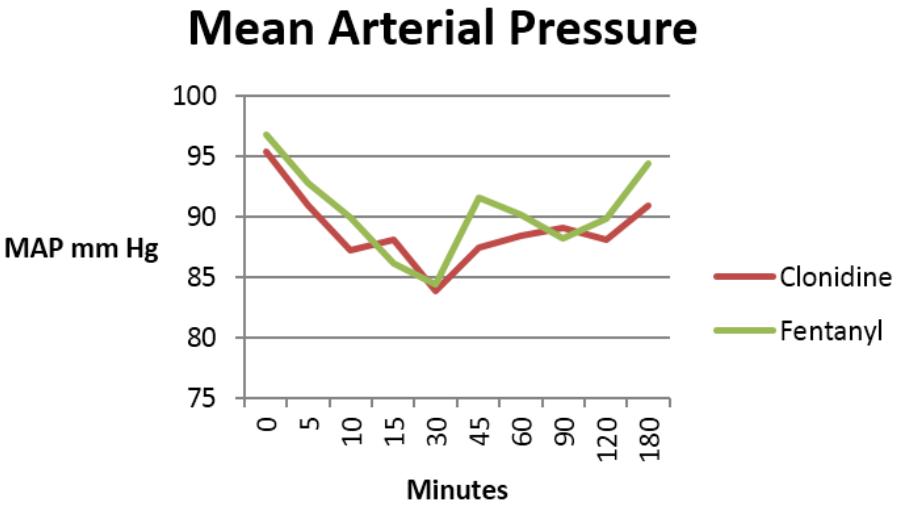


Graph 6: Mean Heart Rate

Table 6: Mean arterial Blood pressure (MBP) among the groups

MBP	Study group	Mean	SD	t – value	P - value
0 minute	Clonidine	95.49	9.06	0.525	0.602
	Fentanyl	96.79	10.10		
5 minutes	Clonidine	90.97	8.75	0.855	0.396
	Fentanyl	92.86	8.37		
10 minutes	Clonidine	87.28	10.40	1.118	0.268
	Fentanyl	89.93	7.82		
15 minutes	Clonidine	88.09	11.57	0.651	0.518
	Fentanyl	86.10	12.09		
30 minutes	Clonidine	83.91	9.06	0.222	0.825
	Fentanyl	84.44	9.58		
45 minutes	Clonidine	87.42	12.64	1.392	0.169
	Fentanyl	91.61	10.57		
60 minutes	Clonidine	88.47	7.42	1.004	0.320
	Fentanyl	90.23	6.16		
90 minutes	Clonidine	89.03	6.79	0.526	0.601
	Fentanyl	88.18	5.78		
120 minutes	Clonidine	88.10	6.07	1.140	0.259
	Fentanyl	89.87	5.93		
180 minutes	Clonidine	90.98	6.95	1.838	0.071
	Fentanyl	94.41	7.41		

The mean arterial pressure variation between the two groups were comparable.



Graph 7: Mean arterial pressure of groups

Premedication and intra operative medication used, as shown in Table

Table 7: Medications used while conducting Anaesthesia

Medicines	Clonidine		Fentanyl	
	Number	Percentage	Number	Percentage
GLYCO	2	6.7	0	0.0
GLYCO+KETAMINE	0	0.0	1	3.3
MEPH 6+6	5	16.7	6	20.0
MEPH6	3	10.0	2	6.7
MIDAZ	1	3.3	2	6.7
NIL	19	63.3	19	63.3
Total	30	100.0	30	100.0

Glyco-glycopyrrolate (0.2mg), Glyco+ketamine – glycopyrrolate (0.2mg) + ketamine (30mg) , MEPH 6 & MEPH 6+6 –mephentermine 6 mg & 12mg respectively, MEPH6-mephentermine 6mg, MIDAZ-midazolam 1 mg.

Medications used pre or intra operative

38 patients had no requirement for pre medications, 16 participants required Mephentermine for tackling hypotension intra operatively. Bradycardia was evident in 2 patients in the clonidine group and glycopyrrolate was administered. 2 patients in fentanyl group, due to anxiety showed elevated SBP as compared to 1 in clonidine group with similar cause was given midazolam. Only 1 patient in fentanyl group was supplemented with Ketamine & glycopyrrolate.

Table 8: Ramsay sedation score of the study groups

Ramsay sedation score	Clonidine		Fentanyl	
	Number	Percentage	Number	Percentage
1	1	3.3	3	10.0
2	16	53.3	18	60.0
3	9	30.0	7	23.3
4	4	13.3	2	6.7
Total	30	100.0	30	100.0

Ramsay sedation score between the two study groups were similar and comparable.

Table 9: PONV episodes among the study groups

PONV	Clonidine		Fentanyl	
	Number	Percentage	Number	Percentage
1 EPISODE	1	3.3	2	6.7
NIL	29	90.0	28	90.0
Total	30	100.0	30	100.0

Incidence of PONV were similar between the two groups.

Table 10: VAS score recorded among the groups

Study group	Mean	SD	t - value	P - value
Clonidine	3.33	1.12	0.955	0.344
Fentanyl	3.60	1.04		

VAS score: that was recorded at the time of administering first analgesic, were similar in both the groups

Discussion

Time of sensory blockade onset: Clonidine group has a mean value of 102.06±16.1 seconds.

Bajwa et al [7] attained a value of 54.6±10.8sec with 12.5 mg of 0.5% Hyperbaric Bupivacaine and 50 µcg of clonidine faster compared to our study, probably because of increased clonidine concentration.

In Sachan P et al [2] with value of 62.17±6.6 sec with 75 µcg of clonidine and 10 mg 0.5% Hyperbaric Bupivacaine faster compared to our study, probably because of increased clonidine concentration.

In Singh R et al [1] et al study of same drug 10.20±1.00 minutes i.e [612 sec±60] where they used 75 µcg of clonidine with 7.5 mg 0.5% Hyperbaric Bupivacaine, slower than compared to our study, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Agarwal D et al[3] study had 12.8 ±3.8 min [768 sec ±228] with 30 µcg of clonidine with 9 mg 0.5% Hyperbaric Bupivacaine slower compared to our study, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Fentanyl group has a mean value 100.73±10.46 seconds.

Bajwa et al [7] attained a value of 54±11.6 sec with 25 µcg fentanyl and 12.5 mg 0.5% Hyperbaric Bupivacaine which is faster compared to our study.

In Singh R et al [1] et al study with value of 13.80±2.61 min [828±156 sec] with 7.5 mg 0.5% Hyperbaric Bupivacaine and 25 µcg of fentanyl slower than our study, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Hence between clonidine & fentanyl, Fentanyl as a spinal adjuvant has faster onset of sensory blockade as observed in our study, which is clinically & statistically significant.

Time of motor blockade onset: Clonidine group has a mean value of 123.13±13 sec.

Bajwa et al [7] attained a value of 102.6±29.4 sec with 12.5 mg of 0.5% Hyperbaric Bupivacaine and 50 µcg of clonidine showing that above 10 mg of 0.5% Hyperbaric Bupivacaine, probably the onset is faster with given 50 µcg of clonidine when compared to our study.

Sachan P et al [2] with a value of 1.66±0.30 min [99.6 ± 18 sec] 75 µcg of clonidine with 10 mg 0.5% Hyperbaric Bupivacaine faster than our study, probably the onset is faster with given 75 µcg of clonidine,

In Singh R et al [1] et al study 14.00±2.04 min [840 ± 120 sec] used 75 µcg of clonidine with 7.5 mg 0.5% Hyperbaric Bupivacaine, slower onset compared to our study. Probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Agarwal D et al [3] 11 min ±3.1 [660 sec±180] with 30 µcg of clonidine with 9 mg 0.5% Hyperbaric Bupivacaine slower than our study, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Fentanyl group has a mean value of 126.3±14.77 sec. Bajwa et al[7] attained a value of 94.8±27 sec with 25 µcg fentanyl and 12.5 mg 0.5% Hyperbaric Bupivacaine faster compared to our study.

In Singh R et al [1] et al study, a value of 15.40±2.86 min [924±171.6 sec] with 7.5 mg 0.5% Hyperbaric Bupivacaine and 25 µcg of fentanyl, slower when compared to our study, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Hence with respect to motor blockade onset fentanyl group is faster than clonidine group in our study, which is clinically significant but not statistically.

Maximum Height of Dermatome Attained

Clonidine group average height of dermatome was T4 at the end of 30 min, compared to Sachen P et al[2] attained height was T5, with Agarwal D et al[3] T5 was the maximum height, which are almost similar and Singh R et al[1] et al T7 was the maximum height, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Fentanyl group average height of dermatome was T4 at end of 30 min compared to Singh et al attained a height of T7, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Hence maximum height of dermatome safely attained without significant side effects is T4 with clonidine and fentanyl as adjuvant in our study.

Time of Maximum Sensory Height

Clonidine group has a mean time of 8.5±0.7 min.

Sachan P et al [2] attained a value of 4.43±0.26 min almost half the duration of our study 75 µcg of clonidine with 10 mg 0.5% Hyperbaric Bupivacaine, faster than our study, probably because of increased clonidine concentration and or the studied mothers posted for cesarean section.

Bajwa et al [7] had attained maximum sensory height within 7.56±1.78 minutes with 12.5 mg of 0.5% Hyperbaric Bupivacaine and 50 µcg of clonidine, which is relatively faster than our study.

In Agarwal D et al [3] 28.8±12.3 min with 30 µcg of clonidine with 9 mg 0.5% Hyperbaric Bupivacaine slower than compared to our study, because of increased clonidine concentration.

Fentanyl group had a mean time of 7.015±0.41 min in our study.

Bajwa et al [7] had a mean time of 7.34±0.96 min, relatively similar to our study.

In our study, fentanyl group attained maximum height of sensory blockade faster than clonidine group, which is both clinically and statistically significant.

Two Segments Regression

Clonidine group has a mean value of 125.9±17.04 min.

Singh R et al [1] et al attained 128.20±14.85 min with clonidine additive is longer than our study, which is due increased clonidine concentration.

Bajwa et al [7] had a mean of 136.56±12.67 min longer than our study, probably because of increased clonidine concentration.

Agarwal D et al [3] study 89.3 ±27.7 min shorter compared to our study, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Fentanyl group has a mean value of 111.06±8.87 min.

Bajwa et al [7] had a mean 132±14.56 min which longer compared to our study.

In Singh R et al [1] et al study 89.00±9.68 min was the mean value which is shorter than our study, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Hence Clonidine can last longer than Fentanyl as adjuvant, which is clinically significant but not statistically.

Time in first dose of analgesia or rescue analgesia or duration of analgesia: Clonidine group has a mean value of 248.17±29.93 min.

Bajwa et al[7] had a mean value of 497.20±139.78 min using 50 µcg clonidine and 12.5 mg 0.5% Hyperbaric Bupivacaine having longer duration than our study, probably because of increased clonidine concentration.

Sachen P et al had a mean value of 337±18.22 min dose of clonidine 75 µcg is longer duration than our study, probably because of increased clonidine concentration and also their study population were post cesarean mothers.

In Singh R et al [1] et al study had 209.80±26.32 min as mean value, which is shorter duration than our study, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Fentanyl group has a mean value of 201±34.09 min.

Bajwa et al [7] had a mean value 416.87±105.67 min longer duration than our study.

Singh R et al [1] et al study had a value of 199.20±21.92 min shorter duration than our study, probably due to lower dose of 0.5% Hyperbaric Bupivacaine.

Therefore, the clonidine 30 µg as adjuvant can prolong the duration of analgesia longer than fentanyl 25 µg in our study, which is statistically and clinically significant.

Few related studies comparing similar additives with 0.5% hyperbaric bupivacaine are highlighted.

Katiyar S and associates in 2017 concluded that addition of magnesium sulphate at 100 mg dose or fentanyl 25 µg as adjuvant to intrathecal bupivacaine significantly prolongs the duration of analgesia. [4]

Khandelwal M and associates in 2017 concluded that intrathecal clonidine (30 µg) prolonged post-operative analgesia along with earlier onset and prolonged duration of sensory and motor blockade compared to both magnesium (50 mg) and control without any significant adverse effects or hemodynamic perturbation. [8]

Erturkand associates in 2010, studied on 60 patients scheduled for hip arthroplasty were randomly assigned to receive an intrathecal injection of either 12 mg ropivacaine with 20µg Fentanyl or 8mg hyperbaric bupivacaine with 20µg fentanyl concluded that Ropivacaine combination had better hemodynamic stability. [9]

Grandhe and co-workers in 2008, did prospective, randomized double blind study in patients undergoing unilateral spinal anaesthesia for lower limb orthopaedic surgery and found that combination of 1-1.5µg/kg body weight of clonidine and 15mg of 0.5% bupivacaine effectively prolonged the sensory and motor block

and also post operative analgesia while causing minimal adverse effects. [10]

Tuijl and co-workers in 2006, concluded that addition of 75µg of clonidine to hyperbaric prolonged spinal anaesthesia after caesarean section and improved early analgesia but did not reduce the post operative morphine requirements during first 24 hours. [11]

Strebel and associates in 2004, stated that addition of small doses of intrathecal clonidine(150µg) significantly prolonged both sensory and motor blockade after spinal anaesthesia and enhance the analgesia effects of bupivacaine in a dose dependent manner with minimal side effects. [12]

A.M. Korhonen and associates in 2003, observed in their double-blind study of 100 patients undergoing knee arthroscopy received randomly either 4mg of bupivacaine or 3mg of bupivacaine with fentanyl intrathecally. They concluded that, combination of local anaesthetic and opioid enables use of less spinal anaesthetic and increases success of anaesthesia. Addition of small dose of fentanyl does not prolong motor recovery and thus shortens PACU time. [13]

Intra operative hemodynamic: The heart rate variation was minimal in Fentanyl group than compared to the clonidine which was statistically significant from 10 minutes onwards till 180 min.

Even though bradycardia without hemodynamic instability was relatively frequent in 6.7% of Clonidine group, it was symptomatically corrected with glycopyrrolate none required atropine. The mean arterial pressure changes were almost similar in both groups, incidence of hypotension was aborted using mephentermine (meph). Each group had almost equal (26%) requirement of vasoconstrictor. Episode of PONV was minimal in both groups. The sedation produced by the adjuvants Ramsay sedation score of 4 was seen 13.3% from clonidine group and 6.7% from Fentanyl group. Bajwa et al [7] reported higher incidence of drowsiness in 16% in clonidine group than fentanyl group higher than our study, probably due to increased clonidine concentration.

Hence use clonidine or fentanyl as an adjuvant to the spinal anesthetic can help ally the intra operative psychological changes by sedation, from our study.

Although the local anesthetic dose can be reduced and analgesia prolonged, the addition of fentanyl to bupivacaine may increase side effects and delay discharge of the patient postoperatively. [14]

Conclusion

We conclude from our study that Fentanyl as an adjuvant has faster onset of sensory blockade with faster attainment of maximal height of sensory blockade and Clonidine as an adjuvant has longer duration of analgesia, however both the drugs didn't have any significant hemodynamic side effects but sedation was more common with clonidine.

Conflict of Interest

There are no conflicts, except for variation in observed values.

References

1. Singh R, Kundra S, Gupta S, Grewal A. Effect of clonidine and/or fentanyl in combination with intrathecal bupivacaine for lower limb surgery. J Anaesthesiol Clin Pharmacol 2015;31(4):485-90.
2. Sachan P, Kumar N, Sharma JP. Intrathecal clonidine with hyperbaric bupivacaine administered as a mixture and sequentially in caesarean section: A randomized controlled study. Indian J Anaesth 2014;58(3):287-92.
3. Agarwal D, Chopra M, Mohta M, Sethi AK. Clonidine as an adjuvant to hyperbaric bupivacaine for spinal anesthesia in elderly patients undergoing lower limb orthopedic surgeries. Saudi J Anaesth 2014;8(2):209-14.
4. Katiyar S, Dwivedi C, Tipu S, Jain RK. Comparison of different doses of magnesium sulphate and fentanyl as adjuvants to bupivacaine for infraumbilical surgeries under subarachnoid block. Indian J Anaesth 2015;59(8):471‑5.
5. Baheti DK, Laheri VV. Spinal, Epidural and combined spinal-epidural anesthesia. Textbook of understanding anesthetic equipment & procedures. 2nd edn. Jaypee Brothers Medical Publishers 2018:422-5.
6. Comparison of efficacy among various topical anesthetics: an approach towards painless injections in periodontal surgery – Scientific Figure on Research Gate. Available from: https:// www.researchgate. net/figure/Visual-analog-scale_fig1_283752750
7. Bajwa BS, Singh AP, Rekhi AK .Comparison of intrathecal clonidine and fentanyl in hyperbaric bupivacaine for spinal anesthesia and postoperative analgesia in patients undergoing lower abdominal surgeries. Saudi J Anaesth 2017;11(1):37-40.
8. Khandelwal M, Dutta D, Bafna U, Chauhan S, Jetley P, Mitra S. Comparison of intrathecal clonidine and magnesium sulphate used as an adjuvant with hyperbaric bupivacaine in lower abdominal surgery. Indian J Anaesth 2017; 61(8):667‑72.
9. Erturk E, Tutuncu C, Eroglu A, Gokben M. Clinical comparison of 12mg ropivacaine and 8mg bupivacaine, both with 20µg fentanyl, in spinal anaesthesia for major orthopaedic

surgery in geriatric patients. Med Princ Pract 2010;19(2):142-47.
10. Grandhe RP, Wig J, Yaddanapudi LN. Evaluation of bupivacaine- clonidine combination for unilateral spinal anaesthesia in lower limb orthopaedic surgery. J Anaesth Clin Pharmacol 2008;24(2):155-8.
11. Tuijl VI, Van Klej WA, Van der Werff DBM, Kalkman CJ. The effect of addition of intrathecal clonidine to hyperbaric bupivacaine on post-operative pain and morphine requirements after caesarean section. Br J Anaesth 2006;97(3):365-70.
12. Strebel S, Guezdel JA, Schwider MC. Small dose of intrathecal clonidine and isobaric bupivacaine for orthopedic surgery: a dose responsive study. Anaesth Analg 2004;99(4): 12 31-8.
13. Korhonen AM, Valanne JV, Jokela RM, Ravaska P, Korttila K. Intrathecal hyperbaric bupivaaciane 3mg plus fentanyl 10µg for outpatient knee arthroscopy with tourniquet. Acta Anaesthiol Scand 2003;47(3):342-6.
14. Peng PW, Sandler AN. A review of the use of fentanyl analgesia in the management of acute pain in adults. Anesthesiology 1999;90(2):576-99.